PYRIDINE AND ITS DERIVATIVES

In Four Parts

PART FOUR

This is Part Four of the fourteenth volume in the series

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

A SERIES OF MONOGRAPHS

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PYRIDINE
and Its Derivatives
Part Four

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The Chemistry of Heterocyclic Compounds

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures, and for the physiological and industrial significance of heterocyclic compounds.

A field of such importance and intrinsic difficulty should be made as readily accessible as possible, and the lack of a modern detailed and comprehensive presentation of heterocyclic chemistry is therefore keenly felt. It is the intention of the present series to fill this gap by expert presentations of the various branches of heterocyclic chemistry. The subdivisions have been designed to cover the field in its entirety by monographs which reflect the importance and the interrelations of the various compounds and accommodate the specific interests of the authors.

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ARNOLD WEISSBERGER

Preface

It is hoped that the organization of this monograph will prove to be self-explanatory, but a few general observations are in order.

Chemical compounds are tabulated exhaustively by the principle of latest position. Thus halogenated pyridinecarboxylic acids are found in Chapter X rather than VI, but hydroxy acids in Chapter XII. The principal exceptions are the quaternary compounds, which proved too numerous to be catalogued, and the N-oxides, which are included in Chapter IV irrespective of nuclear substitution. Other exceptions are explained where they occur.

The principle of latest position does not apply to reactions. All reactions for obtaining pyridine derivatives from non-pyridinoid starting materials are covered in Chapter II irrespective of substitution. If the starting material *is* a pyridine derivative, the reaction is discussed instead in the appropriate later chapter or chapters. Thus the conversion of aminopyridines to pyridinols is discussed in Chapters IX and XII.

Nomenclature follows Chemical Abstracts.

The editor wishes to express his gratitude to Prof. D. S. Tarbell of the University of Rochester for the impetus he gave to this undertaking, to the chemists in many parts of the world who have been so generous with reprints, to the staff of Interscience Publishers for their cooperation, and finally to Dr. R. S. Long and Dr. J. J. Leavitt of American Cyanamid for their patience.

ERWIN KLINGSBERG

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CHAPTER XIII

Pyridine Alcohols

By Ellis V. Brown
University of Kentucky, Lexington, Ky.

A. PREPARATION

1. From Non-Pyridine Starting Materials

By the condensation of hydroxylamine with glutaraldehydes carrying either an α-(2-hydroxyethyl) or an α-(3-hydroxypropyl) group, Paul and Tchelitcheff (*1*) were able to prepare 3-pyridineethanol and 3-pyridinepropanol. From the proper keto aldehydes, in the same manner, were prepared 2-pyridinepropanol and 2-methyl-3-pyridinepropanol.

The reaction of butyraldehyde with amonia furnished 3-(3,5-diethyl-2-pyridyl)heptanol-4 (*2*). 5-Methyl-2-pyridineethanol has been isolated from cevine (*3,4*) and a product believed to be 2-(3-carboxy-3-hydroxy-2-methylpropyl)nicotinic acid has been isolated from wilfordine (*5*). Pyrones containing alcohol groups may be converted to the corresponding pyridines by heating with ammonia (*6–8,503, 504*). In one case the product of a pyrone and hydrazine was treated with HNO_2 to give a pyridine (*505*). Certain furan derivatives have been opened and recyclized to pyridines (*506*).

2. Oxidation of Side-Chains

Oparina has prepared a di-alcohol by the oxidation of 3,5-di-*i*-propylpyridine with 3% permanganate solution (*9*).

3. Hydrolysis of Side-Chain Halides

Occasionally one prepares a pyridine alcohol by hydrolysis of a side-chain halide, although the reverse reaction is more common. Dehnel (*10*) hydrolyzed 3-bromomethylpyridine to the corresponding alcohol, and Knudsen (*12,507*) hydrolyzed the bromination product of aldehyde collidine to α,6-dimethyl-3-pyridinemethanol. 2-Methyl-3-pyridineethanol has been prepared from the corresponding chloride (*11,13,14*). In the same way 2-pyridinemethanol (*15*), α-methyl-2-pyridinemethanol (*508,509*), and 4-methyl-3-pyridineethanol (*16*) have been prepared. In some cases replacement of halogen by acetoxy is followed by hydrolysis, as in the preparation of 2,6-dichloro-4-methyl-3-pyridineethyl acetate (*16,510*).

4. From Side-Chain Amines and Nitrous Acid

LaForge (*17*) treated 3-(α-aminobenzyl)pyridine with nitrous acid to prepare α-phenyl-3-pyridinemethanol. The reaction has since

been used for the preparation of 2-pyridinemethanol, 4-pyridinemethanol (*18,19,622*), 2,6-dichloro-4-pyridinemethanol, 2,6-dibromo-4-pyridinemethanol (*20,21*), and some 3-hydroxymethylpyridines containing carbocyclic rings fused at the 5,6 position (*511*).

These last two preparations were used by Nieman *et al.* (*22*) in the syntheses of the respective β-pyridylalanines. The synthesis of 3-pyridinemethanol by this procedure has been patented (*23*).

2-Methyl-3-pyridineethanol was prepared by the reaction of nitrous acid on 2-methyl-3-(β-aminoethyl)pyridine (*14*) and also by reduction of the corresponding 4,6-dichloro compound (*11,13*).

5. Reduction of Aldehydes and Ketones

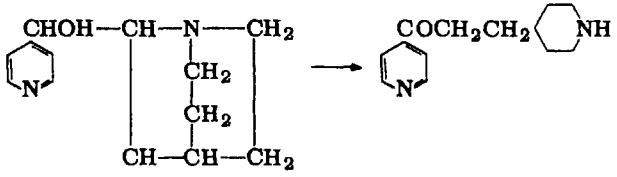
Picolinaldehyde has been hydrogenated over a nickel catalyst to 2-pyridinemethanol (*24*). 6-Carbomethoxypicolinaldehyde has also been reduced to the methanol, the ester group remaining unaffected (*25*). These seem to be the only examples of the preparative reduction of pyridine aldehydes to alcohols, although 2-pyridinemethanol (*26*), 4-pyridinemethanol (*27*), 5-methyl-3-pyridinemethanol (*513*), and various halogenated pyridinemethanols (*28,29*) have been obtained by the Cannizzaro reaction.

Ketones have been reduced by a number of methods. α-Methyl-3-pyridinemethanol was prepared by catalytic hydrogenation (Adams catalyst) and converted to the benzoate, *p*-nitrobenzoate, and *p*-aminobenzoate for evaluation as local anesthetics (*30*). Nickel catalyst may also be used and may give further reduction to the hexahydrocarbinol (*31*). Boekelheide and Mason (*32*) reduced 5-(2-pyridyl)-2-pentanone to the corresponding alcohol. 2-Benzoylpyridine has been hydrogenated to the alcohol over both nickel and platinum catalysts (*33,34*) as has 4-benzoyl-2,6-lutidine (*35*). Rubtsov and Volskova (*36*) reduced 5-ethyl-2-quinuclidyl 2-pyridyl ketone and 2-quinuclidinyl 2-pyridyl ketone to the carbinols.

The Meerwein-Ponndorf-Verley reaction and catalytic hydrogenation were used by Clemo and Hoggarth (*37*) to prepare α-methyl-4-pyridinemethanol. 3-Acetyl-5-bromopyridine (*38*), 2-benzoylpyridine (*39*), and 4-benzoylpyridine (*512*) have likewise been reduced by aluminum *i*-propoxide. Kegelman and Brown (*40*) found that reduction of 4-benzoylpyridine gave α-phenyl-4-pyridinemethanol instead of the expected pinacol. Copper-bronze was used to

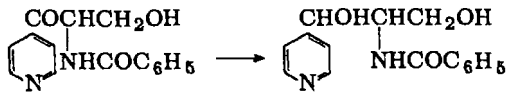
convert 2-naphthyl 4-pyridyl ketone to the alcohol (*41*). Zinc and sodium ethoxide were used to prepare α-phenyl-4-pyridinemethanol (*42*) and α-phenyl-2-pyridinemethanol (*43*), and the tertiary alcohols were resolved (*623*). Engler and Bauer (*44*) found that ethyl 2-pyridyl ketone could be reduced by zinc and alcohol to the carbinol alone, while sodium amalgam in alcohol gave both the carbinol and the pinacol. With sodium amalgam and propyl 2-pyridyl ketone, these authors obtained the carbinol, while Engler and Majmon (*45*) obtained both carbinol and pinacol. Palladium and hydrogen were used to reduce 6-methyl-3-pyridyl propyl ketone to the carbinol (*19*). Platinum catalyst was used for the reduction of 3-acetyl-4-picoline (*46,47*). Benary and Psille (*48*) used zinc to reduce 2-phenyl-5-benzoylpyridine to the alcohol. 3-Acetylpyridine and a number of its ring homologs have been reduced to the carbinols (*49*). Both zinc with acid and lithium aluminum hydride have been used to reduce pyridine ketones (*514,612*).

The reduction of aminoketones of the pyridine series has been used to prepare various aminoalcohols, including substitution products of 2-aminoethanol (*54,55*), 3-aminopropanol (*56*), and 4-aminobutanol (*57*). Aminoethanol derivatives have also been prepared by the reduction of α-nitrosoketones (*58*). In the reduction of 4-pyridyl 2-quinuclidyl ketone, hydrogen (*N* HCl) and palladium catalyst gave two racemic carbinols, A and B, while aluminum *i*-propoxide gave only one, A (*59*). This carbinol underwent hydramine fission to give β-(4-piperidyl)ethyl 4-pyridyl ketone (XIII-1).



(XIII-1)

The reduction of the ketone XIII-2 was employed during the synthesis of a pyridine analog of chloramphenicol (XIII-3); the final product proved low in activity (*60*). Pyridine amino alcohols are tabulated in Table XIII-25 (p. 80).



(XIII-2) (XIII-3)

6. Reduction of Acids and Esters

3-Pyridinemethanol is obtained by the reduction of methyl thiolnicotinate with Raney nickel (*61*) or (in trace amounts) from nicotinic acid with tin and hydrochloric acid (*62*); the latter method also reduces 2,6-dichloroisonicotinic acid to 2,6-dichloro-4-pyridinemethanol (*62*). Both picolinic and isonicotinic acids are smoothly reduced to the alcohols with zinc in acetic acid (*63*). Reduction of nicotinonitrile with hydrogen over palladium-charcoal in aqueous mineral acid at 30° C. or below gave a 90% yield of 3-pyridinemethanol (*64*).

Esters of all three nuclear pyridine acids (*65–68*) and 3-pyridineacetic acid (*68,69*) are reduced to the corresponding alcohols by lithium aluminum hydride. Nicotinic ester is covered in a number of patents (*69–71*). 2,4-Bis(2-pyridyl)-1-butanol has also been prepared in this manner from the corresponding ester (*72*). This type of reduction proceeds normally with nuclear methyl (*73*), phenyl, and amino (*74,515–518*) derivatives of ethyl nicotinate. A single ester group of diethyl 2,6-dimethyl-3,5-pyridinedicarboxylate may be reduced selectively (*68*), although pyridinedimethanols have also been obtained by lithium aluminum hydride reduction (see page 14). 6-Methyl-2-hydroxynicotinic acid, but not its ester, could be reduced to the methanol (*75*). The diethylamide of nicotinic acid gave 3-pyridinemethanol as a by-product (*76*). 4-Pyridinemethanol has been prepared by reductive desulfurization of ethyl thioisonicotinate over Raney nickel (*19*).

7. Aldol Condensation of Alkylpyridines with Aldehydes

The condensation of formaldehyde with 2-picoline at approximately 200° gives 2-vinylpyridine and di- and trihydric compounds in addition to 2-pyridineethanol (*68,72,77–85,594*). 4-Bromo-2-picoline gave a mixture of 4-bromo-2-pyridineethanol and 4-hydroxy-2-

pyridineethanol (*595*). 4-Picoline gives 4-pyridineethanol (*86–88*) and 2-ethylpyridine gives α-methyl-2-pyridineethanol. 4-Ethylpyridine gives β-methyl-4-pyridineethanol and a diol (*88*). As would be expected, 3-ethyl-4-picoline (*89*), 2,5-lutidine (*618*), and 5-ethyl-2-picoline (*90–92,599,625*) react only at the methyl group. 2,6-Lutidine reacts once (*88,93*), or twice (*94*). 2,4-Lutidine reacts at the 2-methyl but also at the 4-methyl (*91,95,96,596,624,626*). s-Collidine reacts at the 2-methyl (*97*) and to some extent at the 4-methyl (*97,597, 598,627*). 3-Nitrocollidines apparently react at a 6-methyl rather than a 2-methyl (*97*). 2-Benzylpyridine gave a diol and 4-benzylpyridine gave both a mono- and diol (*98*). Low yields of α-methyl-2-pyridineethanol have been obtained by several authors (*77,79,99–101*) from acetaldehyde and 2-picoline. Propionaldehyde reacts similarly (*102,103*). Both 2- and 4-methylpicolinic acid have been condensed with formaldehyde and acetaldehyde to give alcohol derivatives which were cyclized to naphthyridines (*600,601*). Chloral condenses with 2-picoline to give α-(trichloromethyl)-2-pyridineethanol (*84,104–112*), with 4-picoline to give α-(trichloromethyl)-4-pyridineethanol (*46,113–120*), and similarly with 2,6-lutidine (*121*), aldehyde collidine (*122*), *s*-collidine (*123,124*), 3-ethyl-4-picoline (*114,125*), 4-methyl-3-pyridineethanol (*16*), and 6-phenyl-2-picoline (*429*) to give the corresponding trichloropropanols.

A large number of aryl-substituted pyridineethanols have been prepared by the condensation of 2-picoline, 4-picoline, and various homologs with aromatic aldehydes. This reaction is summarized in Table XIII-1 (p. 27).

8. From Organometallic Compounds and Pyridine Aldehydes, Ketones, and Esters

These addition reactions proceed normally, generally in good yield, and offer a flexible source of pyridine alcohols. They are summarized in Tables XIII-2 and XIII-3 (pp. 28–30).

9. From Metallopyridine Compounds

A great many alcohols have been prepared by the normal addition reactions of metallopyridine compounds with aldehydes, ketones, and esters.

Similarly the expected substituted propanol is obtained from ethylene oxide and 2-picolyllithium (*126–128*) or the sodium derivative of 2-benzylpyridine (*129*). Cyclohexene oxide reacts normally (*130*). 3-Picolylpotassium with aldehydes gave the carbinols (*519*). Neither Finkelstein and Elderfield (*131*) nor Gilman and Towle (*126*) found any evidence for Tiffeneau rearrangement in the reaction of 2-picolyllithium with formaldehyde, acetaldehyde, acetyl chloride, or ethylene oxide.

Ethers are obtained in the coupling reaction between metallopyridine compounds and alkoxyalkyl halides. In this way, for example, 2- and 4-picolylsodium are converted to the ethoxypropylpyridine by reaction with 2-ethoxyethyl chloride (*132*). 2-Picolylpotassium has been used to prepare longer-chain ethers (*128*). Similar reactions have been described with 2-picolyllithium (*133*) and 4-picolyllithium (*134*). The air oxidation of 2-picolyllithium to 2-pyridinemethanol (*135*) should also be noted.

These reactions are tabulated in Chapter VII: Tables VII-1–3 (pp. 445 ff.) give the reactions of pyridyllithium compounds; Tables VII-4–9 (pp. 449 ff.) give the reactions of picolyllithium compounds, Tables VII-11, VII-12 and VII-13 give the reactions, respectively, of 2-, 3-, and 4-picolylsodium, Table VII-14–17 gives the reactions of picolylpotassium compounds. The reactions of the Grignard compounds are given in Table VII-17–18 (pp. 460 ff.).

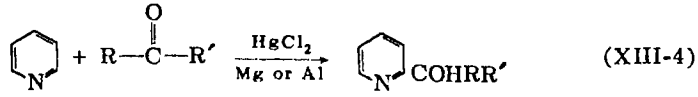
10. Aldol Condensation of Pyridine Aldehydes

Nitromethane condenses with picolinaldehyde and isonicotinaldehyde to give 1-(2-pyridyl)-2-nitroethanol (*136*) and 1-(4-pyridyl)-2-nitroethanol (*137*), respectively. Nicotinaldehyde and other pyridine aldehydes have also been condensed with nitromethane and substituted nitromethanes (*520,521*). Contrary to an earlier report by Dornow and Boberg (*523*), Robertson (*522*) showed that phenylnitromethane gives normal condensation products with pyridine aldehydes. They also condense with hydroxy and methoxy acetophenones (*524*). *Cf.* Chapter XIV (p. 141).

11. Emmert-Asendorf Reaction

In this reaction (*138,139,629*) secondary and tertiary pyridine alcohols are prepared by condensing pyridine with aldehydes and

ketones in the presence of mercuric chloric and either magnesium or aluminum (XIII-4). Generally the 2-pyridyl carbinols are the main

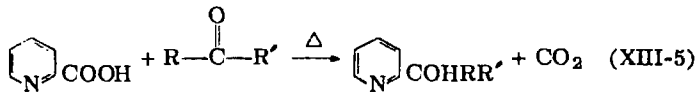


(XIII-4)

products, although with aromatic ketones substantial amounts of the 4-pyridyl carbinols have been isolated. The yields are in the range of 10–30% based on the ketones, with 2-picolines giving somewhat lower yields. 3-Picoline gives both the 2,3- and the 2,5-isomers, with the latter predominating (*140*). Tables XIII-4–6 (pp. 30–32) summarize the literature on this method. In a somewhat related reaction, heating benzaldehyde with *t*-butyl peroxide and pyridine gave the benzoate of α-phenyl-4-pyridinemethanol and another compound from which this carbinol could be obtained by hydrolysis (*141*).

12. Hammick Reaction

In this reaction, an acid is decarboxylated in the presence of an aldehyde or ketone to give the corresponding alcohol (XIII-5). It



(XIII-5)

was first applied to quinaldic and isoquinaldic acids (*142*) and then to picolinic acid (*143*). From isonicotinic acid, α,α-diphenyl-4-pyridinemethanol has been obtained in a yield of 3.5% of theoretical (*144*). Cantwell and Brown (*145*) have shown that the reaction fails in the pyrimidine and thiazole series, that not all ketones and aldehydes react, and that solvents have a beneficial effect (*146*). Yields are from 15 to 60% in the case of picolinic acid with aldehydes and ketones that do react. Picolinic acid 1-oxide was found to undergo the Hammick reaction with acetophenone while neither the 3- nor the 4-acid 1-oxides showed the reaction (*525*). Table XIII-7 summarizes the literature on this reaction (p. 33).

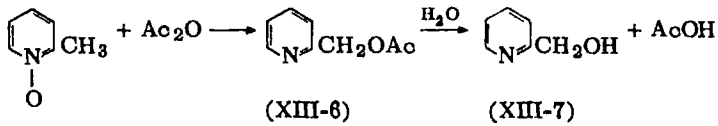
13. From Vinylpyridines

Ethers can be prepared by the addition of alcohols to vinylpyridines. A reported example of this reaction is the addition of ethyl

alcohol in the presence of sodium ethoxide to 2-vinylpyridine to give 2-(2-ethoxyethyl)pyridine (*147*).

14. Rearrangement of Alkylpyridine 1-Oxides

Pyridine 1-oxides, alkylated in the 2 and 4 position, rearrange in refluxing acetic anhydride to the corresponding acetoxyalkylpyridine (XIII-6), which is readily hydrolyzed to the alcohol (XIII-7). The oxygen migrates to the carbon attached to the ring; in other words, the major product is a pyridylcarbinol (*148–151*).



Berson and Cohen studied the rearrangement of 4-picoline 1-oxide in detail, and found a 20% yield of the expected 4-pyridinemethyl acetate, but also a 14% yield of 4-methyl-3-pyridinol (*152*).

Carrying this rearrangement a step further, the 2-acetoxymethylpyridine 1-oxide was converted in 46% yield to the diacetate of picolinaldehyde; similar behavior was shown by 2-acetoxymethyl-3-hydroxypyridine 1-oxide (*630*), while 6-methyl-2-acetoxymethylpyridine 1-oxide was converted to 2,6-di-(acetoxymethyl)pyridine, which was hydrolyzed to 2,6-pyridinemethanol. The rearrangement apparently proceeds by attack of acetoxy anion on the *o*-acetate of the 1-oxide (*150,152*). However, Boekelheide and Hamington favor a free radical mechanism (*153*), but other suggestions have been offered (*532,533*).

Fifty grams of 2,4-lutidine 1-oxide was converted to 15 grams of 4-methyl-2-pyridinemethanol, 3 grams of 2-methyl-4-pyridinemethanol, and 1 gram of 2,4-dimethyl-3-pyridinol (*155*). The reaction with 2-pyridineethanol 1-oxide, the corresponding propanol, and 4-pyridineethanol 1-oxide has been patented (*156*). In a similar way 4-benzyl-2,6-lutidine 1-oxide (*157*), 2-ethyl-3,5-diphenylpyridine 1-oxide (*158*) and 2,3-lutidine 1-oxide (*159*) were rearranged to the alcohols, while the acetates of 3-methyl-2-pyridinemethanol 1-oxide and 3-hydroxy-2-pyridinemethanol 1-oxide were converted to the aldehydes (*159*), as was 4-methyl-2-acetoxymethylpyridine 1-oxide (*531*). 2,6-Dimethyl-α-phenyl-4-pyridinemethanol 1-oxide gave ketone

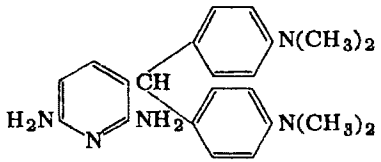
as well as dicarbinol (*157*) and a number of substituted pyridine 1-oxides of various kinds have been rearranged to alcohols (*508,515, 526–530*).

B. PROPERTIES

The properties of the pyridine alcohols are those to be expected of alcohols containing a tertiary amino group. For physical properties, see Tables XIII-9–XIII-31 (pp. 37–105).

Fromherz and Spiegelberg (*160*) discuss the pharmacology of 3-pyridinemethanol and list the boiling points of a number of its esters and ethers. Several 3-pyridylmethyl esters of dibasic acids have also been prepared (*161*), and the phosphate salts have been suggested as vasodilators (*631*). The chelating abilities of 2-pyridinemethanol, 6-methyl-2-pyridinemethanol and α-methyl-2-pyridinemethanol are reported by Erlenmeyer and co-workers (*149*).

Bis(2-dimethylamino-5-pyridyl)phenyl carbinol was prepared, but had only a slight tendency to give the quinoid form, the pyridine analog of malachite green (*163*). Bis(2-dimethylamino-5-pyridyl)-carbinol was treated with aniline and sulfuric acid to give 4-aminophenyl-bis(2-dimethylamino-5-pyridyl)methane, while Michler's hydrol and 2,6-diaminopyridine gave XIII-8 (*164*). The ultraviolet



(XIII-8)

spectra of 2- and 4-hydroxymethyl-3-hydroxypyridines have been reported and discussed (*534*).

C. REACTIONS

1. Oxidation

3-Pyridinemethanol has been oxidized to the aldehyde in yields of 70 and 77% by heating over silver or copper (*165*). Oxidation by manganese dioxide or selenium dioxide has also proved effective

in the preparation of aldehydes and ketones (*166–168,527,536*). Lead tetraacetate has been used to convert 4-methyl-3-pyridinemethanol and other pyridine alcohols (*632*) to the aldehydes (*517*). The alcohols can be oxidized to the corresponding acids with permanganate, as, for example, 2-pyridinepropanol to 2-pyridinepropionic acid (*9,169*). Nitric acid has likewise been used to convert alcohols to acids (*9,170,504,633*). In one case, NaOBr was used to oxidize a secondary pyridine alcohol to the pyridinecarboxylic acid (*530*), and in another case biological oxidation converted 2-(2-methoxyethyl)-pyridine to 2-pyridineacetic acid (*537*). The preparation of side-chain acids from alcohols is further discussed in Chapter XI (p. 349).

Both dehydrogenation and chromium trioxide oxidation have been used to prepare ketones from alcohols such as α-(*p*-nitrophenyl)-2-pyridineethanol (*171*) and various pyridyl alkyl (*44,172*) and pyridyl aryl (*42,173*) carbinols. Manganese dioxide oxidized methyl η-hydroxy-5-methoxy-6-methyl-2-pyridineoctanoate to the ketone (*168*). Dehydrogenation over palladium converted 1-(2-pyridyl)-4-phenyl-3-butene-2-ol to the ketone (*174*). α-(3,4-Methylenedioxyphenyl)-2-pyridinemethanol was oxidized by acetone and aluminum *i*-propoxide to the ketone (*175*).

The preparation of aldehydes and ketones is further discussed in Chapter XIV (p. 123).

The acetates of 2-pyridinemethanol, α-methyl-2-pyridinemethanol (*150*), 2-pyridinepropanol, and other alcohols were oxidized to the 1-oxides (*156,160,509,515,535*).

2. Reduction

Hydrogen iodide is the reagent most commonly used to replace side-chain hydroxyl by hydrogen, both in pyridyl alkyl (*37,176–178*) and pyridyl aryl (*179,180*) carbinols, but palladium and hydrogen also do this (*538,539*). Lithium aluminum hydride can be used to reduce the alcohol directly (*67*) or as the *p*-toluenesulfonate (*181*). This reduction can also be accomplished by sodium in butanol or ethanol (*37,182*), although in other cases this method has been found to saturate the pyridine ring without affecting side-chain hydroxyl (*84,86,170,183*) or ethoxyl (*133*) groups. Pyridine alcohols containing side-chain nitro groups can be reduced to the alkanolamines by palladium and hydrogen without further reduction (*520*).

α-Methyl-2-pyridinemethanol has been hydrogenated to the piperidine alcohol over a nickel catalyst in alcohol (*84*); the 3-pyridine isomer could be hydrogenated only in the presence of hydrochloric acid (*30*). Platinum and hydrogen generally reduce the pyridine to a piperidine (*184–186,540*). Palladium on carbon or barium sulfate has been the catalyst for ring reduction in several cases (*542,543*). Using nickel at 200°, 2-pyridinepropanol was cyclized to octahydropyrrocoline (*187*). Rhodium on carbon with hydrogen has been used to reduce the pyridine ring to piperidine (*541*).

1-(2-Pyridyl)-4-phenylbutene-3-ol-2 was reduced at the double bond with palladium and hydrogen in acetic acid (*174*) while 1-(2-pyridyl)cyclohexanol was reduced over Adams catalyst in glacial acetic acid to 1-(2-piperidyl)cyclohexanol (*140*). The hydrogenolysis of nuclear halogen is seen in the conversion of 2,6-dichloro-4-pyridinemethanol to 4-pyridinemethanol over platinum catalyst (*62*).

Replacement of side-chain methoxy by hydrogen has been accomplished with sodium amalgam (*188*) or hydrogen iodide and phosphorus (*189*).

The following alcohols and derivatives were reduced to the corresponding piperidines: 2-pyridinepropanol (*128,187*), 2-methyl-4-pyridineethanol (*190*), 2,6-di(2-phenyl-2-hydroxyethyl)pyridine (*33*), α-methyl-2-pyridineethanol methosulfate (*101*), 2,4-di(2-pyridyl)-1-butanol (*72*), α-phenyl-2-pyridineethanol (*134*), 2-(2-pyridyl)-5-ethoxy-2-pentanol (*191*), α-methyl-3-pyridinemethanol (*30*), 4-pyridinemethanol (*62*), 2-(2-pyridyl)pentanol-2 (*192*), α-methyl-α-phenyl-2-pyridinemethanol (*146*), α,α-diphenyl-2-pyridinemethanol (*146*), 2-(7-methoxyheptyl)pyridine, 2-(6-methoxyhexyl)pyridine, 2-(4-methoxybutyl)pyridine, 4-(3-methoxypropyl)pyridine (*128*), and 5-ethyl-2-pyridinepropanol (*193*). α-(Trichloromethyl)-2-pyridineethanol with sodium in alcohol was reduced to α-methyl-2-piperidineethanol (*84*).

3. Esterification and Etherification

These reactions are carried out in the usual way. The diphenylacetic esters and 9-fluorenecarboxylic esters of a number of pyridine alcohols have been prepared (*194*), including 2-pyridineethanol, 2-pyridinepropanol, α-methyl-2-pyridineethanol, 4-pyridineethanol,

and 4-pyridinepropanol. Barnden prepared a number of pyridine alcohol esters of penicillin-G (*195*), and many additional esters have been prepared (*544,545,634*).

Ethers may be prepared by the action of sodium on the pyridine alcohol, followed by treatment with a halide (*198,546,547*). In this manner, ethers of 3-pyridinemethanol were prepared from the following halides (*196*): dimethylaminoethyl chloride, 2-dimethylamino-1-chloropropane, 1-(chloroethyl)morpholine, 1-chloroethylpiperidine, and β-chloroethyl nicotinate (*197*). Certain 4-pyridinemethanol ethers have been prepared (*635*). Sodium phenolate and 3-(α-chlorethyl)-4-picoline gave an ether (*47*). Sulfuric acid and methanol also produce ethers in some cases (*512*). Some 2- and 4-pyridinemethyl ethers have been rearranged to the secondary alcohols by heating with sodamide (*636*).

As previously shown (p. 7), pyridine ethers can be prepared by the action of alkoxyalkyl halides on pyridine organometallic compounds.

4. Replacement of Hydroxyl Group by Halogen

This reaction proceeds normally with the usual reagents, and is summarized in Table XIII-8 (p. 34). *Cf.* Chapter VI (p. 329).

5. Dehydration to Olefins

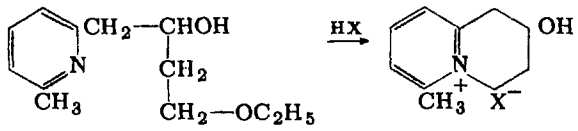
Several reagents have been used to dehydrate pyridine alcohols to the olefins, including phosphorus pentoxide, (*37,67,448*), potassium acid sulfate (*448,507*), zinc chloride (*422,507*), phosphorus pentachloride (*105*), potassium hydroxide (*46,85,92,117,551*), aluminum oxide (*92*), sulfuric acid (*38,138,140,524,548*), and plain heat (*549,550*). This reaction is further discussed in Chapter V (pp. 203, 204).

Attempts to distill ethyl β-hydroxy-3-pyridinepropionate, obtained by hydrogenation of ethyl β-oxo-3-pyridinepropionate, resulted in dehydration to the acrylic ester (*199*).

6. Synthesis of Polycyclic Systems

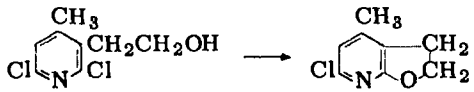
2-Pyridinepropanol has been cyclized with nickel at 200° to give octahydropyrrocoline (*187*). α-Methyl-2-pyridineethanol reacted with ω-bromoacetophenone to give the quaternary salt, which was cyclized

to 2-phenylpyrrocoline (*200,552*). Ring closure of α-(2-ethoxethyl)-6-methyl-2-pyridineethanol gave a 2-hydroxy-6-methyl-1,2,3,4-tetrahydroquinolizinium halide (XIII-9) (*201*). 2,6-Dichloro-4-methyl-3-

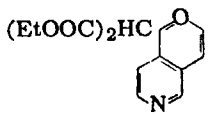


(XIII-9)

pyridineethanol was ring closed with potassium *tert*-amylate to an azadihydrobenzofuran (XIII-10) (*202*). Somewhat similarly a pyridinodihydropyran was obtained (*16,203*) (XIII-11) and also a 3-pyri-



(XIII-10)



(XIII-11)

dylmorpholine (*553*). Condensation of *p*-methoxyphenyl-2-pyridyl carbinol with phenols gave the triarylmethanes which were pharmacologically evaluated (*554*).

D. DIHYDRIC AND POLYHYDRIC ALCOHOLS CONTAINING ONE PYRIDINE NUCLEUS

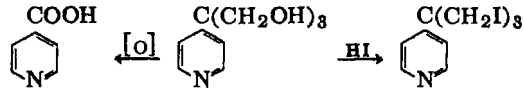
Compounds of this type are prepared by simple extensions of the synthetic methods already discussed. Lithium aluminum hydride has been used, for example, to prepare the isomeric pyridinedimethanols (*65,68,85,204,205,515*) and their nuclear substitution products (*65,68,206,207*) by reduction of the corresponding dicarboxylic esters. Similarly the aldol condensation with aldehydes may engage more than one nuclear methyl group (*170,208*), or formaldehyde may react repeatedly at a single methyl group, giving rise to 1,3-glycols of the type 2-PyCH(CH_2OH)$_2$ (*209*) or 4-PyCH(CH_2OH)$_2$ (*86,181, 210*). 2-Ethylpyridine (*82*), 4-ethylpyridine (*211,212*), 2-benzylpyri-

dine, and 4-benzylpyridine (*98*) have also been converted to the 1,3-glycol by reaction of the α-carbon with two molecules of formaldehyde. 3-Nitro-2,5,6-collidine reacts with two molecules of formaldehyde at the 6-methyl group; the nitro group apparently inhibits the reaction of the adjacent 2-methyl group (*97*). Reaction with three molecules of formaldehyde converts both 2-picoline (*80,81, 209*) and 4-picoline (*86,170*) to the triol $PyC(CH_2OH)_3$.

Other preparative methods that have been less widely applied include the catalytic reduction of dicarbonyl compounds (*25,31*) and the conversion of 2,6-dibromopyridine to the dimagnesium compound, followed by reaction with benzaldehyde (*213,214*). Decarboxylation of pyridylglycolic acid in the presence of an aldehyde has also been used (*637*). Appropriate organometallic reactions may also serve to introduce side-chains containing one or more ether linkages, as in the reaction of 2-picolyllithium with β-ethoxypropionaldehyde (*215*), the alkylation of 4-picoline with two moles of β-chloroethyl ether in the presence of sodamide (*132*) or the reaction of picolyllithium with 4-(bromoethyl)-2,2-dimethyl-1,3-dioxane followed by hydrolysis (*216*). 2-Picolyllithium reacted with tetracetylglucosyl halide to give a crude product that was presumably an acetate of a polyhydroxy ketone (*217*).

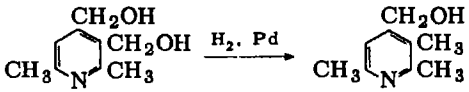
Olefins have been converted to 1,2-glycols by electrolysis (*218*), the Prevost method (*219*), or by bromine followed by silver oxide (*220*). 1-Phenyl-2-(2-pyridyl)ethylene glycol prepared in this way could be oxidized to the diketone (*220*). Electrolytic reduction of pyridine ketones with phenyl ketones gave glycols which could be cyclized to pyridylindenes (*555*). 3,5-Dibromo-4,6-di(methoxymethyl)-2-pyridinol was prepared by the action of sodium methylate on the corresponding di(bromethyl) compound (*221*).

The reactions of these compounds require little comment. The triol (XIII-12) may be oxidized to isonicotinic acid (*18*) or converted to the corresponding triiodide (XIII-13) (*170*).



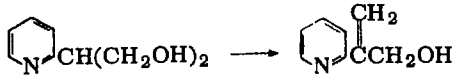
(XIII-12) (XIII-13)

The partial hydrogenolysis of a diol is shown in Equation XIII-14 (*73*).



(XIII-14)

The dehydration of the 1,3-glycol (XIII-15) occurred on distillation at 10 mm. pressure (*80,81,211*). The pyridine-3-(2-amino)-ethanol from the reduction of the product of nicotinaldehyde and nitromethane was treated with ethylene oxide to give the aminoglycol which could be cyclized to 3-pyridylmorpholine (*556*).

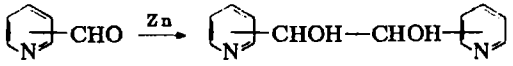


(XIII-15)

E. DIHYDRIC ALCOHOLS CONTAINING TWO PYRIDINE NUCLEI

The pinacol reduction has been performed on pyridine ketones with various reagents. Electrolytic reduction converted 3-acetylpyridine to the pinacol (*222,557*), while sodium amalgam has been used with ethyl 2-pyridyl ketone and the corresponding propyl and phenyl ketones (*44,45*). 3-Benzoylpyridine ketone gives the pinacol on exposure to sunlight in *i*-propyl alcohol solution (40).

All three pyridine aldehydes have been found to undergo bimolecular reduction by zinc to the glycol (XIII-16) (*223*). Starting



(XIII-16)

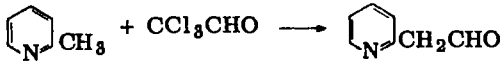
with picolinaldehyde or its 6-methyl derivative, the same result is achieved in two stages, the pyridoin condensation followed by reduction (*224,225*). The action of potassium cyanide on nicotinaldehyde gave the glycol directly, presumably by a crossed Cannizzaro reaction on the pyridoin, since isonicotinic acid was also formed (*226*). Pyridylglycollic acids react with pyridine aldehydes to give dipyridylglycols (*558,637*).

Vigorous oxidation of these 1,2-glycols gives the carboxylic acids as would be expected; lead tetraacetate gives the aldehyde instead (*224,513*).

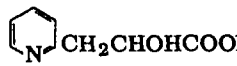
In the pinacol rearrangement, the 2-pyridyl and 3-pyridyl radicals have been found to migrate much less readily than the phenyl radical (*40*). The pinacol rearrangement has also been used preparatively to make pyridyl ketones (*559*).

F. SIDE-CHAIN HYDROXYACID DERIVATIVES

Compounds with hydroxyacid side chains are obtained by reduction (*227*) or catalytic hydrogenation (*228*) of ketoacid side chains, or more generally by condensation of methylpyridines with appropriately substituted carbonyl compounds. Thus 2-picoline reacts with chloral to give the trichloropropanol (XIII-17), which may be hydrolyzed to the lactic acid (XIII-18) (*84,105,107*). *s*-Collidine re-



(XIII-17)

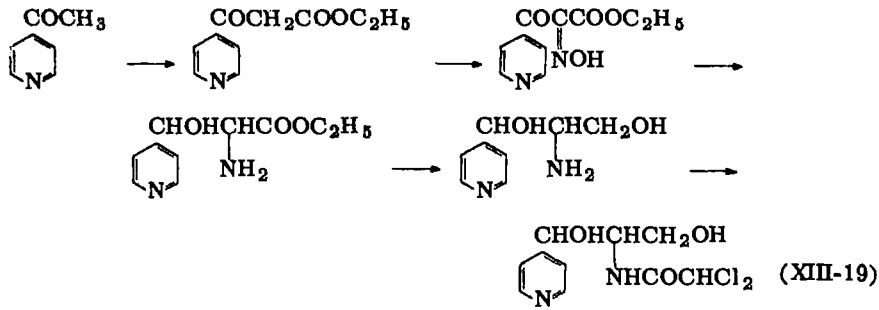


(XIII-18)

acts with chloral at the 2-methyl group; another unidentified product was also obtained (*91*). Pyridylic acid rearrangement has been used in two cases to obtain the hydroxy acids (*560*). The Reformatsky reaction on pyridine ketones also yields hydroxy acids (*561*).

Picolines may also be condensed with ketoesters, such as ethyl benzoylacetate, to give hydroxyesters (*229*). Picoline containing additional side chains with hydroxy groups may furnish hydroxyacid derivatives by reaction with chloral and hydrolysis or with dihydroxymalonic ester (*203,230*).

An analog of chloramphenicol was prepared as shown (*231*) (XIII-19).



(XIII-19)

Addition of hydrogen cyanide to 5-methylnicotinaldehyde, followed by hydrolysis of the cyanohydrin, gave 5-methyl-3-pyridineglycolic acid (*232*). Cyanohydrins from a number of picolinaldehydes have also been prepared (*166,638*). (*Cf.* Chapter XIV, p. 137.)

The introduction of a side-chain containing an ether linkage is seen in the alkylation of ethyl 2-pyridineacetate at the α-carbon atom by 3-phenoxypropyl bromide (*233*). Ring opening of 6-hydroxyquinoline produced compound (XIII-20) (*234*).

(XIII-20)

These hydroxyacids shown the properties that would be expected. Replacement of hydroxyl by bromine (*105,107*) and dehydration to unsaturated acids (*84,105,199,228*) were described in the older literature.

G. DERIVATIVES CONTAINING BOTH NUCLEAR AND SIDE-CHAIN HYDROXYL

1. Preparation and Reactions

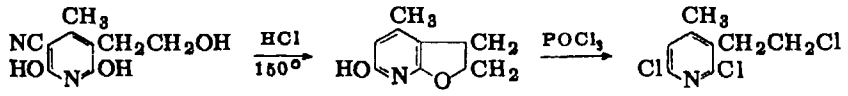
In a number of instances nuclear hydroxy groups are found to activate the ring sufficiently to permit direct hydroxymethylation by formaldehyde. Thus 3-pyridinol gives a 51% yield of 3-hydroxy-2-pyridinemethanol; 6-methyl-3-pyridinol also gives the 2-methanol (*235,236*). 2,4-Dihydroxy-6-chloronicotinonitrile hydroxymethylates at the 5 position (*237*) and 5-hydroxy-8-(2-pyridyl)octanoic acid hydroxymethylates at the 6 position (*238*).

Most other compounds of this type have been prepared by applications of the nuclear synthetic methods discussed at length in Chapter II. Thus 5-butoxy-4-hydroxy-2-pyridinemethanol (*239*), 5-ethoxy-4-hydroxy-2-pyridinemethanol (*189*), 5-methoxy-2,4-pyridinedimethanol, and 2-hydroxymethyl-5-methoxy-1-methyl-4(1*H*)-pyridone (*188*) have been prepared from the corresponding pyrone and ammonia. 5-Hydroxy-2-pyridinemethanol has been obtained by the action of ammonia and heat upon 5-ethoxymethylfurfural or 5-chloromethylfurfural (*240*). A number of pyridinols containing side-

chain ether functions have been obtained by cyclization of appropriately substituted starting materials (*11,241–244*).

As might be expected, a side-chain hydroxyl group can be replaced successively by bromine and hydrogen, without interference by nuclear hydroxyl in the 3 position (*235,236*). It is interesting that a 2-hydroxymethyl group can be oxidized to carboxy without interference by nuclear hydroxyl in the 3 (*235*) or 4 (*236*) position.

The triol (XIII-21) was cyclized to the dihydrofuran with loss of the cyano group; this was then converted to the trichloride (XIII-22) (*243*).

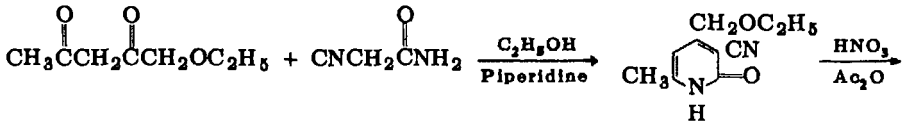


(XIII-21) (XIII-22)

2. Pyridoxol and Related Compounds. Codecarboxylase

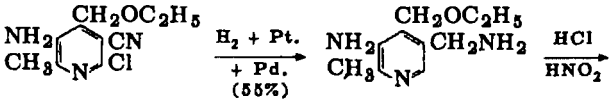
Pyridoxol (pyridoxine, vitamin B_6, adermin) was isolated from rice bran as the hydrochloride ($C_8H_{12}O_3Cl$, m.p. 204–206°) of a base ($C_8H_{11}O_3N$, m.p. 160°) by several groups of workers (*245–248*). Its structure was shown by two groups to be 5-hydroxy-6-methyl-3,4-pyridinedimethanol because of its analysis, ultraviolet spectrum, chemical behavior, and comparison with certain model substances (*249–253*). Pyridoxol is optically inactive and gives negative tests for methoxy, primary and secondary amine groups, ester, and aldehyde groups. It has one C-methyl group and three active hydrogens by the Zerewitinow procedure, and is a tertiary amine. It gives a red ferric chloride test. Its ultraviolet absorption spectrum resembles that of 3-pyridinol. Etherification with diazomethane forms a methyl ether which can be oxidized to a methoxypyridinedicarboxylic acid; this was proved by synthesis to be 5-methoxy-6-methylcinchomeronic acid (*252,254*). Total synthesis by Harris and Folkers confirmed the structure assigned (*253*) (XIII-23). Subsequently these authors (*255*) were able to convert XIII-29 to XIII-32 in the two steps of splitting the ether and treating with nitrous and hydrochloric acids. XIII-25 has been hydrolyzed by 50% sulfuric acid to the hydroxymethyl acid and its lactone (*256*) and the cyano group in XIII-25 has been reduced to the aminomethyl group (*257,564*). The

Merck & Company patents are covered in the bibliography (*258–288, 565,566*).

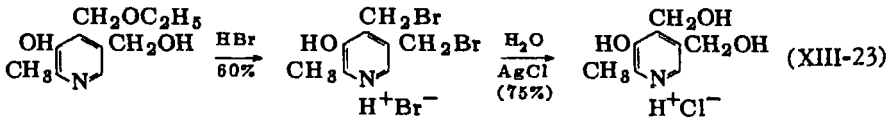


(XIII-24) (XIII-25)

(XIII-26) (XIII-27)



(XIII-28) (XIII-29)



(XIII-30) (XIII-31) (XIII-32)

Starting with 6-hydroxy-5-cyano-4-phenoxymethyl-2-methyl-nicotinic acid, converting the carboxy group to the carbethoxyamino group by the Schmidt reaction, removing the 6-hydroxy group, and reducing the cyano group in the usual manner gave 6-methyl-5-carbethoxyamino-4-phenoxymethyl-3-pyridinemethanol which could be converted by the action of hydrobromic acid and then nitrous acid to pyridoxol (*289*).

A second general synthesis of pyridoxol involves the reduction of derivatives of the 5-substituted 6-methylcinchomeronic acids. One approach of this kind was the use of lithium aluminum hydride on the proper pyridine diester (*290,291,571–574*), and in this way the following were reduced to pyridoxol directly or with the appropriate second step: dimethyl 5-hydroxy-6-methylcinchomeronate, dimethyl 5-amino-6-methylcinchomeronate (*292*), dimethyl 5-acetoxy-6-methylcinchomeronate, and ethyl 5-amino-3-cyano-6-methylisonicotinate (*293,562,563*).

Another approach is the catalytic reduction of an appropriate 3,4-dicyanopyridine (*294*). In one case 5-methoxy-6-methylcinchomeronic acid, obtained in a series of reactions from 3-methyl-4-methoxyisoquinoline, was converted to the diamide and dinitrile in the usual manner, reduced to the di(aminomethyl) compound, and treated with nitrous acid to give the di(hydroxymethyl) compound; ether cleavage gave pyridoxol (*295–297*). A related synthesis is the preparation of 5-methoxy-4-methoxymethyl-6-methylnicotinic acid starting from an amino or hydroxy substituted 3-methoxy-4-methoxymethylquinaldine, followed by conversion to pyridoxol through the cyano derivative, reduction, nitrous acid treatment, and removal of the ether groups in the conventional manner (*298*).

Similarly, Carlson converted ethyl 2-hydroxy-3-cyano-6-methylisonicotinate to the 3,4-dinitrile which was nitrated, converted to 2-methyl-3-amino-4,5-di(aminomethyl)pyridine in the usual manner, and treated with nitrous acid to give pyridoxol (*299,300*). In still another related synthesis, *N*-alkylalanine esters are condensed with α-formylsuccinic esters to give *N*-alkyl-*N*-(1-carbalkoxyethyl)aminomethylenesuccinic esters which are cyclized to basic ketoesters and dehydrogenated to pyridinium salts. Hydrogenolysis of the 1-benzylpyridinum salts gave 5-hydroxy-6-methylcinchomeronates, which can be converted to pyridoxol through the dicyano compound in the previously outlined manner or by reduction with lithium aluminum hydride (*301*). Stevens (*302,303*) has cyclized 4-formyl-3-oxo-tetrahydrofuran with certain amino compounds to make cyclic ethers which could be converted to pyridoxol.

Pyridoxol has been obtained in 76% overall yields from 2-(α-acetamidoethyl)-3,4-bis(acetoxymethyl)furan in a three step process (*304,639*), 2-(α-aminoethyl)3,4-bis(hydroxymethyl)-2,5-dimethoxy-2,5-dihydrofuran also gave pyridoxol (*305*), and 3,4-bishydroxymethylfuran (*568*). Other attempts to obtain pyridoxol from furans were unsuccessful (*305*). (*Cf.* Chapter II, pp. 154–172.) In an attempt to prepare pyridoxol, McElvain and co-workers unsuccessfully attempted to replace a 4-chloro group by a cyano (*306*). The 1-oxide of the vitamin has been prepared and found to have only 15% activity (*642*).

Pyridoxol has been quantitatively determined by means of the Gibbs color test with 2,6-dichloroquinone chloromide (*307–313*).

Other color reactions and chemical tests have been used but have not acquired the importance of the Gibbs test (*314–317*).

Microbiological tests have been very useful for the determination of pyridoxol and related compounds (*313,318,319*).

The stability (*313,320*), toxicity (*321*), and metabolism (*322, 323*) of pyridoxol have been investigated.

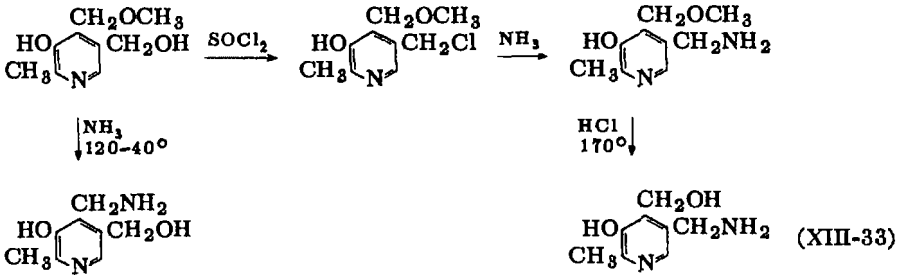
Hydrogenation of pyridoxol with Adams catalyst reduces its 4-hydroxymethyl group to methyl (*324,325,538*), whereas oxidation converts the 5-hydroxymethyl to the carboxy group and a lactone results (*252*). Pyridoxol base, when treated with methyl, butyl, and benzyl alcohols at 125° or reflux temperature, produced the 4-alkoxymethyl compound (*324,326*), while acetic anhydride gave a triacetate which was different from 6-methyl-5-hydroxy-3,4-di(acetoxymethyl)pyridine hydrochloride prepared from the corresponding 3,4-di(bromomethyl) compound (*324*). Pyridoxol hydrochloride yields an *i*-propylidene derivative with acetone (*327,328*). Methyl iodide with silver carbonate gives the same *N*-methyl derivative in good yield that is obtained from pyridoxol in low yield with diazomethane. Chemical and physical properties indicate that this compound is a phenol betaine or zwitterion (*329,330*); pyridoxol hydrochloride also is apparently a zwitterion at pH 6.8 in aqueous solution. The action of methyl iodide at 110–115° converted the phenol betaine to the 3-methyl ether methiodide; the latter was also prepared from methyl iodide and pyridoxol-3-methyl ether (*317,329*). The *N*-methylation of pyridoxol destroys its biological activity (*329*). The alcoholic hydroxyl groups of pyridoxol have been replaced by halogens using halogen acids and other halogen compounds (*567*).

Neutral aqueous solutions of the vitamin polymerize at 120° by losing the elements of water. In the same way the 4-methyl ether loses the elements of methyl alcohol to polymerize, but the 4-desoxy compound does not polymerize (*326*).

Long chain fatty acid derivatives of pyridoxol, pyridoxal, and 4-desoxypyridoxol have been prepared (*331,332*).

Snell found natural substances similar to pyridoxol with increased growth-promoting powers and showed that such substances could be obtained by amination or oxidation of pyridoxol. He named the amine "pyridoxamine" and the aldehyde "pyridoxal,"

and showed that they were interconvertible by a transamination reaction (*333–335*). Seeking to establish the position of the amine and aldehyde groups, Harris and co-workers (*336,337*) synthesized both the 3- and 4-aminomethyl analogs of pyridoxol and showed that the 4-isomer had the activity of pyridoxamine (XIII-33).



Careful permanganate oxidation of pyridoxol gave the 4-aldehyde, which was shown to be pyridoxal. The isomeric 5-aldehyde was inactive in promoting the growth of lactic-acid bacteria. The 4-aldehyde may have a cyclic hemiacetal structure and is readily converted to the cyclic ethyl acetal (*336*). A synthesis of the lactone of 4-pyridoxic acid from the oxime of pyridoxal has been developed (*338*) and pyridoxal oxime has been reduced to pyridoxamine electrolytically (*569*). Pyridoxal has been reductively coupled with a number of amines including amino acids and amino esters (*339–345, 570,641*). (Table XIII-29, p. 98.) Schiff bases are also obtained (*341,342,345,346,575,576*). (Table XIII-30, p. 101.) Metal complexes of Schiff bases are believed to be intermediate in transamination reactions (*345–350,577,578*); these reactions have been discussed by Snell and co-workers in a series of papers (*351–356*). The enzymic conversion of pyridoxal to its 5-phosphate (codecarboxylase) has been observed (*357,579,580*).

The antibacterial properties of irradiated pyridoxamine have been studied (*358*). Pyridoxol, pyridoxamine, and pyridoxal have been compared as to growth promoting properties for many organisms (*359*), and a differential bacterial assay has been developed for materials in which they may occur naturally (*360*).

Nicotinyl and isonicotinyl hydrazones of pyridoxal have been prepared (*361*). The hydrazide of 4-pyridoxic acid and the thio-

semicarbazone of pyridoxal were also prepared (*362*), and specific reaction rates for pyridoxal-5-phosphate with several hydrazides have been determined (*363*). The action of *p*-nitrobenzoyl chloride on pyridoxal gave a di-*p*-nitrobenzoate of the hemiacetal; mild hydrolysis gave the monoester of the hemiacetal (*364*).

The methyl group of pyridoxol, pyridoxal, and pyridoxamine has been replaced by the ethyl group and the resulting compounds examined for biological activity (*365–368*) . The methyl group has also been replaced by *i*-propyl, phenyl, *i*-butyl (*369,370*), *n*-amyl (*370*), and benzyl groups (*371*). 4-Desoxypyridoxol has been shown to be an effective pyridoxol antagonist for some organisms but not for others (*372–376,588–590*), and has likewise been modified by replacing the 6-methyl groups by ethyl, *i*-butyl (*365*), and *n*-amyl (*370, 377*). It is reported that 5-desoxypyridoxol, 5-desoxypyridoxal, and 5-desoxypyridoxamine are less effective antagonists (*378,379*).

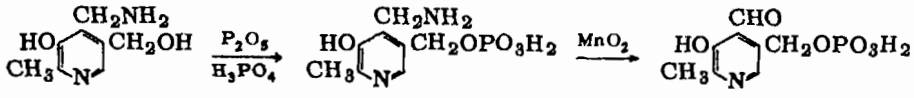
Numerous pyridoxol analogs have been prepared in which various groups are replaced, removed, or changed in position, including 5-hydroxy-3,4-pyridinedimethanol (*591,592*), 6-methyl-3,4-pyridinedimethanol (*380*), 5-hydroxy-6-methyl-3-pyridinemethanol (*381*), 4,6-dimethyl-3-pyridinemethanol (no activity), 5,6-dimethyl-3-pyridinemethanol (weak antagonism) (*382*), 6-hydroxy-4-methyl-2-pyridinemethanol (*383*), a number of derivatives of 2-hydroxy-6-methyl-3,4-pyridinedimethanol (*383,593*), 2-hydroxy-4,6-dimethyl-3-pyridinemethanol (*384*), 4,6-di(methoxymethyl)-2-pyridinol (inactive) (*385*), 5-hydroxy-6-methyl-2,3-pyridinedimethanol (*386*), 4-amino-6-methyl-2,5-pyridinedimethanol (*386*), 5-hydroxy-6-methyl-2,3,4-pyridinetrimethanol (no activity, slight antagonism), 5-amino-6-methyl-2,3-pyridinedimethanol, 5-amino-6-methyl-2,3,4-pyridinetrimethanol, 5-amino-6-methyl-3,4-pyridinedimethanol (*386*), and various others (*387,388,640*).

The antidermatitic effects of a number of derivatives and analogs have been determined (*389*).

Codecarboxylase (XIII-34) is a coenzyme in a number of important enzymes (*390–396*). It was originally prepared by the action of adenosine triphosphate on pyridoxal (*397*) and then by the use of phosphorus oxychloride on pyridoxal (*398*) or its acetal (*399*). A free aldehyde group was indicated (*400*) and the structure further shown by the difference between codecarboxylase, and the nuclear

phosphate of pyridoxal (*401–404*). The question of phosphorylation at the aldehyde or carbinol positions was finally decided by synthesis, and the structure confirmed (*405–408*). Phosphorylation of pyridoxal oxime gave the oxime of codecarboxylase, which can also be prepared from codecarboxylase itself (*405*).

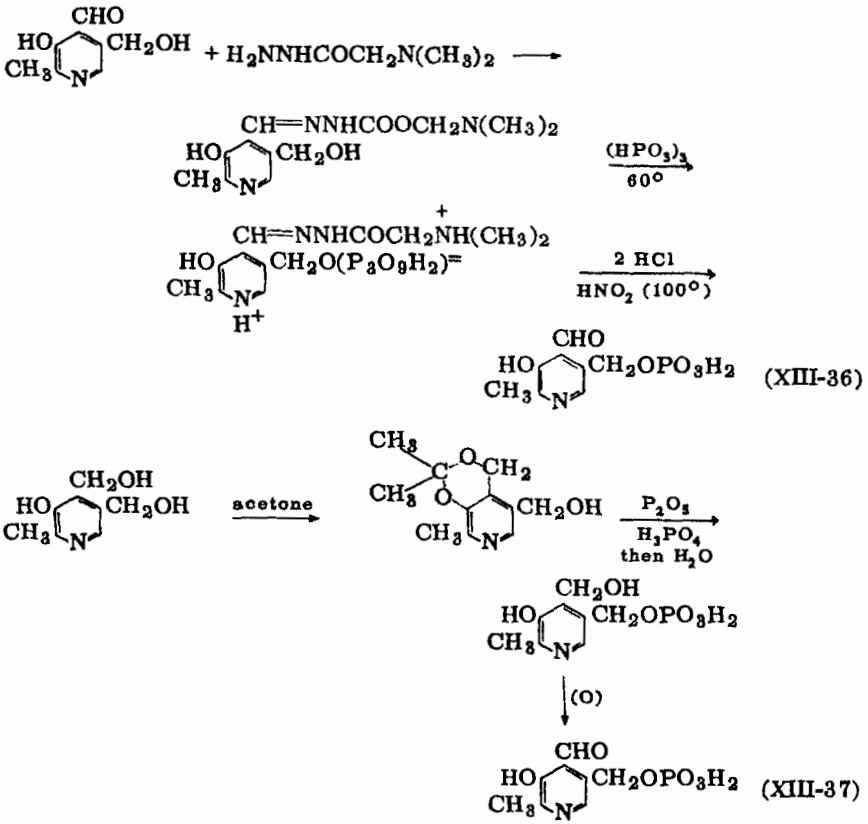
The synthesis of codecarboxylase from pyridoxamine (XIII-35) is shown (*403,409,410*).



(XIII-35) (XIII-34)

Codecarboxylase

It has also been synthesized from pyridoxal by an unambiguous method (XIII-36) (*407*) and from pyridoxol (XIII-37) (*408*).



Magnesium, calcium (*411*), and acridine (*412*) salts of codecarboxylase have been reported. Phosphates of pyridoxol, pyridoxamine, and 4-deoxypyridoxine have also been prepared (*413,414*).

In codecarboxylase as well as pyridoxal, the formyl group is replaced by a hydroxyl group on treatment with hydrogen peroxide (*415*).

H. TABLES

TABLE XIII-1. Condensation of 2- and 4-Picolines with Aromatic Aldehydes $PyCh_3 + RCHO \longrightarrow PyCH_2CH_2OHR$

Py	R	Ref.
2-Py	Ph	416,420
2-Py	*p*-MeC_6H_4	417,420
2-Py	*p*-(*i*-Pr)C_6H_4	421
2-Py	*o*-$NO_2C_6H_4$	416,417,420,422
2-Py	*m*-$NO_2C_6H_4$	420
2-Py	*p*-$NO_2C_6H_4$	171
2-Py	PhCH : CH	174
2-Py	2-furyl	423
4-Py	PhCH : CH	174
2-Pyridyl 1-methiodide	Ph	425
4-Methyl-2-pyridyl	*p*-MeC_6H_4	96
6-Methyl-2-pyridyl	Ph	424,425
6-Methyl-2-pyridyl	*m*-$NO_2C_6H_4$	426
6-Methyl-2-pyridyl	PhCH : CH	426
6-Methyl-2-pyridyl	*p*-$NO_2C_6H_4$	427
6-Methyl-2-pyridyl 1-methiodide	Ph	425
5-Ethyl-2-pyridyl	Ph	426
5-Ethyl-2-pyridyl	*o*-$NO_2C_6H_4$	417
5-Ethyl-2-pyridyl	*p*-$NO_2C_6H_4$	417
4,6-Dimethyl-2-pyridyl	Ph	208
6-Phenyl-2-pyridyl	*p*-MeC_6H_4	427
6-Phenyl-2-pyridyl	*o*-$NO_2C_6H_4$	428
6-Phenyl-2-pyridyl	*p*-$NO_2C_6H_4$	429

TABLE XIII-2. Addition of Organometallic Compounds to Pyridine Aldehydes and Ketones PyCOR + R′M⟶PyC(OH)RR′

Py	R	R′M	Ref.
2-Py	H	MeMgCl	149
2-Py	H	PhMgBr	628
2-Py	H	*p*-ClC_6H_4MgBr	628
2-Py	H	$PhCH_2MgCl$	419
2-Py	H	*i*-PrMgBr	136
2-Py	H	*p*-$PrOC_6H_4MgBr$	136
2-Py	H	*p*-$CH_3OC_6H_4MgBr$	554
2-Py	Me	MeMgBr	38
2-Py	Me	EtMgCl	430
2-Py	Me	PrMgBr	431
2-Py	Me	$EtOCH_2CH_2CH_2MgBr$	191
2-Py	Me	PhMgLi	67,432
2-Py	Ph	PhMgCl	179,186,512
2-Py	o-$NH_2C_6H_4$	MeMgBr	438
2-Py	o-$NH_2C_6H_4$	$PhCH_2MgBr$	438
2-Py	Ph	*p*-MeC_6H_4MgCl	186
2-Py	Ph	$PhCH_2MgCl$	186
2-Py	Ph	*p*-$MeOC_6H_4MgCl$	186
2-Py	Ph	*p*-$EtOC_6H_4MgCl$	186
2-Py	Ph	β-indolyl-MgCl	186
2-Py	Ph	4-methylcyclohexyl MgCl	186
2-Py	*p*-$MeOC_6H_4$	cyclopropyl-MgCl	186
2-Py	Ph	cyclopropyl-MgCl	186
2-Py	Ph	o-MeC_6H_4Li	186
2-Py	Ph	*m*-MeC_6H_4Li	186
2-Py	Ph	*p*-EtC_6H_4Li	186
2-Py	Ph	2,5-$(Me)_2C_6H_3Li$	186
2-Py	Ph	2,4,6-$(Me)_3C_6H_2Li$	186
2-Py	Ph	1-$C_{10}H_7Li$	186
2-Py	Ph	*m*-ClC_6H_4Li	186
2-Py	Ph	*p*-$(Me)_2NC_6H_4Li$	186
2-Py	Ph	*p*-$(Me_3Si)C_6H_4$	186
2-Py	Ph	cyclopropyl-Li	186
2-Py	Ph	1-cycloheptenyl-Li	186
2-Py	2-Py	EtMgCl	440
2-Py	2-Py	4-PyLi	605
2-Py	4-Py	4-PyLi	605
3-Py	Me	PhMgCl	432,433
3-Py	Me	$PhCH_2MgBr$	436
3-Py	Me	1-$C_{10}H_7(C_6H_5)C:CHMgBr$	434
3-Py	Me	*p*-MeC_6H_4MgCl	433
3-Py	Et	PhMgCl	433
3-Py	Me	1-$C_{10}H_7MgCl$	433

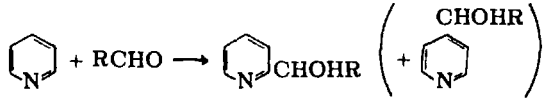
TABLE XIII-2. (*Continued*)

Py	R	R′M	Ref.
3-Py	Ph	4-biphenyl	606
3-Py	3-Py	3-PyLi	605
3-Py	3-Py	4-PyLi	605
3-Py	4-Py	4-PyLi	605
4-Py	Me	EtMgCl	177
4-Py	Ph	MeMgBr	146,435
4-Py	Ph	PhMgCl	177,436,437
4-Py	o-$NH_2C_6H_4$	MeMgBr	438,439
4-Py	o-$NH_2C_6H_4$	EtMgBr	438,439
4-Py	4-Py	4-PyLi	605
4-Py	Me	4-biphenyl	606
4-Py	Et	4-biphenyl	606
4-Py	Pr	4-biphenyl	606
4-Py	Ph	4-biphenyl	606
4-Py	$PhCH_2$	4-biphenyl	606
6-Methyl-3-pyridyl	Me	MeMgCl	176
2,4,6-Triphenyl-2,3,4,5-tetrahydro-3-pyridyl	Ph	MeMgBr	32

TABLE XIII-3. Addition of Organometallic Compounds to Pyridinecarboxylic Esters PyCOOR + R'M ⟶ PyC(OH)R'_2

Py	R	R'M	Ref.
2-Py	Et	MeMgI	441
2-Py	Et	EtMgBr	136,440
2-Py	Et	PrMgBr	136
2-Py	Et	$PhCh_2MgBr$	136
2-Py	Et	p-$CH_3C_6H_4MgBr$	186
2-Py	Et	p-$CH_3OC_6H_4MgBr$	554
3-Py	Me	MeMgI	9,18
3-Py	Et	EtMgBr	441
6-Methyl-3-pyridyl	Et	MeMgI	176
4-Py	Ft	MeMgI	37
1-Methyl-4-(tetrahydropyridyl)	Me	PhMgBr	442
2-Py	Et	o-Me C_6H_4Li	186
2-Py	Et	p.$EtOC_6H_4Li$	186
2-Py	Et	p-$(Me)_2NC_6H_4Li$	186
6-Methyl-2-pyridyl	Et	PhLi	186
Methyl-3,5-pyridine dicarboxylate		MeMgI	9

TABLE XIII-4. Emmert-Asendorf Reaction with Aldehydes



Pyridine reactant	R	Yield, %	Ref.
Pyridine	Ph	22-39 (2-isomer) 19 (4-isomer)	146,175
Pyridine	o-ClC_6H_4	23 (2-isomer)	146
Pyridine	p-(i-Pr)C_6H_4	14 (2-isomer)	146
Pyridine	o-$MeOC_6H_4$	18 (2-isomer)	146
Pyridine	p-$MeOC_6H_4$	51 (2-isomer)	146
Pyridine	2,3-$(MeO)_2C_6H_3$	12 (2-isomer)	146
Pyridine	3,4$(CH_2O_2)C_6H_3$	29–37 (2-isomer)	175
Pyridine	$PhCH_2Me$	6 (2-isomer)	146
4-Ethylpyridine	Ph	19 (2-isomer)	186

TABLE XIII-5. Emmert-Asendorf Reaction with Open-Chain Ketones

PyH + RCOR′ ⟶ 2-PyC(OH)RR′ (+ 4-PyC (OH)RR′)

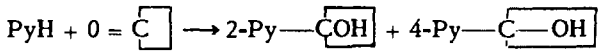
PyH	R	R′	Yield%	Ref.
Pyridine	Me	Me	29	38,138, 140
Pyridine	Me	Et	10	138
Pyridine	Me	hexyl	69 (2-isomer)	146
Pyridine	Me	cyclopropyl	16 (2-isomer)	146
Pyridine	Me	cyclohexyl	56 (2-isomer)	146
Pyridine	Me	1-cyclohexenyl	16 (2-isomer)	146
Pyridine	Me	Ph	44,53 (2-isomer)	138,146
			12 (4-isomer)	439
Pyridine	Me	o-MeC_6H_4	21 (2-isomer)	146
Pyridine	Me	m-MeC_6H_4	38 (2-isomer)	146
Pyridine	Me	p-MeC_6H_4	51 (2-isomer) 8 (4-isomer)	146
Pyridine	Me	3,4-$Me_2C_6H_3$	31 (2-isomer)	146
Pyridine	Me	2-Me-5-*i*-PrC_6H_3	40 (2-isomer)	146
Pyridine	Me	o-ClC_6H_4		146
Pyridine	Me	m-ClC_6H_4	26 (2-isomer)	146
Pyridine	Me	p-ClC_6H_4	15 (2-isomer) 7 (4-isomer)	146
Pyridine	Me	m-BrC_6H_4	31 (2-isomer)	146
Pyridine	Me	o-$MeOC_6H_4$		146
Pyridine	Me	m-$MeOC_6H_4$	28 (2-isomer)	146
Pyridine	Me	p-$MeOC_6H_4$	62 (2-isomer) 4 (4-isomer)	146
Pyridine	Me	3,4-$(MeO)_2C_6H_3$	39 (2-isomer)	146
Pyridine	Me	2-MeO-4-MeC_6H_3		146
Pyridine	Me	2-MeO-5-MeC_6H_3		146
Pyridine	Me	1-$C_{10}H_7$	25 (2-isomer)	146
Pyridine	Me	2-$C_{10}H_7$	14 (2-isomer)	146
Pyridine	Me	2-thienyl	16–17 (2-isomer)	146
Pyridine	Me	5-bromo-2-thienyl		146
Pyridine	Et	Ph	50 (2-isomer)	146
Pyridine	*i*-Pr	*i*-Pr	26 (2-isomer)	146
Pyridine	*i*-Pr	Ph	44 (2-isomer)	146
Pyridine	Ph	Ph		138
Pyridine	$PhCH_2$	Ph	36 (2-isomer)	138
Pyridine	$PhCH_2$	$PhCH_2$	33 (2-isomer)	146
2-Picoline	Me	Me	2–3 (6-isomer)	140
2-Picoline	Me	Ph	13 (6-isomer)	146

(*continued*)

TABLE XIII-5. (*Continued*)

PyH	R	R′	Yield %	Ref.
3-Picoline	Me	Me	8.5 (2- and 6-isomer)	140
4-Picoline	Me	Me	8.5 (2-isomer)	140
4-Picoline	Me	Ph	58 (2-isomer)	146
4-Picoline	Ph	Ph	38	186
4-Picoline	*p*-Me C_6H_4	*p*-Me C_6H_4	52	186
3-Chloropyridine	Me	Ph		138
3-Bromopyridine	Me	Ph	13 (2- or 6-isomer)	146

TABLE XIII-6. Emmert-Asendorf Reaction with Cyclic Ketones



PyH	Ketone	Yield, %	Ref.
Pyridine	cyclopentanone	23 (2-isomer) 0.1 (4-isomer)	140,443,444
Pyridine	cyclohexanone	29–55 (2-isomer) 0.25 (4-isomer)	140,146,443
Pyridine	2-cyclohexylidenecyclohexanone	24 (2-isomer)	146
Pyridine	*l*-indanone	35 (2-isomer)	146
Pyridine	*l*-tetralone	23 (2-isomer)	146
Pyridine	*dl*-fenchone	52 (2-isomer)	146
Pyridine	*dl*-camphor	35 (2-isomer)	146,443
2-Picoline	cyclopentanone	2.3 (6-isomer) 0.56 (4-isomer)	140
3-Picoline	cyclopentanone	4 (2-isomer) 11 (6-isomer)	140
4-Picoline	cyclopentanone	23 (2-isomer)	140

TABLE XIII-7. Hammick Reaction PyCOOH + RCOR′⟶PyC(OH)RR′

Py	R	R′	Yield, %	Ref.
2-Py	Ph	H	49, 54	143,145,432
2-Py	Ph	Me	17, 50	143,145,432
2-Py	Ph	Ph	14.5, 48	143,145,432
2-Py	*m*-MeC_6H_4	H	29	432
2-Py	*p*-MeC_6H_4	H	49	432
2-Py	*p*-*i*-PrC_6H_4	H	24.5	432
2-Py	*o*-ClC_6H_4	H	45	432
2-Py	*p*-ClC_6H_4	H	37, 58	145,432
2-Py	*p*-ClC_6H_4	Me	13	432
2-Py	*m*-$NO_2C_6H_4$	H	48[a]	145
2-Py	*m*-$NO_2C_6H_4$	Me	42	145
2-Py	*o*-$MeOC_6H_4$	H	27	445
2-Py	*p*-$MeOC_6H_4$	H	33, 59	145,432
2-Py	3,4-$(MeO)_2C_6H_3$	H	2.4, 15	432,446
2-Py	3,4-$(CH_2O_2)C_6H_3$	H	26	432
2-Py	—$(CH_2)_5$—		33	446
2-Py	2-Py	Me	17	432
2-Py	2-thienyl	Me	12	432
4-Py	Ph	Ph	3.5	144
3-Methyl-2-pyridyl	*p*-$MeOC_6H_4$	H	35	145
4-Methyl-2-pyridyl	*p*-$MeOC_6H_4$	H	53	145
5-Methyl-2-pyridyl	*p*-$MeOC_6H_4$	H	47	145
5-Methoxy-6-methyl-2-pyridyl	$(CH_2)_6CO_2Me$	H	25	168
6-Methyl-2-pyridyl	*p*-$MeOC_6H_4$	H	57	145
6-Methyl-2-pyridyl	$(CH_2)_5Me$	H	24	168
6-Methyl-2-pyridyl	$(CH_2)_7CO_2Me$	H	9	168
4,6-Dimethyl-2-pyridyl	*p*-$MeOC_6H_4$	H	49	145
2-Py 1-oxide	Ph	Cl_3	m.p. 112–113°	525

[a]Product is *m*-nitrophenyl 2-pyridyl ketone.

TABLE XIII-8. Side-Chain Replacement of Hydroxyl by Halogen

ROH ⟶ RX

ROH	Reagent	X	Ref.
2-$PyCH_2OH$	$POCl_3$	Cl	447
2-$PyCH_2OH$	HBr	Br	63,509
2-PyCHROH[a]	$SOCl_2$	Cl	445
2-$PyCH_2CH_2OH$	HBr	Br	99
2-$PyCH_2CH_2OH$	HI	I	99
2-$PyCOH(CH_3)_2$	HBr	Br	99
2-$PyCOH(CH_3)_2$	HI	I	82
2-$PyCOH(CH_3)CH_2CH_3$	HBr	Br	102,103
2-$PyCH_2CHOHCH_2CH_3$	HI	I	102,103
3-$PyCH_2OH$	$SOCl_2$	Cl	65
3-$PyCHOHCH_2CH_2CH_2NHCH_3$	HI	I	57
4-$PyCH_2OH$	HBr	Br	22,63
4-$PyCH_2CH_2OH$	HCl	Cl	86
α,4-Dimethyl-3-pyridinemethanol	HBr	Br	47
α,6-Diphenyl-3-pyridinemethanol	$SOCL_2$	Cl	35
2,6-Dimethyl-α-phenyl-4-pyridinemethanol	PCl_5	Cl	48

[a]R = Phenyl or, substituted phenyl.

TABLE XIII-9. 2-Pyridinemethanols (1-carbon side-chain) 2-PyC(OH)RR′

Py	R	R′	Physical properties, derivatives	Ref.
2-Py	H	H	b.p. 60–65°/1 mm.; picrate, m.p. 159–61°; acetate, b.p. 112–17°/5 mm.; chloroplatinate, m.p. 177°; *p*-nitrobenzoate, m.p. 92°; benzoate, b.p. 196–98°/17 mm.; penicillin-*G* ester m.p. 94–96°; α_D^{20} + 150°, ethers	15,18,22,24,26, 63,65,66,68, 148,150,195, 453,532,533, 604,619,632, 634,636
3-Methyl-2-pyridyl	H	H	acetate, b.p. 118–24°/12–14 mm.	159
4-Methyl-2-pyridyl	H	H	b.p. 100–7°/4 mm.	155,531
6-Methyl-2-pyridyl	H	H	b.p. 126–27°/16 mm.; acetate, b.p. 110–114°/15 mm.	94,150
5-Ethyl-2-pyridyl	H	H	b.p. 116–17.5/5 mm.; acetate, b.p. 120–27°/5 mm.	453
6-Chloro-2-pyridyl	H	H	HCl, m.p. 143–4°	530
4,6-Dichloro-2-pyridyl	H	H	m.p. 84°; benzoate, m.p. 53–54°	28
4,5,6-Trichloro-2-pyridyl	H	H	m.p. 84°	29
3-Hydroxy-2-pyridyl	H	H	acetate, b.p. 109–10°/0.8 mm.; m.p. 137–9°	159,235,236, 630,640
5-Hydroxy-2-pyridyl	H	H	m.p. 124°	240,505
4-Methyl-6-hydroxy-2-pyridyl	H	H	m.p. 225°; picrate, m.p. 127°	241,383

(*continued*)

TABLE XIII-9. (*Continued*)

Py	R	R′	Physical properties, derivatives	Ref.
6-Methyl-3-hydroxy-2-pyridyl	H	H	m.p. 154°; hydrochloride, m.p. 162°; hydrobromide, m.p. 164°; picrate, m.p. 173–74°	235,236
4,5-Dihydroxy-2-pyridyl	H	H	m.p. 246°; benzyl ether, m.p. 224–226°	505
3-Ethyl-4-methoxy-2-pyridyl	H	H	b.p. 140°/5 mm, picrate m.p. 73°; acetate, b.p. 140°/6 mm., picrate, m.p. 184–6°	527
3-Ethyl-4-ethoxy-2-pyridyl	H	H	b.p. 135–8/4 mm.; picrate, m.p. 53–5°; acetate, b.p. 150–4°/7 mm.	527
3-Ethyl-4-chloro-2-pyridyl	H	H	b.p. 132–4°/6 mm.	527
3-Methoxy-4-hydroxy-2-pyridyl	H	H	m.p. 171–3°	503
3-Methyl-2-pyridyl	Ph	H	m.p. 57–58°; b.p. 134–37°/1; acetate, b.p. 118–24°/12–14 mm.	159,445,456
3-Methyl-2-pyridyl	*p*-methoxyphenyl	H	m.p. 68°	145
4-Methyl-2-pyridyl	Ph	H	m.p. 89–90°	456
4-Methyl-2-pyridyl	*p*-methoxyphenyl	H	m.p. 96°	145

4-Methyl-2-pyridyl	*p*-tolyl	*p*-tolyl	m.p. 107–9°; hydrochloride, m.p. 180–83°	186
5-Methyl-2-pyridyl	*p*-methoxyphenyl	H	m.p. 75°	145
6-Methyl-2-pyridyl	Ph	H	m.p. 86°	456
6-Methyl-2-pyridyl	*p*-methoxyphenyl	H	m.p. 95°	145
6-Methyl-2-pyridyl	1-*nitro*cyclohexyl	H	HCl, m.p. 165–82°	520
6-Methyl-2-pyridyl	6-methyl-2-pyridyl	H	m.p. 90–92°; HCl, 169–71°; picrate, m.p. 136–8°	560
4-Ethyl-2-pyridyl	Ph	H	m.p. 131–33°	186
5-Chloro-2-pyridyl	β-indolyl	H	m.p. 166–7°	645
2-Py	Ph	H	m.p. 107–8°; m.p. 82°; b.p. 133–38°/1 mm. *l*-, m.p. 66°; α^{18}_{6563} −67.8° *d*-, m.p. 66°; α^{18}_{D} + 84.8° metal chelates	33,34,39,43, 143,145,146, 213,432,454, 455,610,623, 628,642
2-Py	*m*-tolyl	H	m.p. 105–6°	432
2-Py	*p*-tolyl	H	b.p. 146–152°/1 mm.	432
2-Py	*p*-*i*-propylphenyl	H	m.p. 102.5–3°; b.p. 166–70°/2 mm.; 142–45°/0.15 mm.; hydrochloride, m.p. 150–53°; dimethylaminoethyl ether, b.p. 159-63°/0.01 mm.; hydrochloride, m.p. 122–23[c]	143,145,146, 432

(*continued*)

TABLE XIII-9. (*Continued*)

Py	R	R′	Physical properties, derivatives	Ref.
2-Py	*o*-chlorophenyl	H	m.p. 63–64°; b.p. 145–48°/0.2 mm.; hydrochloride, m.p. 174–75°; dimethylaminoethyl ether, b.p. 174–76°/0.15 mm.; hydrochloride, m.p. 116–18°	146,432
2-Py	*p*-chlorophenyl	H	m.p. 83°	145,432,628
2-Py	*o*-anisyl	H	b.p. 144–48°/0.3 mm.; m.p. 81–81.5°; hydrochloride, m.p. 170–71°; dimethylaminoethyl ether, b.p. 152–54°/0.2 mm.; hydrochloride, m.p. 133–35°	146,445
2-Py	*p*-anisyl	H	m.p. 133–34°; b.p. 180–85°/1 mm.; hydrobromide, m.p. 132–34°	146,432,500, 554
2-Py	*p*-propoxyphenyl	H	m.p. 65°	136
2-Py	2,3-dimethoxyphenyl	H	m.p. 138–39°; b.p. 152–56°/0.15 mm.; hydrochloride, m.p. 166–68°	146
2-Py	3,4-methylenedioxyphenyl	H	m.p. 142–42.5°; b.p. 178–81°/0.3 mm.; hydrochloride, m.p. 182–84°; dimethylaminoethyl ether, b.p. 182–85°/0.1 mm.; hydrochloride, m.p. 147–49°	146,432

2-Py	3,4-dimethoxy-phenyl	H	m.p. 92–93°	432,446
2-Py	*m*-nitrophenyl	H	m.p. 118°	145
2-Py	1-nitrocyclo-hexyl	H	m.p. 127–28.5°	520
2-Py	β-indolyl	H	m.p. 160–1°	645
2-Py	2-Py	H	m.p. 39–41°	560
2-Py	Ph	Ph	m.p. 104–6°; hydrochloride, m.p. 181–82°; dimethylaminoethyl ether, b.p. 180–88°/0.3 mm.	146,186,512, 647
2-Py	Ph	*o*-tolyl	m.p. 95–96°; hydrochloride, m.p. 190–92°	186
2-Py	Ph	*m*-tolyl	m.p. 90–91°; hydrochloride, m.p. 193–95°	186
2-Py	Ph	*p*-tolyl	m.p. 83–85°; hydrochloride, m.p. 193–95°	186
2-Py	Ph	*p*-ethylphenyl	m.p. 59–61°; hydrochloride, m.p. 156–57°	186
2-Py	Ph	2,5-dimethyl-phenyl	m.p. 93–95°; hydrochloride, m.p. 175–77°	186
2-Py	Ph	mesityl	m.p. 147–48°; hydrochloride, m.p. 192–93°	186
2-Py	Ph	1-naphthyl	m.p. 148–49°; hydrochloride, m.p. 186–88°	186

(*continued*)

TABLE XIII-9. (*Continued*)

Py	R	R′	Physical properties, derivatives	Ref.
2-Py	Ph	*p*-chlorophenyl	m.p. 110–11°; hydrochloride, m.p. 215–16°	186
2-Py	Ph	*o*-chlorophenyl	m.p. 125–27°; hydrochloride, m.p. 208–209°	186
2-Py	Ph	*m*-chlorophenyl	hydrochloride, m.p. 194–96°; b.p. 166–76°/10 mm.	186
2-Py	Ph	*p*-bromophenyl	m.p. 96°; hydrochloride, m.p. 203–204°	186
2-Py	Ph	*p*-fluorophenyl	m.p. 93–95°; hydrochloride, m.p. 187–89°	186
2-Py	Ph	*p*-hydroxyphenyl	hydrochloride, m.p. 165–67°	186
2-Py	Ph	*p*-anisyl	m.p. 120–22°; hydrochloride, m.p. 158–60°	186
2-Py	Ph	*p*-phenetyl	m.p. 110–12°	186
2-Py	Ph	3,4-methylene-dioxyphenyl	m.p. 112–14°; hydrochloride, m.p. 190–92°	186
2-Py	Ph	3,4,5-trimethoxy-phenyl	m.p. 137°	540
2-Py	Ph	2-methoxy-1-naphthyl	m.p. 103–105°; hydrochloride, m.p. 142–44°	186
2-Py	Ph	*p*-trimethylsilyl-phenyl	m.p. 74–76°; hydrochloride, m.p. 171–73°	186
2-Ph	Ph	β-indolyl	m.p. 178–79°	186

2-Py	Ph	2-furyl	m.p. 60–62°; hydrochloride, m.p. 164–66°	186
2-Py	Ph	2-thienyl	m.p. 84–86°; hydrochloride, m.p. 156–58°	186
2-Py	Ph	cyclopropyl	m.p. 82–84°; hydrochloride, m.p. 122–24°	186
2-Py	Ph	cyclopentyl	m.p. 65–67°; hydrochloride, m.p. 110°	186
2-Py	Ph	cyclohexyl	m.p. 71–73°	186
2-Py	Ph	1-cycloheptenyl	b.p. 135–50/0.2 mm.; hydrochloride, m.p. 166–67°	186
2-Py	Ph	1-methyl-3-(2-propyl)-cyclopentyl	m.p. 71–76°	186
2-Py	Ph	4-methylcyclohexyl	m.p. 109–11°	186
2-Py	Ph	bicyclo (2,2,1)-5-hepten-2-yl	m.p. 91–92°	186
2-Py	Ph	2-Py	m.p. 96°; hydrochloride, m.p. 181–82°	186
2-Py	o-tolyl	o-tolyl	m.p. 119–20°; hydrochloride, m.p. 193–94°	186
2-Py	*p*-tolyl	*p*-tolyl	m.p. 119–21°; hydrochloride, m.p. 181–83°	186

(*continued*)

TABLE XIII-9. (*Continued*)

Py	R	R′	Physical properties, derivatives	Ref.
2-Py	*p*-chlorophenyl	*o*-chlorophenyl	m.p. 110–12°; hydrochloride, m.p. 182–92°	186
2-Py	*p*-chlorophenyl	*p*-chlorophenyl	m.p. 88–89°; hydrochloride, m.p. 187–93°	186
2-Py	*p*-bromophenyl	*p*-bromophenyl	m.p. 102–3°	186
2-Py	*p*-anisyl	cyclopropyl	m.p. 95–96°; hydrochloride, m.p. 172–73°	186
2-Py	*p*-anisyl	*p*-anisyl	m.p. 90–91°; hydrochloride, m.p. 154–56°	186,554
2-Py	*p*-phenetyl	*p*-phenetyl	m.p. 93–94°	186
2-Py	*p*-benzyloxyphenyl	*p*-benzyloxyphenyl	m.p. 123–26°; hydrochloride, m.p. 146–47°	186
2-Py	cyclohexyl	cyclohexyl	m.p. 79–81°; hydrochloride, m.p. 237–240°	186
2-Py	CRR′ = 1-Indanylidene		m.p. 79–81°; hydrochloride, m.p. 164–66°	186
2-Py	1-tetralylidene		m.p. 77–78°; hydrochloride, m.p. 186–87°	186
2-Py	9-fluorenylidene		m.p. 130–31°; hydrochloride, m.p. 222–23°	186
2-Py	10-thioxanthylidene		m.p. 186–87°; hydrochloride, m.p. 190–92°	186
2-Py	9-anthrylidene		m.p. 126–28°; hydrochloride, m.p. 240°	186

2-Py	2-Py	2-Py	m.p. 127–28°; dipicrate, m.p. 114–15°	459
2-Py	2-Py	4-Py	m.p. 146.3–146.7°	605
2-Py	4-Py	4-Py	m.p. 209.3–209.7°	605
4-Methyl-2-pyridyl	Ph	Ph	m.p. 112–14°; hydrochloride, m.p. 205–7°	186
6-Methyl-2-pyridyl	Ph	Ph	m.p. 88–91°; hydrochloride, m.p. 171–76°	186

TABLE XIII-10. 3-Pyridinemethanols (1-carbon side-chain) 3-PyC(OH)RR′

Py	R	R′	Physical properties, derivatives	Ref.
3-Py	H	H	b.p. 92–94°/2–3 mm; b.p. 112–14/2 mm.; picrate, m.p. 158–59°, 58–60°; hydrochloride, m.p. 176–80°; chloroplatinate, m.p. 210–11°	10,23,64,161, 195,196,197
			dimethylaminopropyl ether, b.p. 110°/1 mm.; diethylaminopropyl ether, b.p. 116°/1 mm.; morpholinoethyl ether, b.p. 126°/2 mm.; piperidylethyl ether, b.p. 117°/2 mm.; diethylaminoethyl ether, b.p. 109°/1 mm.; dimethylaminoethyl ether, b.p. 105°/1 mm.; *dl*-mandelate, m.p. 69–72°; bis-succinate-picrate, m.p. 190–92°; acid succinate, m.p. 140–42°; bis-phthalate, m.p. 70°; penicillin-G ester, α_D^{20} + 99.5°.	545,546,604
2-Methyl-3-pyridyl	H	H	m.p. 59–60°; hydrochloride, m.p. 118–21°; picrate, m.p. 158–60°	11,61,62,65,66, 67,68,69,70,71
4-Methyl-3-pyridyl	H	H	b.p. 125–7°/2 mm., m.p. 44–6°; HCl, m.p. 191–2°; picrate, m.p. 160.5–2°	517
5-Methyl-3-pyridyl	H	H	b.p. 125°/1.3 mm.	513
6-Methyl-3-pyridyl	H	H	m.p. 46°; HCl, m.p. 119–20°	306,515,526
4,6-Dimethyl-3-pyridyl	H	H	m.p. 38.5–39.5°; nitrate, m.p. 162–63°; hydrochloride, m.p. 225–27°	382,383
5,6-Dimethyl-3-pyridyl	H	H	b.p. 108°/0.5 mm., hydrochloride, m.p. 103–6°	382
2,4,6-Trimethyl-3-pyridyl	H	H	m.p. 87–88.5; hydrochloride, m.p. 168–70°	73
5,6-Dichloro-3-pyridyl	H	H	m.p. 76–78°; benzoyl derivative, m.p. 103–4°	28

3-Py	Ph	H	m.p. 56–58°; b.p. 120–22°/0.25 mm., picrate, m.p. 156.5–57°; hydrochloride, m.p. 156–58°; dimethylaminoethyl ether, b.p. 160–65°/0.02 mm.; hydrobromide, m.p. 79–81°	17,146,173,213, 432,455,457
6-Phenyl-3-pyridyl	Ph	H	m.p. 115–16°; hydrochloride, m.p. 173–74°; picrate, m.p. 175–76°	28
3-Py	Ph	Ph	m.p. 115°; hydrochloride, m.p. 150–55°	173,458,459
3-Py	Ph	biphenyl	m.p. 186–7°	606
3-Py	3-Py	Ph	m.p. 128.5–30°; dipicrate, m.p. 197–98.5°	459
3-Py	3-Py	3-Py	picrate m.p. 202–3°, hydrate, m.p. 81–5°	459,605
3-Py	3-Py	4-Py	picrate, m.p. 249–50°	605
3-Py	4-Py	4-Py	m.p. 185.6–188.6°	605

TABLE XIII-11. 4-Pyridinemethanols (1-carbon side-chain) 4-PyC(OH)RR′

Py	R	R′	Physical properties, derivatives	Ref.
4-Py	H	H	m.p. 57°; b.p. 140–42°/12 mm.; hydrochloride, m.p. 164°, 41°; picrate, m.p. 165–66°, 137–39°; acetate, b.p. 112–17°/5 mm.; ethers.	18,19,22,27,63, 66,68,148,150, 152,453,461, 632,636
3-Hydroxy-4-pyridyl	H	H	HCl, m.p. 198–202°	640
2-Methyl-4-pyridyl	H	H	b.p. 131–40/4 mm.	155
2,3,6-Trimethyl-4-pyridyl	H	H	m.p. 127–28°	73
2-Chloro-4-pyridyl	H	H	m.p. 68–70°; HCl, m.p. 156–7°	530
2,6-Dichloro-4-pyridyl	H	H	m.p. 131–32°; benzoate, m.p. 119–20°	20,21,28,62
2,6-Dibromo-4-pyridyl	H	H	m.p. 111–12°	21
4-PyCHOH(1-nitrocyclohexyl)			m.p. 179°	520
4-Py	Ph	H	m.p. 123–25°; b.p. 140–50°/0.5 mm.; hydrochloride, m.p. 166–67°; *d*-, m.p. 131–32°; α_D^{18} + 52.4°; *l*-, m.p. 131–32°; α_D^{18} – 55.5°; picrate, m.p. 145°; dimethylaminoethyl ether, b.p. 145–48°/0.2 mm.; hydrochloride, m.p. 103–5°.	39,40,42,146, 461,512,623
4-Py	2-Naphthyl	H	m.p. 174–75°; picrate, m.p. 200°	41
2,6-Dimethyl-4-pyridyl	Ph	H	b.p. 140–50°/0.1 mm.; m.p. 97–99°; picrate, m.p. 155–56°; acetate, b.p. 140–44°/1 mm.; *p*-nitrobenzoate, 158–64°	35,157

4-Py	Ph	Ph	m.p. 237–38°	144,177,435,436, 437,461
4-Py	Ph	biphenyl	m.p. 162°; HCl, m.p. 216°	606
4-Py	Ph	*p*-ClC_6H_4-	m.p. 207–8°	620
			-$CH_2CH_2NEt_3^+Cl$, m.p. 136°	615,635
			ethyl iodide quaternary ethers;	
			-$CH_2CH_2NMe_2Et^+I^-$, m.p. 210°	
			-$CH_2CH_2NEt_3^+I^-$, m.p. 166°	
			-$CH_2CH_2NEtPr_2^+I^-$, m.p. 150°	
			-$CH_2CH_2CH_2NEtMe_2^+I^-$, m.p. 164°	
			-$CH_2CH_2NEt(CH_2CH_2)_2O^+I^-$, m.p. 166°	
			-Et, m.p. 194–7°	
			-*iso*-Pr, m.p. 150°	
			-CH_2Ph, m.p. 120°	
4-Py	*p*-ClC_6H_4-		C_6H_4—$CO_2(CH_2)_2NEt_3^+I^-$, m.p. 136°	615
1-Methyl-tetrahydro-4-pyridyl	Ph	Ph	m.p. 176–78°	442
4-Py	4-Py	Ph	m.p. 214.3–14.9°; dipicrate, 217–17.9°	461
4-Py	4-Py	4-Py	m.p. 262–3°	605

TABLE XIII-12. α-(2-Pyridyl) ethanols (2-carbon side-chain) 2-PyC(OH)RCHR′R″

Py	R	R′	R″	Physical properties, derivatives	Ref.
2-Py	H	H	H	b.p. 85–89°/5 mm.; chloroplatinate, m.p. 169–72°; acetate, b.p. 89–93°/3 mm.; hydrochloride, m.p. 196–98; chloroaurate, m.p. 153–55°	148,149,150, 170,453, 508
2-Py	H	H	NO_2	m.p. 68°	136
2-Py	H	Ph	H	dimethylaminoethyl ether, no constants.	499,500,636
2-Py	Ph	H	H	m.p. 40°; b.p. 133–36°/0.5 mm., 152°/745 mm.; *d*-, m.p. 16–18°; α_D^{22} + 38.4; picrate, m.p. 178°; dimethylaminoethyl ether, b.p. 145–53°/0.4 mm.; diethylaminoethyl ether, b.p. 150–56/0.2 mm.; 1-(2-dimethylamino)propyl ether, b.p. 148–51°/.05 mm.; piperidylethyl ether; b.p. 160–66°/0.08 mm.; morpholylethyl ether, b.p. 168–74°/0.1 mm.; pyrrolidylethyl ether; b.p. 156–62°/0.1 mm.	39,67,138, 143,145, 146,432, 439
2-Py	*o*-methylphenyl	H	H	m.p. 86–8°; b.p. 130–32°/0.2 mm.; hydrochloride, m.p. 217–19°	146
2-Py	*m*-methylphenyl	H	H	b.p. 132–35°/0.18 mm.; hydrochloride, m.p. 162–64°; dimethylaminoethyl ether, b.p. 152–56°/0.1 mm.; hydrochloride, m.p. 134–36°	146

2-Py	*p*-methylphenyl	H	H	m.p. 67–68°; b.p. 134–38°/0.3 mm.; hydrochloride, m.p. 166–67°; dimethylaminoethyl ether, b.p. 145–55°/0.2 mm.; hydrochloride, m.p. 178–79°	146
2-Py	3,4-dimethylphenyl	H	H	m.p. 55–57°; b.p. 148–52°/0.3 mm.; hydrochloride, m.p. 185–87°; dimethylaminoethyl ether, b.p. 162–64°/0.08 mm.; hydrochloride, m.p. 152–54°	146
2-Py	2-methyl-5-*i*-propylphenyl	H	H	m.p. 92–95°; b.p. 145–50°/0.5 mm.; hydrochloride, m.p. 168–69°; dimethylaminoethyl ether, b.p. 160–65°/0.15 mm.; hydrochloride, m.p. 184–86°	146
2-Py	*m*-nitrophenyl	H	H	m.p. 130°	145
2-Py	*m*-chlorophenyl	H	H	b.p. 145–48°/0.3 mm.; hydrochloride, m.p. 155–57°; dimethylaminoethyl ether, b.p. 158–62°/0.1 mm.; hydrochloride, m.p. 137–38°	146
2-Py	*p*-chlorophenyl	H	H	b.p. 145–48°/2 mm., 134–38°/0.5 mm.; hydrochloride, m.p. 202–4°; dimethylaminoethyl ether, b.p. 154–56°/0.2 mm.; hydrochloride, m.p. 162–64°	146,432
2-Py	*m*-bromophenyl	H	H	b.p. 165–72°/0.7 mm.; hydrochloride, m.p. 162–65°; dimethylaminoethyl ether, b.p. 180–85°/0.2 mm.; hydrochloride, m.p. 126–28°	146

(*continued*)

TABLE XIII-12. *(Continued)*

Py	R	R′	R″	Physical properties, derivatives	Ref.
2-Py	*m*-methoxyphenyl	H	H	b.p. 145–52°/0.4 mm.; hydrochloride, m.p. 166–68°; dimethylaminoethyl ether, b.p. 167–73°/0.2 mm.; hydrochloride, m.p. 130–32°	146
2-Py	*p*-methoxyphenyl	H	H	m.p. 54–55°; b.p. 165–68°/0.4 mm.; hydrochloride, m.p. 171–72°; dimethylaminoethyl ether, b.p. 173–75°/0.2 mm.; hydrochloride, m.p. 152–53°	146
2-Py	3,4-dimethoxyphenyl	H	H	b.p. 160–65°/0.3 mm.; hydrochloride, m.p. 156–57°; dimethylaminoethyl ether, b.p. 175–80°/0.2 mm.; hydrochloride, m.p. 174–75°	146
2-Py	α-naphthyl	H	H	m.p. 130–31°; b.p. 185–98°/0.4 mm.; hydrochloride, m.p. 194–96°; dimethylaminoethyl ether, b.p. 185–95°/0.3 mm.; hydrochloride, m.p. 229–30°	146
2-Py	β-naphthyl	H	H	b.p. 175–210°/0.4 mm.; hydrochloride, m.p. 177–78°; dimethylaminoethyl ether, b.p. 185–95°/0.2 mm.; hydrochloride, m.p. 161–62°	146
2-Py	2-Py	H	H	b.p. 118–25°/1.0 mm.;hydrochloride, m.p. 200–2°; dimethylaminoethyl ether; trihydrobromide, m.p. 154–56°	146

2-Py	2-thienyl	H	H	b.p. 130–36°/0.5 mm.; hydrochloride, m.p. 155–57°; dimethylaminoethyl ether, b.p. 155–58°/0.05 mm.; hydrochloride, m.p. 119–20°	146
2-Py	Ph	Ph	H	m.p. 104–5°; hydrochloride, m.p. 188–90°	186
4-Methyl-2-pyridyl	Ph	H	H	m.p. 70–71°; b.p. 138–42°/0.1 mm.; hydrochloride, m.p. 185–87°; dimethylaminoethyl ether, b.p. 152–56°/0.1 mm.; hydrochloride, m.p. 162–64°	146
5-Methyl-2-pyridyl	H	H	H	b.p. 107–9°/4 mm.; picrate, m.p. 126–7°	618
6-Methyl-2-pyridyl	H	H	H		507
6-Methyl-2-pyridyl	H	Ph	Ph	m.p. 122–24; hydrochloride, m.p. 220–22°	462
6-Methyl-2-pyridyl	Ph	H	H	b.p. 134–36/0.2 mm.; hydrochloride, m.p. 125–27°; dimethylaminoethyl ether, b.p. 145–50° 0.3 mm.; hydrochloride, m.p. 153–55°	146
5-(or 3-) Bromo-2-pyridyl	Ph	H	H	b.p. 148–52°/0.2 mm.; hydrochloride, m.p. 192–95°	146

TABLE XIII-13. α-(3-Pyridyl)ethanols (2-carbon side-chain) 3-PyC(OH)RCHR′R″

Py	R	R′	R″	Physical properties, derivatives	Ref.
3-Py	H	H	H	b.p. 132°/0.12 mm.	49–53
3-Py	H	H	NO_2	HCl, m.p. 116–17°	520
3-Py	Ph	H	H	m.p. 92–93°; b.p. 144–46°/0.7 mm.; picrate, m.p. 158–59°; hydrochloride, m.p. 163–64°	173,432,433
3-Py	*p*-methylphenyl	H	H	m.p. 108°; hydrochloride, m.p. 160–62°	433
3-Py	1-naphthyl	H	H	m.p. 186–90°	433
2-Methyl-3-pyridyl	H	H	H	b.p. 142–43°/12 mm.	50–53
4-Methyl-3-pyridyl	H	H	H	b.p. 159–61°/13 mm.; m.p. 65.5–67°; picrate, m.p. 133–34°; hydrochloride, m.p. 148–49°; 101–3°	16,46,47
6-Methyl-3-pyridyl	H	H	H		49,507
2,4-Dimethyl-3-pyridyl	H	H	H		49
2,6-Dimethyl-3-pyridyl	H	H	H		49
2,4,6-Trimethyl-3-pyridyl	H	H	H		49
5-Bromo-3-pyridyl	H	H	H	b.p. 134–36°/3 mm.	38
2-6-Dichloro-4-methyl-3-pyridyl	H	H	H	b.p. 182–84°/11 mm.; m.p. 73.5–75°	16
6-Methyl-3-pyridyl	Ph	H	H	m.p. 101–2°, b.p. 197–9°/12 mm.	507

TABLE XIII-14. α-(4-Pyridyl)ethanols (2-carbon side-chain) 4-PyCOHRCHR′R″

Py	R	R′	R″	Physical properties, derivatives	Ref.
4-Py	H	H	H	m.p. 54 °; b.p. 138–40 °/30 mm.; picrate, m.p. 125; picrolonate, m.p. 232 °; chloroplatinate, m.p. 206 °	37
4-Py	H	H	NO_2	m.p. 95 °; hydrochloride, m.p. 142 °	137
4-Py	H	H	Ph	picrate, m.p. 162–3 °	636
4-Py	Ph	H	H	m.p. 146–47 °; b.p. 165–69 °/0.5 mm.; hydrochloride, m.p. 186–89 °; propionate, b.p. 147–51 °/11 mm.; dimethylaminoethyl ether, b.p. 158–60 °/0.3 mm.; dihydrochloride, m.p. 282.5–84.5 °	138,146, 435, 439, 461
4-Py	*p*-MeC_6H_4	H	H	m.p. 165–70 °; b.p. 162–68 °/0.3 mm.; hydrochloride, m.p. 173–75 °	146
4-Py	*p*-ClC_6H_4	H	H	m.p. 140 °; b.p. 165–68 °/1.0 mm.; hydrochloride, m.p. 224–26 °	146
4-Py	*p*-$MeOC_6H_4$	H	H	m.p. 130 °; b.p. 185–88 °/0.4 mm.; hydrochloride, m.p. 198–99 °	146
4-Py	biphenyl	H	H	m.p. 217–18 °	606
4-Py	Ph	H	Ph	m.p. 154 °	607
4-Py	*p*-ClC_6H_4	H	Ph	m.p. 175–6 °	620
4-Py	biphenyl	H	Ph	m.p. 200 °	606

TABLE XIII-15. β-(2-Pyridyl)ethanols (2-carbon side-chain) 2-PyCHRC(OH)R′R″

Py	R	R′	R″	Physical properties, derivatives	Ref.
2-Py	H	H	H	b.p. 118–21°/15 mm., 88–90°/2 mm.; picrate, m.p. 120–21°, 176° (dec.) chloroplatinate, m.p. 164–68°; penicillin-G ester, α_D^{20} + 140°	77–85,131,195
2-Py	H	Ph	H	m.p. 108–110°; dipicrolonate, m.p. 229–30° (dec.); chloroplatinate, m.p. 104°	146,416,420,425, 463,464,465
2-Py	H	*p*-methyl-phenyl	H	m.p. 96°	417,420
2-Py	H	*p*-*i*-Propyl-phenyl	H		421
2-Py	H	o-nitro-phenyl	H	m.p. 139°	171,416,417,420, 421,422
2-Py	H	*m*-nitro-phenyl	H	m.p. 98°	420
2-Py	H	*p*-nitro-phenyl	H	m.p. 165°	171,417
2-Py	H	*p*-methoxy-phenyl	H	m.p. 108°	535
2-Py	H	4-dimethylamino-phenyl	H	m.p. 126°	535
2-Py	H	o-chlorophenyl	H	b.p. 120°/0.5 mm.	535
2-Py	H	*p*-bromophenyl	H	m.p. 129°	535
2-Py	H	3-cyclohexenyl	H	hydrobromide, m.p. 71–74°	462
2-Py	H	2-furyl	H	m.p. 41–43°	423
2-Py	H	2-Py	H	b.p. 190–91°	465

2-Py	H	Ph	Ph	m.p. 152–53°; hydrochloride, m.p. 221–22°	462,467
2-Py	H	Ph	*p*-tolyl	m.p. 117–19°; hydrochloride, m.p. 206–207°	462
2-Py	H	Ph	*p*-phenetyl	m.p. 122–24°; hydrobromide, m.p. 169–70°	462
2-Py	H	Ph	*p*-chlorophenyl	m.p. 111–12°; hydrochloride, m.p. 213–15°; methylbromide, m.p. 202–204	462
2-Py	H	Ph	bicyclo(2.2.1)-5-hepten-2-yl	m.p. 111–13; hydrochloride, m.p. 183–84°	462
2-Py	H	Ph	cycloheptyl	m.p. 78–79°; hydrochloride, m.p. 184–86°	462
2-Py	H	Ph	4-methylcyclohexyl	m.p. 120–21°; hydrochloride, m.p. 165–67°	462
2-Py	H	Ph	cyclohexyl	m.p. 107–109°; hydrochloride, m.p. 179–81°; methylbromide, m.p. 222–23°	462
2-Py	H	Ph	1-methyl-3-*i*-propyl-cyclopentyl	hydrochloride, m.p. 205–207°	462
2-Py	H	Ph	cyclopentyl	m.p. 87–88°; hydrochloride, m.p. 193–94°	462
2-Py	H	*p*-tolyl	*p*-tolyl	m.p. 137–39°; hydrochloride, m.p. 197–98°	462

(*continued*)

TABLE XIII-15. (*Continued*)

Py	R	R′	R″	Physical properties, derivatives	Ref.
2-Py	H	*p*-anisyl	*p*-anisyl	m.p. 111–12°; hydrochloride, m.p. 207–208°; methylbromide, m.p. 205–208°	462
2-Py	H	*p*-anisyl	*m*-bromophenyl	m.p. 106–7°; hydrochloride, m.p. 139–43°; methylbromide, m.p. 209–10°	462
2-Py	H	cyclohexyl	cyclohexyl	m.p. 66–67°; hydrochloride, m.p. 195–97°; methylbromide, m.p. 210–12°	462
2-Py	H	cyclohexyl	hexyl	hydrochloride, m.p. 148–50°	462
		CR′R″			
2-Py	H	1-indanylidene		hydrochloride, m.p. 143–44°	462
2-Py	H	9-fluorenylidene		m.p. 84–86°; hydrochloride, m.p. 167–69°	462
2-Py	H	1-acenaphthenylidene		hydrochloride, m.p. 166–67°	462
2-Py	H	9-xanthylidene		m.p. 108–10°	462
2-Py	H	2-cyclohexylcyclohexylidene		m.p. 92–93°; hydrochloride, m.p. 210–12°	462
2-Py	H	2-*p*-anisylcyclohexylidene		m.p. 85–87°	462
2-Py	H	*d*-bornylidene		m.p. 67–68°; hydrochloride, m.p. 196–99°	462
2-Py	H	*dl*-fenchylidene		m.p. 110–11°	462
2-Py	2-Py	2-Py	H	m.p. 184°; picrate, m.p. 235°	465

3-Methyl-2-pyridyl	H	H	H	b.p. 94–95°/1 mm.; picrate, m.p. 137–38°	131
4-Methyl-2-pyridyl	H	H	H	b.p. 130–32°/16 mm.	95,96,596,624
4-Methyl-2-pyridyl	H	Ph	H	m.p. 92.1–92.3°	602
4-Methyl-2-pyridyl	H	*p*-tolyl	H	m.p. 64°; mercuric chloride, m.p. 197°; chloroplatinate, m.p. 181°	96
4-Methyl-2-pyridyl	H	*p*-nitrophenyl	H	m.p. 168–69°	427
6-Methyl-2-pyridyl	H	H	H	m.p. 55°; b.p. 121–22°/12 mm.; hydrochloride, m.p. 196–98°; chloraurate, m.p. 153–55°	93,170
6-Methyl-2-pyridyl	H	Ph	H	hydrochloride. m.p. 188°	424
6-Methyl-2-pyridyl	H	*m*-nitrophenyl	H	m.p. 96°, hydrochloride, m.p. 205°; picrate, m.p. 139–40°; mercuric chloride, m.p. 199°; chloroplatinate, m.p. 208°	426
4,6-Dimethyl-2-pyridyl	H	H	H	m.p. 51–55°; b.p. 132°/13 mm.	97,597

(*continued*)

TABLE XIII-15. (*Continued*)

Py	R	R′	R″	Physical properties, derivatives	Ref.
4,6-Dimethyl-2-pyridyl	H	Ph	H	b.p. 188–89°/9 mm.	208,602
5-Ethyl-2-pyridyl	H	H	H	b.p. 103/1 mm.; picrate, m.p. 101–2°	90,91,92
5-Ethyl-2-pyridyl	H	Ph	H	m.p. 88°	426
5-Ethyl-2-pyridyl	H	*o*-nitrophenyl	H	m.p. 110°	417
5-Ethyl-2-pyridyl	H	*p*-nitrophenyl	H	m.p. 147°; hydrochloride, m.p. 103°; chloroplatinate, m.p. 141°; picrate, m.p. 126°	417
4-bromo-2-pyridyl	H	H	H	b.p. 95–8°/14 mm.; m.p. 54.5°	595
5-Nitro-3,6-dimethyl-2-pyridyl	H	H	H	m.p. 86°; picrate, m.p. 122.5°	97
5-Nitro-4,6-dimethyl-2-pyridyl	H	H	H	b.p. 150–54°/5 mm.; benzoate, m.p. 86°; picrate, m.p. 133°, 144°	97
6-Phenyl-2-pyridyl	H	*p*-tolyl-phenyl	H	chloroplatinate, m.p. 202°	427
6-Phenyl-2-pyridyl	H	*o*-nitrophenyl	H	chloraurate, m.p. 175° chloroplatinate, m.p. 156°	428

TABLE XIII-16. β-(3-Pyridyl)ethanols (2-carbon side-chain) 3-PyCHRC(OH)R′R″

Ph	R	R′	R″	Physical properties, derivatives	Ref.
3-Py	H	H	H	b.p. 160–61°/20 mm.; phenylurethan, m.p. 104°; picrate, m.p. 118°; penicillin-G ester, α_D^{22} + 144°	1,68,69,195
3-Py	H	H	Ph	b.p. 180–5°/3 mm.; m.p. 120.6–121°	539
				MeI salt, m.p. 170–1°	536
3-Py	H	Ph	Ph	m.p. 143.8–144.4°	539
				hydrochloride, m.p. 256–57°; methylbromide, m.p. 250–51°	462
2-Methyl-3-pyridyl	H	H	H	m.p. 60–61°; b.p. 120–25°/0.5 mm.; picrate, m.p. 125°	1,11,13,14,68
6-Methyl-3-pyridyl	H	H	H	b.p. 103°/2 mm.	501
				acetate, b.p. 95–99°/0.3 mm.	69,501
2,6-Dichloro-4-methyl-3-pyridyl	H	H	H	b.p. 186–87°/10 mm.; m.p. 73–75°; benzoate, m.p. 110°	202

TABLE XIII-17. β-(4-Pyridyl)ethanols (2-carbon side-chain) 4-PyCHRC(OH)R′R″

Py	R	R′	R″	Physical properties, derivatives	Ref.
4-Py	H	H	H	b.p. 151–52°/13 mm.; picrate, m.p. 134–35°; chloroplatinate, m.p. 171° (dec.); penicillin-*G* ester, α_D^{20} + 114°	86,87,468,624, 195
4-Py	Ph	H	H	m.p. 89–90°; chloroplatinate, m.p. 178°	98
4-Py	H	Ph	Ph	m.p. 122–24°; hydrochloride, m.p. 265–66°; methylbromide, m.p. 213–15°	462
2-Methyl-4-pyridyl	H	H	H	mercuric chloride, m.p. 212°; chloroplatinate, m.p. 164°	190,596
3-Ethyl-4-pyridyl	H	H	H	chloroplatinate, m.p. 190–92°	89

TABLE XIII-18. 2-Pyridylpropanols (3-carbon side-chain)

Compound	Physical properties, derivatives	Ref.
2-PyCHOHEt	b.p. 213–16°, 135–36°/15 mm., 94–98°/1 mm.	44,45,150, 432,636
2-PyCH$_2$CHOHMe	b.p. 122–25°/20 mm., 110–11°/ 10 mm.	77,79,99–101,112, 127,465, 612
2-PyCHOHCHNO$_2$Me	HCl, m.p. 136–49°	520
2-PyCH$_2$CH$_2$CH$_2$OH	b.p. 190–95°/20 mm.; phenylurethan, m.p. 155°	1,126,127, 128,643
2-PyCHMeCH$_2$OH	picrate, m.p. 120–22°	82,89
2-PyC(OH)Me$_2$	m.p. 50–51°; b.p. 204–205°; 130/10 mm.	38,138,441
2-PyCHPhCH$_2$CH$_2$OH	b.p. 201°/7 mm.	129,603,644
2-PyCH(*p*-ClC$_6$H$_4$)-CH$_2$CH$_2$OH	b.p. 183–90°/3 mm.; ethyl ether, b.p. 148–51°/1 mm.	603,644
2-PyC(OH)PhEt	m.p. 80–81°; b.p. 134–40°/0.4 mm.; hydrochloride, m.p. 142–45°; picrate, m.p. 105–6°; *d*-, m.p. 68°; α_D^{22} + 65.9°; *l*-, m.p. 68°; α_D^{22} – 66.2°; dimethylaminoethyl ether, b.p. 150–53°/.09 mm.; hydrochloride, m.p. 201–2°	39,146,607, 623
2-PyC(OH)PhC≡CH	m.p. 47°	607,617
2-PyCHOHCHPhMe	m.p. 46–48°; b.p. 121–23°/0.3 mm.; hydrochloride, m.p. 196–98°; dimethylaminoethyl ether, b.p. 146–55°/0.3 mm.; hydrochloride, m.p. 144–46°	146,465
2-PyCHOHCH$_2$CH$_2$Ph	b.p. 148–52°/1 mm.	432
2-PyC(OH)MeCH$_2$Ph	m.p. 68–72°, b.p. 129–34°/0.3 mm.; hydrochloride, m.p. 183–85°; diethylaminoethyl ether, b.p. 146–155°/0.3 mm.; hydrobromide, m.p. 118–20°	146
2-Py-C(OH)Ph(CH$_2$)$_2$Ph	picrate, m.p. 148–9°	607

(*continued*)

TABLE XIII-18. (*Continued*)

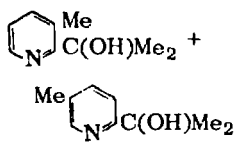
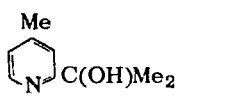
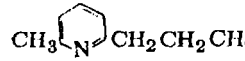
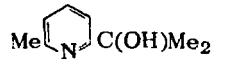
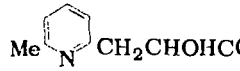
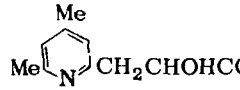
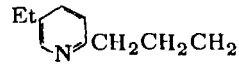
Compound	Physical properties, derivatives	Ref.
2-Py-C(OH)PhC≡CPh	m.p. 110°	607
2-PyC(OH)$(CH_2Ph)_2$	m.p. 118.5–19°; b.p. 230–35°/15 mm.; 165–70°/0.4 mm.; hydrochloride, m.p. 220–23°; chloroplatinate, m.p. 211–12°; dimethylaminoethyl ether, b.p. 175–80°/0.25 mm., dihydrochloride, m.p. 267–68°	136,146,458
2-$PyCH_2CHOHCCl_3$	m.p. 86–87°	230,234,285-288,302,303,332,544
	b.p. 119–23.5°/23 mm. (mixture)	140
	b.p. 119–21°/23 mm.	140
5-Me-2-$PyCH_2(CH_2)$-CH_2OH	b.p. 100–1°/3 mm.; acetate, b.p. 115–16°/3 mm.	618
5-Me-2-$PyCH(CH_3)CH_2OH$	b.p. 110–12°/7 mm.	618
	b.p. 75–76°/3 mm.	552
	b.p. 98–100°/14 mm.	140
6-Me-2-PyCHOHCHNO$_2$Me	HCl, m.p. 176–79°	520
	m.p. 105.5°; hydrochloride, m.p. 134°; chloroplatinate, m.p. 210°; chloroaurate, m.p. 165°	121
	m.p. 139.5°	123,124
	b.p. 98–110°/0.1 mm.; picrolonate, m.p. 158–59°	293,643

TABLE XIII-18. *(Continued)*

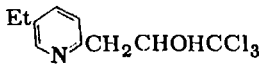
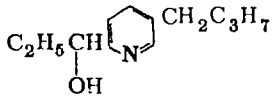
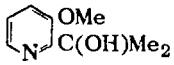
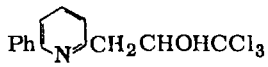
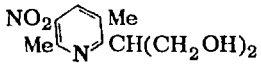
Compound	Physical properties, derivatives	Ref.
	m.p. 86°; hydrobromide, m.p. 188°; hydroiodide, m.p. 174°; chloroplatinate, m.p. 208°; picrate, m.p. 150°	122
	b.p. 99–112°/high vac.	530
	b.p. 105–25°/0.1 mm.	494
	m.p. 65°; chloroplatinate, m.p. 201°	429
	m.p. 96°; dibenzoate, m.p. 139°	97

TABLE XIII-19. 3-Pyridylpropanols (3-carbon side-chain)

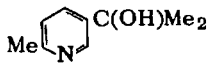
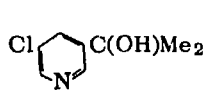
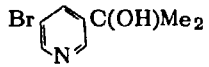
Compound	Physical properties, derivatives	Ref.
3-$PyCH_2CH_2CH_2OH$	b.p. 130–33°/3 mm.; picrate, m.p. 97°	1,643
3-$PyC(OH)Me_2$	m.p. 53°; b.p. 130°/11 mm.; benzoate, m.p. 53°; *p*-nitrobenzoate, m.p. 157°; picrate, m.p. 112–23°	9,18
3-$PyCHOHCHNO_2Me$	HCl, m.p. 152–54°	520
3-PyCHMeCHOHPh	b.p. 164–7°/3 mm; picrate, m.p. 147.2–47.8	539
3-$PyC(OH)MeCH_2Ph$	b.p. 160–65°/2 mm.	432
3-PyC(OH)EtPh	m.p. 104–106°; b.p. 171–72°/0.9 mm.; hydrochloride, m.p. 126–27.5	433,607
3-$PyC(OH)PhCH_2CH_2Ph$	m.p. 118.5–119°; chloroplatinate, m.p. 160–62°	440
3-PyC(OH)PhC≡CH	m.p. 143°	607,617
3-PyC(OH)PhC≡CPh	m.p. 140°	607
3-$PyC(OH)CMe_2Py$-3	m.p. 104–5°	550
3-PyCHMeCHOH(2-thienyl)	b.p. 160–4°/2 mm.; m.p. 98.4–98.8	539
3-$PyCHOHCMe_2Py$-3	m.p. 104–105°	514
	m.p. 61–62°; b.p. 138–40°/15 mm.	176,507
6-Me-3-Py-C≡CCOHME$_2$	m.p. 101–2°	614
	b.p. 115°/3 mm.	38
	b.p. 135–40°/3 mm.; methiodide, m.p. 208–10° (dec.)	38

TABLE XIII-20. 4-Pyridylpropanols (3-carbon side-chain)

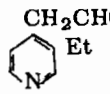
Compound	Physical properties, derivatives	Ref.
4-PyCH(Me)CH_2OH	b.p. 117°/0.35 mm.	37,212
4-PyC(OH)Me_2	m.p. 132°; b.p. 136°/25 mm.; picrate, m.p. 124.4–24.7°; picrolonate, m.p. 236°; chloroplatinate, m.p. 194°	37,461
4-Py(Ph)COHEt	m.p. 153–55°, 161°	39,607, 623
4-PyCHOH—CH_2CH_3	b.p. 125–6°/6 mm.; picrate, m.p. 113–15°	636
4-Py$CH_2CH_2CH_2OH$		643
4-Py$CPh_2CH_2CH_2OH$		
4-PyC(OH)Et(4-ClC_6H_4)	m.p. 169–72°	620
4-PyCHEtCHOH(biphenyl)	m.p. 180–2°	606
4-Py$CH_2CHOHCHCl_2$	m.p. 134–36°	470
4-Py$CH_2CHOHCCl_3$	m.p. 166°; chloraurate, m.p. 189° (dec.); chloroplatinate, m.p. 250° (dec.)	46,113–119, 121
4-PyCHOHCHEtNO_2	m.p. 149–51°	520
4-PyCHOHCHNO_2Me	m.p. 165–66°; HCl, m.p. 158–59°	520
4-PyC(OH)PhC≡CH	m.p. 165°	607,617
4-PyC(OH)PhC≡CPh	m.p. 206°	607
	m.p. 139°; hydrochloride, m.p. 105°; chloraurate, m.p. 173°	125,502

TABLE XIII-21. Pyridylbutanols (4-carbon side-chain)

Compound	Physical properties, derivatives	Ref.
2-PyC(OH)MeEt	b.p. 216–20°, 90.5–93.5°/10 mm.; chloroplatinate, m.p. 190°	138,430
2-PyCHOHPr	b.p. 212–24°	45
2-PyCHOHCHMe$_2$	b.p. 116–17°/15 mm.	136
2-PyCH$_2$CHOHEt	b.p. 125–27°/18 mm.	102,103, 612
2-PyCH$_2$CH$_2$CHOHMe	m.p. 83°	32
2-PyCH$_2$COHMe$_2$	b.p. 64–66°/0.3 mm.	465
2-PyC(OH)PhCHMe$_2$	m.p. 66–68°; b.p. 138–42°/0.15 mm.; hydrochloride, m.p. 156–58°; dimethylaminoethyl ether, b.p. 158–62°/0.1 mm.; hydrochloride, m.p. 161–63°	146
2-PyCH$_2$CHOHCH : CHPh	m.p. 82–83°	174,535
2-PyCH$_2$CHOHCH$_2$CH$_2$Ph	picrate, m.p. 107–109°	174
2-PyCH$_2$CH$_2$CH$_2$CHOHPy-2		69
2-PyCHOHCHNO$_2$Et	HCl, m.p. 137–45°	520
(2-PyCH$_2$)C(OH)Me	b.p. 175–78°/2.5 mm., 154–56°/1.9 mm.; picrate, m.p. 216–18°	126,173, 451,465, 466,471, 472,473, 474
2-PyCH$_2$CHOHCH : CH$_2$	b.p. 75°/.02 mm.	535
3-PyCHOHCHNO$_2$Et	HCl, m.p. 146–52°	
3-PyC(OH)MeCH : CPh(1-C$_{10}$H$_7$)	m.p. 159–61°	434
(3-Py)$_2$CMeCHOHMe	m.p. 165–6°; b.p. 140/0.1 mm.	514,550
(4-PyCH$_2$)$_2$C(OH)Me	b.p. 130–40°/1 mm.; dipicrate, m.p. 214°	471
4-PyC(OH)MeEt	m.p. 99.5–100.5°; b.p. 104–5°/3 mm.	177
4-PyCH$_2$CHOHCH : CHPh	m.p. 115–16°; picrate, m.p. 155–56° (dec.)	174
4-PyCH$_2$CHOHCH$_2$CH$_2$Ph	m.p. 109–10°	174
4-PyCHOHCH$_2$CH : CH$_2$	b.p. 122–3/3 mm.; picrate, m.p. 114–16°	636

TABLE XIII-21. (*Continued*)

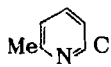
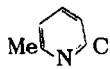
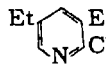
Compound	Physical properties, derivatives	Ref.
4-PyCOHPr(biphenyl)	m.p. 204–5°	606
4-PyCH(CH_3)CH_2CH_2OH		643
4-PyC$Ph_2CH_2CHOHMe$		644
 $CH_2CHOHCH:CHPh$	b.p. 120–40°/0.03 mm., picrate, m.p. 162°	174
 $CH_2CHOHCH_2CH_2Ph$	picrate, m.p. 117–18°	174
	b.p. 180–85°/26 mm.	2
6-Me-3-Py-C≡CCOHMe_2	m.p. 101–2°	614

TABLE XIII-22. Higher Pyridine Alcohols (side-chain with more than 4 carbons including non-aromatic and partly aromatic rings)

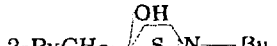
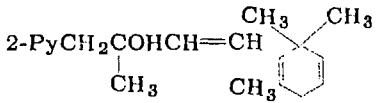
Compound	Physical properties, derivatives	Ref.
2-$PyCH_2CHOHCH:CHMe$	b.p. 140–45°/11 mm.; picrate, m.p. 119–20°	450,535
2-$PyC(OH)Et_2$	b.p. 110–14°/15 mm.; mercuric chloride, m.p. 152–54°; picrate, m.p. 103.5°	440,607
2-PyC(OH)MePr	b.p. 102–3°/10 mm.; hydrobromide, m.p. 168°; hydrochloride, m.p .180–81°; benzoate, b.p. 174–75°/10 mm.	431
2-$PyCH_2COHMeEt$	b.p. 73–75°/0.3 mm., 123–25°/20 mm.	465
2-$PyCH_2CH_2CH_2CHOHMe$	b.p. 83°/0.1 mm.	32
2-$PyC(OH)Pr_2$	b.p. 136–39°/20 mm.	136
2-$PyCH_2CHOHCH:CHCH:CHMe$	b.p. 115–22°/0.01 mm.	450
2-$PyC(OH)(CHMe_2)_2$	b.p. 85–88°/0.2 mm.; hydrochloride, m.p. 300°; dimethylaminoethyl ether, b.p. 95–103°/0.3 mm.; hydrochloride, m.p. 187–88°	146
2-$PyC(OH)Me(CH_2)_5Me$	b.p. 120–24°/0.2 mm.	146
2-$PyCH_2CH(2\text{-}Py)CH_2OH$		72
$(2\text{-}PyCHMe)_2CHOH$	b.p. 162–64°/2.3 mm.	477
2-$PyCH_2CH_2CH_2C(OH)MePh$	m.p. 74–75°; picrate, m.p. 120–21°	32
$(2\text{-}PyCHMe)_2C(OH)Me$	b.p. 144–50°/1 mm.; dipicrate, m.p. 177.3–78°	477
$(2\text{-}PyCH_2)_2C(OH)Et$	b.p. 162.5–164°/1.7 mm.; dipicrate, m.p. 196–98°	466,471
$(2\text{-}PyCH_2)_2C(OH)Pr$	b.p. 160–70°/0.5–1 mm.; dipicrate, m.p. 196–98°	471
$(2\text{-}PyCH_2)_2C(OH)CHMe_2$	b.p. 168–72°/22 mm.	466

$(2\text{-PyCHMe})_2C(OH)Et$	b.p. 124–40°/1.3 mm.; dipicrate, m.p. 169–69.6°	477
$(2\text{-PyCH}_2)_2C(OH)CH_2CHMe_2$	b.p. 168–71°/2 mm.	466
$2\text{-PyCHOHCHCH}_3CH_2CH_3$	b.p. 84–8°/2 mm; HCl, m.p. 121–3°	636
$2\text{-PyCH}_2COHEt(CH_2)_7CH_3$	hydrochloride, m.p. 90–93°	462
$2\text{-PyCH}_2COH(C_7H_{15})_2$	hydrochloride, m.p. 95–97°	462
$2\text{-PyCH}_2COH(C_6H_{13})_2$	hydrochloride, m.p. 95–96°	462
$2\text{-PyCH}_2COH(CH_2CH(CH_3)_2)_2$	hydrochloride, m.p. 156–97°	462
$2\text{-PyCH}_2COH(C(CH_3)_3)_2$	m.p. 63–65°; hydrochloride, m.p. 214–16°	462
$2\text{-PyCOH}(CHCH_3C_2H_5)_2$	m.p. 78–80°; hydrochloride, m.p. 144–45°	186
$2\text{-PyCH}_2CHOH(CH_2)_2CH_3$	b.p. 103–5°/.5 mm.	535,612
$2\text{-PyCH}_2CHOH(CH_2)_3CH_3$	b.p. 67°/.007 mm.	535,612
$2\text{-PyCH}_2CHOH(CH_2)_4CH_3$	b.p. 73°/.0025 mm.	535,612
$2\text{-PyCH}_2CHOH(CH_2)_5CH_3$	b.p. 76–77°/.002 mm.	535
$2\text{-PyCH}_2CHOH(CH_2)_6CH_3$	b.p. 105°/.008 mm.	535
$2\text{-PyCH}_2CHOH(CH_2)_7CH_3$	b.p. 113°/.05 mm.	535
$2\text{-PyCH}_2CHOH(CH_2)_8CH_3$	b.p. 103°/.002 mm.	535
$2\text{-PyCH}_2CHOH(CH_2)_{10}CH_3$	b.p. 110°/.001 mm.	535
$2\text{-PyCH}_2CHOHCH(CH_3)_2$	b.p. 89–92°/.08 mm.	535
$2\text{-PyCH}_2CHOHCH(CH_3)(CH_2)_8CH_3$	b.p. 142–44°/.08 mm.	535
$2\text{-PyCH}_2COHPhCH(CH_3)_2$	hydrochloride, m.p. 209–11°	462
$2\text{-PyCH}_2COHPh(CH_2)_4CH_3$	m.p. 75–77°; hydrochloride, m.p. 122–24°	462
$2\text{-PyCH}_2COHPh(CH_2)_5CH_3$	m.p. 74–75°; hydrochloride, m.p. 149–50°	462
$2\text{-PyCH}_2COHPhC_8H_{17}$	m.p. 57–59°; hydrochloride, m.p. 142–44°	462
$2\text{-PyCH}_2COHPhC_{11}H_{23}$	m.p. 66–68°; hydrochloride, m.p. 142–44°	462
$2\text{-Py(CH}_2)_5C{\equiv}CC(OH)Me_2$	b.p. 149°/.7 mm.	616

(*continued*)

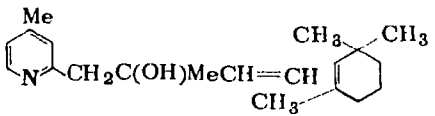
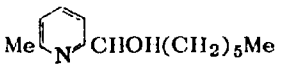
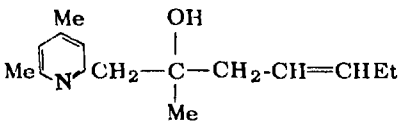
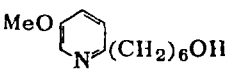
TABLE XIII-22. (*Continued*)

Compounds	Physical properties, derivatives	Ref.
1-(2-Pyridyl)cyclopentanol	m.p. 84°; b.p. 137–38°/13 mm.	140,443,444
1-(2-Pyridyl)cyclohexanol	m.p. 43°; b.p. 157°/34 mm.; hydrochloride, m.p. 157–59°; picrate, m.p. 86–87°	140,146,443,446
1-(2-Picolyl)cyclohexanol	m.p. 48°; b.p. 105–10°/.01 mm.; picrolonate, m.p. 190° (dec.)	130,535
1-(2-Picolyl)cyclopentanol	picrolonate, m.p. 182–84° (dec.); b.p. 108°/.5 mm.	130,535
2-(2-Picolyl)cyclohexanol	b.p. 125°/0.3 mm.; picrolonate, m.p. 172–74°	130
1-Cyclopropyl-1-(2-pyridyl)ethanol	b.p. 83–87°/0.2 mm.; hydrochloride, m.p. 172–74°; dimethylaminoethyl ether, b.p. 95–102°/0.28 mm.; hydrochloride, m.p. 95–97°	146
1-Cyclohexyl-1-(2-pyridyl)ethanol	b.p. 118–22°/0.1 mm.; hydrochloride, m.p. 230°; dimethylaminoethyl ether, b.p. 128–32°/0.2 mm.; hydrochloride, m.p. 164–65°	146
1-(1-Cyclohexenyl)-1-(2-pyridyl)ethanol	b.p. 83–87°/0.2 mm.; dimethylaminoethyl ether, b.p. 132–34°/0.2 mm.; hydrochloride, m.p. 136–38°	146
2-Cyclohexylidene-1-(2-pyridyl)-cyclohexanol	m.p. 59–61°; b.p. 154–59°/0.2 mm.; hydrochloride, m.p. 166–69°	146
1-(2-Pyridyl)indanol	b.p. 140–44°/0.3 mm.; hydrochloride, m.p. 154–56°; dimethylaminoethyl ether, b.p. 162–64°/0.3 mm.; hydrochloride, m.p. 137–39°	146
1-(2-Pyridyl)-1-tetralol	b.p. 160–65°/1 mm.; hydrobromide, m.p. 171–72°	146

	b.p. 148–50°/0.9 mm.	476
	m.p. 41–46°	450,479
1-(2-Pyridyl)borneol	b.p. 130–32°/1 mm.; hydrochloride, m.p. 209–10°; dimethylaminoethyl ether, b.p. 134–38°/0.2 mm. hydrochloride, m.p. 146–48°	146,443
1-(2-Pyridyl)fenchyl alcohol	m.p. 54–60°; b.p. 105–10°/0.2 mm.; hydrochloride, m.p. 200–2°; dimethylaminoethyl ether, b.p. 135–38°/0.2 mm.; hydrochloride, m.p. 197–98°; diethylaminoethyl ether, b.p. 150–56°/0.2 mm.; hydrochloride, m.p. 192–94°	146
2-$PyCH_2C(OH)MePr$	b.p. 60°/.03 mm.	535
2-$PyCH_2C(OH)MeBu$	b.p. 72–73°/.008 mm.	535
2-$PyCH_2C(OH)Me(CH_2)_4CH_3$	b.p. 71°/.01 mm.	535
2-$PyCH_2C(OH)Me(CH_2)_8CH_3$	b.p. 85°/.015 mm.	535
2-$PyCH_2C(OH)(Et)_2$	b.p. 53–54°/.1 mm.	535
2-$PyCH_2C(OH)EtPr$	b.p. 70°/.8 mm.	535
2-$PyCH_2C(OH)PrBu$	b.p. 73/.007 mm.	535
2-$PyCH_2C(OH)(CH_2CH_2CH_2CH_2CH_3)_2$	b.p. 78°/.5 mm.	535
2-$PyCH_2C(OH)MeC(CH_3)_3$	b.p. 65–66°/.0035 mm.	535
2-$PyCH_2C(OH)MeCH{=}C(CH_3)_2$	b.p. 64°/.0025 mm.	535
2-$PyCH_2C(OH)MeCH{=}CH(CH_2)_2CH_3$	b.p. 83–6°/.8 mm.	535
2-$Py(CH_2)_4C(OH)MeC{\equiv}CH$	b.p. 145–157°/.6 mm.	607,608
2-$Py(CH_2)_4C(OH)MeC{\equiv}CPh$	b.p. 200–8°/.6 mm.	607,608
2-$Py(CH_2)_3C(OH)MeC{\equiv}CPh$	b.p. 208–18°/.6 mm.	608

(*continued*)

TABLE XIII-22. (*Continued*)

Compounds	Physical properties, derivatives	Ref.
2-PyC(OH)EtC≡CH	b.p. 113–25°/12 mm.	608
1-(3-Methyl-2-pyridyl)cyclopentanol		140
1-(4-Methyl-2-pyridyl)cyclopentanol	m.p. 81–82°; b.p. 120°/4 mm.	140
	b.p. 136–43/0.033 mm.; m.p. 44–51°	450
	b.p. 122–24°/2 mm.; picrate, m.p. 102–3°	168
1-(5-Methyl-2-pyridyl)cyclopentanol		140
1-(6-Methyl-2-pyridyl)cyclopentanol	b.p. 154°/31 mm.	140
	b.p. 98–104°/0.003 mm.	480
3(3,5-Diethyl-2-pyridyl)heptanol-4	b.p. 164–70°/26 mm.	2
	acetate, b.p. 162°/1 mm.	238
3-PyC(OH)Et$_2$	b.p. 152–55°/24 mm., 156–57.5°/16 mm.; picrate, m.p. 112–13°	441,458
3-PyCHOH(CH$_2$)$_5$Me		475
3-PyCH$_2$CHOHCH(CH$_3$)$_2$	b.p. 122–5°/2 mm.	539
3-PyCH$_2$CHOHMeC$_2$H$_5$	b.p. 111–12°/2 mm.	539
3-PyCH$_2$CHOHMeC$_3$H$_7$	b.p. 128–30°/3 mm.	539

3-$PyCH_2CHOHEt_2$	b.p. 118–20°/2 mm.	539
3-$PyCH_2CHOHPhC_2H_5$	b.p. 165–8°/3 mm.	539
3-$PyCH_2CHOH(C_3H_7)_2$	b.p. 133–6°/2 mm.	539
1-(3-Pyridyl)cyclohexanol	m.p. 89–90°; picrate, m.p. 166–67°	458
(6-Me-3-Py)C≡CCOHEtMe	m.p. 98–9°	614
(6-Me-3-Py)C≡CC(OH)PrMe	m.p. 30–2°	614
(6-Me-3-Py)C≡$CC(OH)MeCMe_3$	m.p. 100–1°	614
(6-Me-3-Py)C≡$CC(OH)(CH_2)_5$	m.p. 116–118°	614
(6-Me-3-Py)C≡CC(OH)MePh	m.p. 104–5°	614
(6-Me-3-Py)C≡CCHOHEt	picrate, m.p. 120–3°	614
(6-Me-3-Py)C≡CCHOHPr	phenylurethane, m.p. 103–4°	614
(6-Me-3-Py)C≡CCHOHBu	picrate, m.p. 112–14°	614
4-$PyCHOHCHCH_3C_2H_5$	b.p. 124–7°/5 mm.; HCl, m.p. 142–4°	636
4-$PyCH_2CH_2CHEtCH_2CH_2CH_2OH$		643
4-$Py(CH_2)_4C(OH)MeC{\equiv}CH$	m.p. 89°	607
4-$Py(CH_2)_4C(OH)MeC{\equiv}CPh$	m.p. 78°	607
4-$Py(CH_2)_4C{\equiv}CC(OH)Me_2$	b.p. 166°/1.8 mm.	616
4-$Py(CH_2)_4C{\equiv}CC(OH)MeEt$	b.p. 163–4°/.7 mm.	616
4-$Py(CH_2)_5C{\equiv}CC(OH)Me_2$	b.p. 167°/1.5 mm.; m.p. 54°	616

TABLE XIII-23. Methyl and Ethyl Ethers of Pyridine Alcohols

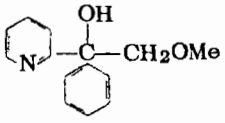
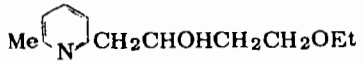
Compound	Physical properties, derivatives	Ref.
2-$PyCH_2OMe$	b.p. 76–8°/18 mm.	538,636
2-$PyCH_2OEt$	b.p. 63–4°/5 mm.	636
2-$PyCH_2OCHCH_3C_2H_5$	b.p. 73–5°/5 mm.	636
2-$PyCH_2OPh$	b.p. 140–3/5 mm.	636
2-$PyCH_2OCH_2Ph$	b.p. 150–60/7 mm.	636
2-$PyCH_2CH_2OEt$	b.p. 106–7°/19 mm.; hydrochloride, m.p. 83.5–84.5°; picrate, m.p. 105–6°	147
2-$PyCH_2CH_2CH_2OEt$	b.p. 230°; picrate, m.p. 180–81°	132
2-$Py(CH_2)_4OMe$	b.p. 122–25°/18 mm.; picrate m.p. 83–84°; chloroaurate, m.p. 77–78°	128
2-$Py(CH_2)_6OMe$	b.p. 120–28°/5 mm.	128
2-$Py(CH_2)_7OMe$	b.p. 122–23°/2 mm.	128
2-$Py(CH_2)_{11}OEt$	b.p. 143–49/0.2 mm.	133
2-$PyC(OH)Me(CH_2)_3OEt$	b.p. 116–20°/10 mm.	191
3-$PyCH_2OMe$	b.p. 92–4°/20 mm.; picrate, m.p. 117–18°	538
3-$PyCH_2OEt$	b.p. 77–8°/5 mm.	636
4-$PyCH_2OEt$	b.p. 78–80°/5 mm.	636
4-$PyCH_2OCHCH_3C_2H_5$	b.p. 81–3°/5 mm.	636
4-$PyCH_2OPh$	b.p. 145–50°/3 mm.	636
4-$PyCH_2OCH_2Ph$	b.p. 153–8°/6 mm.	636
4-$PyCH_2OMe$	b.p. 91–2°/19 mm.; picrate, m.p. 108–9°	538,636
4-$Py(CH_2)_3OMe$	b.p. 121–30°/17 mm.; picrate, m.p. 89–90°	128
4-$Py(CH_2)_3OEt$	b.p. 242°; picrate, m.p. 61–62°	132
	b.p. 155–58°/0.5 mm.	146
	b.p. 135–37°/3 mm., n_D^{20} 1.5009	201

TABLE XIII-23. (*Continued*)

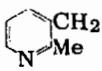
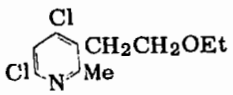
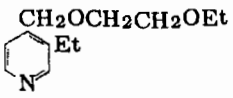
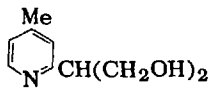
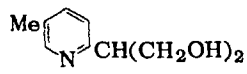
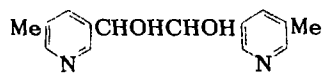
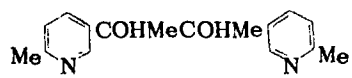
Compound	Physical properties, derivatives	Ref.
	b.p. 72–73°/0.5 mm.	11,13,482
	b.p. 98–99°/0.4 mm.	11,13,481, 482
	b.p. 265°; picrate, m.p. 75°	132

TABLE XIII-24. Pyridine Glycols

Compound	Physical properties, derivatives	Ref.
2-PyCH(CH_2OH)$_2$	m.p. 78°; picrate, m.p. 108–10°	80,81,83,646
2-PyCHOHCH$_2$OH	m.p. 98°	218,558
2-PyCH$_2$CH$_2$CH(CH_2OH)$_2$	m.p. 58–59°; b.p. 163–65°/.01 mm.	85
2-PyC(Me)(CH_2OH)$_2$	b.p. 168–71°; picrate, m.p. 116–17°	82
2-PyCH$_2$CHOHCH$_2$CH$_2$OEt	b.p. 130°/5.5 mm.	215
2-PyCH$_2$CH$_2$CHOHCH$_2$OH	m.p. 52.5°; b.p. 154°/0.1 mm.; mercuric chloride, m.p. 115°; acetone ketal, b.p. 103°/0.1 mm.	216
2-PyC(OH)MeCH$_2$CH$_2$CH$_2$OEt	b.p. 116–20°/10 mm.	82,98,191
2-Py(CH_2)$_9$CHOHCHOHMe	m.p. 87–87.5°	219
2-Py(CH_2)$_{10}$CHOHCH$_2$OH	m.p. 71.5–72°	219
2-PyCPh(CH_2OH)$_2$	m.p. 106–7°	98
2-PyCHOHCHOHPh	m.p. 144–45°; hydrochloride, m.p. 186–87°; diacetate, m.p. 36–37°	220,529,558
2-PyCH(CH_2OH)CH$_2$CH$_2$OH		646
2PyC(CH_3)OHCHOHPh	HCl, m.p. 119–21°	558
2-PyCHOHCHOHCH$_3$	m.p. 101–3°	529
2-PyCHOHCHOHCCl$_3$	m.p. 120°	558,637
2-PyCCH$_3$OHCHOH-(2-quinolyl)	m.p. 209–10°	558
2-PyCCH$_3$OHCHOH-(4-quinolyl)	m.p. 186–7°	558
2-PyCHOHCHOHPy-2	m.p. 153.5–54°	223,224,225, 558,637
2-PyC(OH)EtC(OH)EtPy-2	m.p. 135–36°	44
2-Py-C(OH)PrC(OH)PrPy-2	m.p. 146°	45
2-PyCPh(OH)CPh(OH)Py-2	m.p. 129–30°	40
3-PyCH(CH_2CH_2OH)$_2$		646
p-$CH_3OC_6H_4C(CH_3)OHC(CH_3)$-OH-3Py	b.p. 162°/.001 mm. m.p. 78–80°	555

TABLE XIII-24. (*Continued*)

Compound	Physical properties, derivatives	Ref.
p-$ClC_6H_4C(CH_3)OHC(CH_3)$-OH-3Py	b.p. 160°/.001 mm. m.p. 88–90°	555
$C_6H_5C(CH_3)OHC(CH_3)OH$-3Py	b.p. 130–5°/.001 mm. m.p. 118–120°	555
3-PyCHOHCHOHPy-3	m.p. 245°	223
3-PyCPh(OH)CPh(OH)Py-3	m.p. 187–88°	40
3-PyCMe(OH)CMe(OH)Py-3	m.p. 244–45°	222,514
3-PyCEt(OH)CEt(OH)Py-3	m.p. 188–9°	514,557
4-$PyCH(CH_2CH_2OH)_2$	m.p. 64–66°	132,204,646
4-$PyCH(CH_2OH)_2$		86
4-$PyCMe(CH_2OH)_2$	m.p. 93–95°	211,212
4-$PyCPh(CH_2OH)_2$	m.p. 194°; chloroplatinate, m.p. 185°	98
4-$PyC(CH_3)OHCHOHPh$	m.p. 149.5–51°	558
4-$PyCHOHCHOHCCl_3$	m.p. 189–90.5° HCl,206–7°	558
4-$PyCHOHCOH(CH_3)$-2-Py	m.p. 93–5°	558
4-$PyC(CH_3)OHCHOH$-3-Py	m.p. 188.5	558
4-PyCHOHCHOHPy-4	m.p. 178° and 214° (two forms)	223,226,611, 648,649
4-PyCMeOHCMeOHPy-4	m.p. 219–220°	514
	b.p. 111–13°/.04 mm. m.p. 84–5°	624
	b.p. 155–9°/4 mm.	618
	m.p. 235°	513
	m.p. 139–40°	224
	m.p. 218–19°	557

(*continued*)

TABLE XIII-24. (*Continued*)

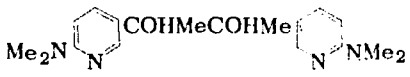
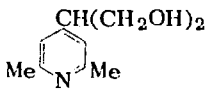
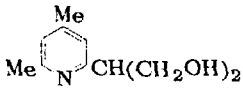
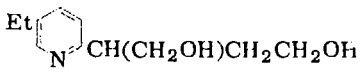
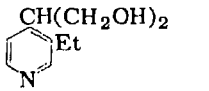
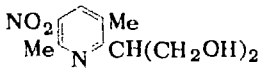
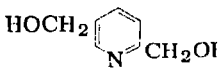
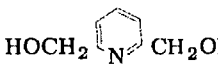
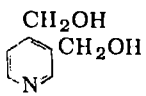
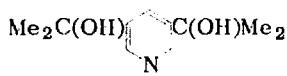
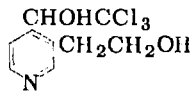
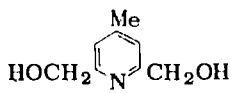
Compound	Physical properties, derivatives	Ref.
	m.p. 247-8°	557
	m.p. 155-6°	597,627
	m.p. 95-95.5; b.p. 120-2°/.05 mm.	597
		646
	ditosyl ester, m.p. 95-96° and 107-8° (two forms)	181,210
	m.p. 86°; picrate, m.p. 122.5°	97
	m.p. 157°	515
	m.p. 114.5-15°; b.p. 185-86°/15 mm.; acetate, b.p. 135-39°/0.3 mm.	25,150,170, 205,213, 214
	m.p. 129.5-30.5°; picrate, m.p. 144-45°	65
	m.p. 146°	9
	m.p. 166.5-68°	16
	m.p. 70-71°	597

TABLE XIII-24. (*Continued*)

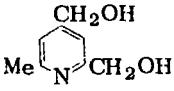
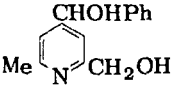
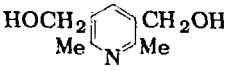
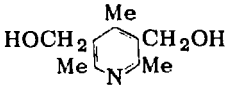
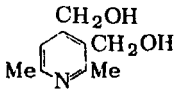
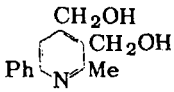
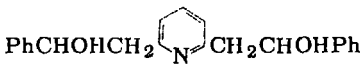
Compound	Physical properties, derivatives	Ref.
	b.p. 121–2/.02 mm.	597
	m.p. 140°	157
	m.p. 141–42°	68
	m.p. 186°	206
	m.p. 182–83°	290,562
	m.p. 95°	207
	m.p. 219°	33

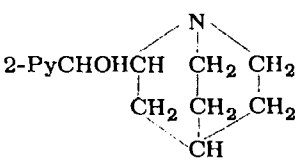
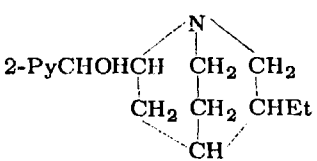
TABLE XIII-25. Pyridine Amino Carbinols

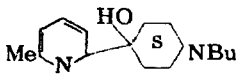
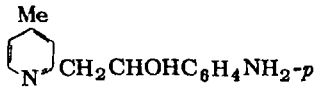
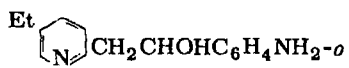
Compound	Physical properties, derivatives	Ref.
2-PyCHOHCH$_2$NH$_2$	b.p. 100°/2 mm.; dihydrochloride, m.p. 189°; picrate, m.p. 179–80°	54,137,520
2-PyCHOHCH(CH$_3$)NH$_2$	m.p. 191°	520
2-PyCHOHCH(Et)NH$_2$	b.p. 92°/0.1 mm.	520
2-PyCHNH$_2$CHOHPh	m.p. 122°	58
2-PyCHNH$_2$CHOHPy-2	dibenzoate, m.p. 181°	58
2-PyCHNH(*i*-oPr)CHOHPy-2	m.p. 89°	58
2-PyCPh(OH)(CH$_2$)$_7$N(CH$_2$)$_4$	m.p. 74–75°	486
2-PyCPh(OH)C$_6$H$_4$NH$_2$-*p*	m.p. 73–75°	186
2-PyCPh(OH)C$_6$H$_4$NMe$_2$-*p*	m.p. 152–53°	186
2-Py(*o*-NH$_2$C$_6$H$_4$)COHMe	m.p. 95–6°	438,439
2-PyCHOHC$_6$H$_4$NMe$_2$-*p*	b.p. 146–52°/0.5 mm.	432
2-Py(2-NH$_2$-5-ClC$_6$H$_3$)COHMe	m.p. 115–16°	439
2-PyCOH(C$_6$H$_4$NMe$_2$-*p*)$_2$	m.p. 148–51°; hydrochloride, m.p. 248–50°	186
2-Py(*o*-NH$_2$C$_6$H$_4$)COHEt	m.p. 83–84°	439
2-Py(*o*-NH$_2$C$_6$H$_4$)COHCH$_2$Ph$_5$	m.p. 131.5°–32°	439
3-Py(*o*-NH$_2$C$_6$H$_4$)COHMe	m.p. 147–48°	439
3-Py(*o*-NH$_2$C$_6$H$_4$)COHEt	m.p. 185–86°	439
4-Py(*o*-NH$_2$C$_6$H$_4$)COHMe	m.p. 199–200°	439
4-Py(*o*-NH$_2$C$_6$H$_4$)COHEt	m.p. 181–82°	439
2-PyCH$_2$CHOH(C$_6$H$_4$NH$_2$-*o*)	m.p. 97–98°	416
2-PyCH$_2$CHOH(C$_6$H$_4$NH$_2$-*p*)	m.p. 135°	171
2-PyCH$_2$COH(*o*-NH$_2$C$_6$H$_4$)(*p*-MeOC$_6$H$_4$)	m.p. 152–53.5°; acetate, m.p. 169–70°	438,439

2-$PyCH_2COH(o\text{-}NH_2C_6H_4)$ (Ph)	m.p. 164–65°; acetate, m.p. 180–81°	438,439,466
2-$PyCH_2COH(p\text{-}MeC_6H_4)$ $(o\text{-}NH_2C_6H_4)$	m.p. 115–16°	438,439
2-$PyCH_2COH(2\text{-}NH_2\text{-}5\text{-}ClC_6H_3)$ (Ph)	m.p. 143–44°	439
2-$PyCH_2C(OH)Me(o\text{-}NH_2C_6H_4)$	m.p. 84–85°	439
2-$PyCH_2COH(C_6H_4NMe_2\text{-}p)_2$	m.p. 190–92°; trihydrochloride, m.p. 160–63°	462
2-$Py(Ph)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 93–94°	483,484
2-$Py(p\text{-}Me_3C_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 119–20°	485
2-$Py(p\text{-}EtC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 112–14°	485
2-$PyCHNH(C_6H_{11})CHOHPy$-2	m.p. 129°	58
2-$Py(p\text{-}i\text{-}PrC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 83–84°	485
2-$Py(t\text{-}BuC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 120–21°	485
2-$Py(m\text{-}MeC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 54–55°	485
2-$Py(3,4\text{-}Me_2C_6H_3)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 104–5°	485
2-$Py(o\text{-}MeC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 106–7°	485
2-$Py(2,4\text{-}Me_2C_6H_3)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 111–12°	485
2-$Py(2,5\text{-}Me_2C_6H_3)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 107–8°	485
2-$Py(p\text{-}ClC_6H_4)C(OH)CH_2CH_2N(CH_2)_4$	m.p. 130–31°	483,484
2-$Py(Ph)C(OH)CH_2CH_2CH_2N(CH_2)_5$	m.p. 84–85°	483
2-$Py(p\text{-}ClC_6H_4)C(OH)CH_2CH_2CH_2N(CH_2)_5$	m.p. 97–98°	483,484
2-$Py(p\text{-}MeC_6H_4)C(OH)CH_2CH_2CH_2N(CH_2)_5$	m.p. 85–86°	485
2-$Py(p\text{-}BrC_6H_4)C(OH)CH_2CH_2N(CH_3)_4O$	m.p. 111–12°	484
2-$Py(Ph)C(OH)CH_2CH_2N(Me)_2$	m.p. 101–2°; b.p. 145–50°/1.5 mm.; dimethylaminoethyl ether hydrobromide, m.p. 244–45°	146,469, 483,484.

(*continued*)

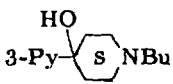
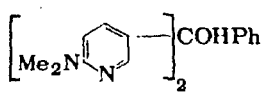
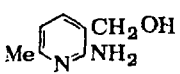
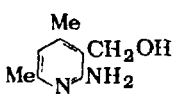
TABLE XIII-25. (*Continued*)

Compound	Physical properties, derivatives	Ref.
2-Py(*p*-MeC_6H_4)C(OH)$CH_2CH_2N(Me)_2$	m.p. 86–87°	484,485
2-Py(*p*-ClC_6H_4)C(OH)$CH_2CH_2N(Me)_2$	m.p. 89–90°	483
2-Py(*p*-$MeOC_6H_4$)C(OH)$CH_2CH_2N(Me)_2$	m.p. 89–90°	483,484
2-Py(2-thienyl)C(OH)$CH_2CH_2N(Me)_2$	b.p. 140–44°/0.1 mm.; m.p. 66–67°	483,484
2-Py(Ph)C(OH)$CH_2CH_2N(Et)_2$	m.p. 61–62°	483
2-Py(*p*-ClC_6H_4)C(OH)$CH_2CH_2N(Et)_2$	b.p. 146–48°/.03 mm.	483,484
2-PyC(OH)Me$CH_2CH_2N(Et)_2$	b.p. 130–34°/.02 mm.	146
2-Py(Ph)C(OH)$CH_2CH_2CH_2N(Me)_2$	m.p. 92–93°	486
2-Py(Ph)C(OH)$CH_2CH_2CH_2N(CH_2)_5$	m.p. 83–84°	486
$(2\text{-Py})_2$C(OH)$CH_2CH_2CH_2CH_2N(Me)_2$		486
$(2\text{-Py})_2$C(OH)$CH_2CH_2CH_2CH_2N(CH_2)_4$		486
2-PyC(OH)PhC≡ $CCH_2N(CH_2)_5$	m.p. 114°	607
2-PyC(OH)Ph$CH_2CH_2CH_2N(CH_2)_5$	m.p. 82°	607
2-Py$(CH_2)_4$C(OH)MeC≡ $CCH_2N(CH_2)_5$	b.p. 203–7°/.7 mm.	607,608
2-PyCHPh($C_6H_4O(CH_2)_2NEt_2$)	m.p. 63–5°	609
	m.p. 69–89°	36
	b.p. 139–43°/0.3 mm.	36

2-Py—CHOH—Et—PyCHOH(1-amino-cyclohexyl)	dipicrate, m.p. 191–2°	520
	b.p. 141–42°/1 mm.	478
	m.p. 130°	427
	m.p. 76°	417
4-NH_2-2-$PyCH_2OH$	m.p. 114–15°; NAc, m.p. 166°	529
6-Me-4-NH_2-2-$PyCH_2OH$	m.p. 141°; NAc, m.p. 178–9°	529
3-$PyCHOHCH_2NH_2$	dihydrochloride, m.p. 189.5–91° (dec.)	54,520
3-$PyCHOHCH_2NHCH_3$	b.p. 115–118°/4 mm.	553
3-$PyCHOHCH_2NHEt$	b.p. 114°/.2 mm.	553
3-$PyCHOHCH_2NHCH_2Ph$	b.p. 189°/.2 mm.	553
3-PyCHOH—$CH_2NHCH_2CH_2CH_3$	b.p. 126–8°/.2 mm.	553
3-PyCHOH—$CH_2NHCH_2CH_2OH$	b.p. 180–5°/.54 mm; m.p. 90°	553
3-$PyCHOHCH_2N(Et)_2$	b.p. 80°/12 mm.	55
3-$PyCHOHCH_2N(CH_2)_5$	m.p. 42.7°; b.p. 162°/16 mm.	55
3-PyCHOHCH(2-Py)N(*i*-Pr)$_2$		55
3-$PyCHOHCH_2CH_2N(Me)_2$	b.p. 140–43°/3 mm.	56
3-Py—CHOH—$CH(CH_3)NH_2$	b.p. 120–22°/0.2 mm.	520
3-PyCHOH—$CH(CH_3)NHCH_3$	b.p. 115/118°/.2 mm.	553

(*continued*)

TABLE XIII-25. *(Continued)*

Compound	Physical properties, derivatives	Ref.
3-PyCHOHCH(CH$_3$)NHEt	b.p. 107–110°/.14 mm.	553
3-PyCHOHCH(CH$_3$)NHCH$_2$Ph	b.p. 163°/.19 mm.	553
3-PyCHOHCH(CH$_3$)NHCH$_2$CH$_2$CH$_3$	b.p. 119–23°/.34 mm.	553
3-PyCHOHCH(CH$_3$)NHCH$_2$CH$_2$OH	b.p. 170–5°/.006 mm.	553
3-PyCHOHCH$_2$CH$_2$CH$_2$NHMe	b.p. 139–40°/1 mm.	154,488
3-PyCHOHCHEtNH$_2$	b.p. 115°/.17 mm.	520,553
3-PyCHOHCH$_2$CH$_2$CH$_2$*N*HMe	*chloroplatinate, no definite m.p.*	57
3-PyCOH(C$_6$H$_4$OMe-*p*)(C$_6$H$_4$NH$_2$-*o*)	m.p. 161–63°	460
3-PyC(OH)Ph(CH$_2$)$_3$piperidyl	dipicrate, m.p. 182–4°	607
3-PyC(OH)PHC≡CCH$_2$piperidyl	m.p. 111°	607
	m.p. 80–81°; acetate hydrochloride, m.p. 215–16°; propionate hydrochloride, m.p. 198–99°	476
	m.p. 123–24°	163,164,487
	m.p. 98°; hydrochloride, m.p. 170.5°	74
	m.p. 120°; picrate, m.p. 175°; hydrochloride, m.p. 188° (dec.); hydrobromide, m.p. 222°	74
	m.p. 76°; hydrochloride, m.p. 300° (dec.)	74

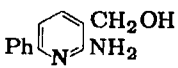
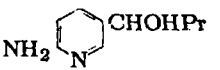
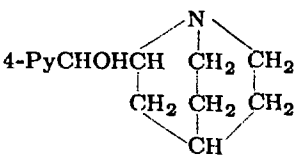
3-PyCOH(p-$C_6H_4O(CH_2)_2NEt_2$)CH_2(p-ClC_6H_4)	m.p. 123–5°	609
3-PyCOH(p-$C_6H_4O(CH_2)_2NEt_2$) CH_2(p-$CH_3OC_6H_4$)	m.p. 124–6°	609
3-PyCOH(p-$C_6H_4O(CH_2)_2NEt_2$)CH_2Py-2	m.p. 70–71°	609
6-Me-4-NH_2-3-PyCH_2OH	m.p. 132–4°	516
	m.p. 76°; hydrochloride m.p. 300° (dec.)	74
	m.p. 71–74°	495
4-PyCHOHCH$_2NH_2$	b.p. 130°/0.2 mm.; dihydrochloride, m.p. 203–5° (dec.)	54,137,520
4-PyCHOHCH(NH_2)CH_2OH	monobenzoate, m.p. 187–89°; monodichloroacetate, m.p. 162–63°	231
4-PyCHOHCHNH_2 CH_2OH	oil; dichloracetamide m.p. 137–39° (dec.)	60
4-PyCHOHCH(CH_3)NH_2	m.p. 123–24°	520
4-PyCHOHCH(NHCOPh)CH_2OH	m.p. 166–67°	60
	racemate A, m.p. 57–58°; dihydrochloride, m.p. 206–7°; racemate B, m.p. 158–59° dihydrochloride, m.p. 167–69°	59
4-PyC(ON)PhC≡ CCH_2piperidyl	m.p. 123°	607
4-Py$(CH_2)_4$C(OH)MeC≡ CCH_2piperidyl	b.p. 215–223°/.5 mm.	607

TABLE XIII-26. Trihydric Pyridine Alcohols

Compounds	Physical properties, derivatives	Ref.
2-$PyC(CH_2OH)_3$	m.p. 68°; chloroplatinate, m.p. 167–68°; chloroaurate, m.p. 140°; picrate, m.p. 111.5–12.5°; tribenzoyl ester, m.p. 94°	77–84, 209
2-$PyCHOHCH_2CH(CH_2OH)CH_2OH$	triacetate, b.p. 171–73 °/0.5	150
4-$PyC(CH_2OH)_3$	m.p. 156–57°; hydrochloride, m.p. 137–38°	86,170
	m.p. 150°	596

TABLE XIII-27. Side-chain Hydroxypyridinecarboxylic Acids and Derivatives

Compound	Physical properties, derivatives	Ref.
2-PyCHOHCOOH	m.p. 108°; methyl ester m.p. 76°; Me ester-HCl 163°	621
2-PyCHOHCN	m.p. 88–89°; acetate, m.p. 47°	166,638
	Benzoyl, m.p. 100–2°	650
2-PyCHOHCONH$_2$	Benzoyl, m.p. 140–2°	650
2-PyCH$_2$CHOHCOOH	m.p. 124–25°	84,105,107
2-PyC(CH$_3$)OHCOOH	HCl, m.p. 131°, nitrile, m.p. 50–51°	621
	m.p. 65–7°	561
	m.p. 51–3°	561
2-Py—C(OH)PhCHPhCOOH	m.p. 162.5°; methyl ester, m.p. 149–51°	561
2-PyCH(CO$_2$Et)CH$_2$CH$_2$CH$_2$OPh	b.p. 205–7°/1 mm.	233
(2-Py)$_2$COHCOOH	Na salt, m.p. 180–200° dec.	560
3-PyCHOHCOOH	m.p. 160°; HCl, m.p. 164° ethyl ester, b.p. 148–9°/.4 mm.; amide, m.p. 152–3°	621
3-PyCHOHCN	Benzoyl, m.p. 94°	650
3-PyCHOHCONH$_2$	Benzoyl, m.p. 163–4°	650
4-PyCHOHCN	m.p. 144–46°	166,638
	Benzoyl, m.p. 130–2°	650
4-PyCHOHCONH$_2$	Benzoyl, m.p. 196–8°	650
4-PyCHOHCH$_2$COOEt	hydrochloride, m.p. 155–57°	228
4-PyCOHEtCH$_2$COOC$_2$H$_5$	m.p. 99–100°	561
4-PyCOHEtCHCH$_3$COOC$_2$H$_5$	m.p. 121–2°	561

(*continued*)

TABLE XIII-27. (*Continued*)

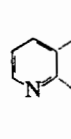
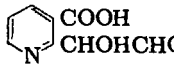
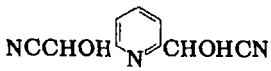
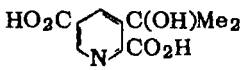
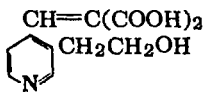
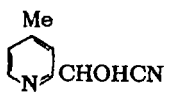
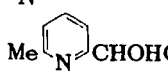
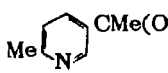
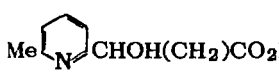
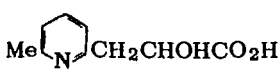
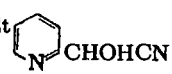
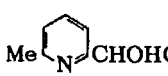
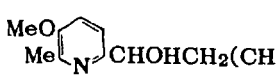
Compound	Physical properties, derivatives	Ref.
4-PyC(OH)PhCHPhCOOH	m.p. 209–13°; methyl ester, m.p. 166–8°	561
	m.p. 153–4°; ethyl ester-acetate, b.p. 133–6°/3 mm.; lactone, m.p. 141–2°	526
	ethyl ester-acetate, b.p. 171–3/7 mm.; lactone, m.p. 118–19°; amide, m.p. 154–5°	526
	amide, m.p. 146–7°; lactone, m.p. 90–2°, b.p. 110–20/3 mm.	600
	lactone-diacetate, m.p. 98–100°, b.p. 100–10°/.06 mm.	600
	lactone, m.p. 83–4°, b.p. 130–5/3 mm.; amide, m.p. 157°	600
	acetate, b.p. 140–50°/.01 mm.	
	methyl ester, m.p. 88°; hydrazide, m.p. 185°	25,68
	acetate-ethyl ester hydrochloride, m.p. 109–10°	203
	m.p. 202–25°; ethyl ester m.p. 100–1°; acetate ethyl ester m.p. 39–41°; b.p. 145–47°/0.3 mm.; hydrochloride, m.p. 140.5–141.5°	16

TABLE XIII-27. (*Continued*)

Compound	Physical properties, derivatives	Ref.
	lactone-acetate, m.p. 177°; lactone-ethyl ester, m.p. 135–36°; lactone-methyl ester, m.p. 152°	234
	m.p. 105°	621
		9
	methyl ether-diethyl ester-hydrochloride, m.p. 98.5–99°; acetate diethyl ester-hydrochloride, m.p. 111–12°; picrate, m.p. 115–16°	230
	m.p. 102°; acetate, m.p. 68.5°	166
	m.p. 102–6°; HCl 138–40°; nitrile, m.p. 134°	621
	m.p. 158–59°; hydrochloride, m.p. 190–91°; chloraurate, m.p. 114°	232
	methyl ester, b.p. 172–73.5°/1.3 mm.	168
	m.p. 166°; chloroplatinate, m.p. 185°; chloraurate, m.p. 143–44°	121
	m.p. 101°	166
	m.p. 134°; acetate, m.p. 62°	166
	methyl ester; b.p. 181.5–82.5°/0.7 mm.	168

(*continued*)

TABLE XIII-27. (*Continued*)

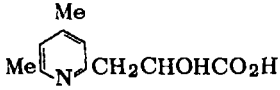
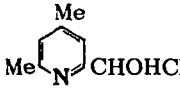
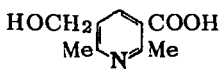
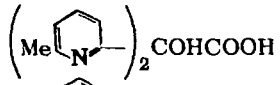
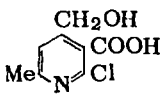
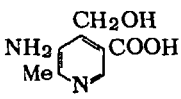
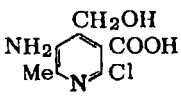
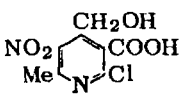
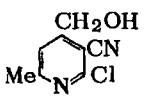
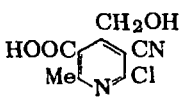
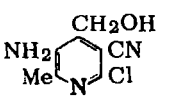
Compound	Physical properties, derivatives	Ref.
	hydrochloride, m.p. 179–81°	91
	m.p. 130°; acetate, m.p. 50.5°	166
	ethyl ester, m.p. 100–1°	68
	Na salt, m.p. 210–240°	560
	m.p. 122–3°; acetate, m.p. 59–61°, b.p. 140–55°/ 14–15 mm.	529
	lactone, m.p. 179°	256
	lactone, m.p. 224–26°; picrate, m.p. 229–30°	252,259
	lactone, m.p. 280–82°	252,281
	lactone, m.p. 176–78°	252,256, 259,271
	ethyl ether, b.p. 160–61°/12 mm.; m.p. 35.5–36.5°; methyl ether, m.p. 66–67°	380,383 490,491
	phenyl ether-ethyl ester, m.p. 155–57°	289
	ethyl ether, m.p. 146–48°	253,255, 258,256, 289

TABLE XIII-27. (*Continued*)

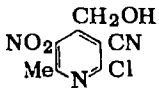
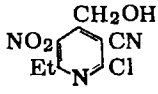
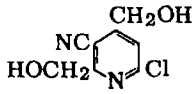
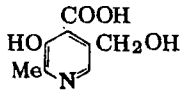
Compound	Physical properties, derivatives	Ref.
	ethyl ether, m.p. 47–48°; methyl ether, m.p. 70–73°	253,257
	methyl ether, m.p. 56–57°	365
	m.p. 77.5°	385
	lactone-3-acetate, m.p. 165–7°	571

TABLE XIII-28. Polyhydroxyl Compounds Related to Pyridoxol

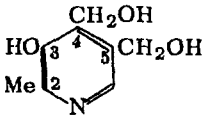
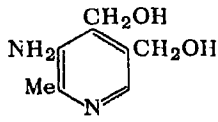
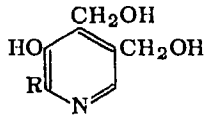
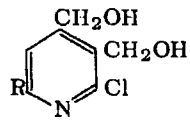
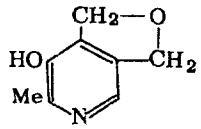
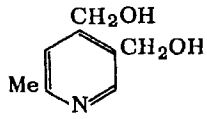
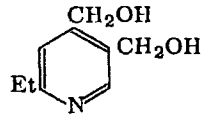
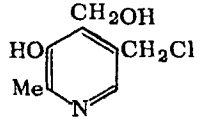
Compound	Physical properties, derivatives	Ref.
	m.p. 160°; hydrochloride, m.p. 208–9°; diacetate-hydrochloride, m.p. 160–61° triacetate m.p. 156–58°; tribenzoate, m.p. 121–22°	253,260, 261,262, 264,283, 285,299
Pyridoxol	4-ethyl ether-hydrochloride, m.p. 135–36°	255,288, 300
	3-methyl ether, m.p. 89.5–90°, 96–7°	257,492
	3-benzyl ether, m.p. 117–20°; HCl, 178°	561,562
	4-benzyl ether, m.p. 166.5°; hydrochloride, m.p. 194–5°	290,291
	4-*n*-butyl ether-hydrochloride, m.p. 127–8°	301,493
	4-methyl ether-hydrochloride, m.p. 181°	295,324, 326
	5-methyl ether-hydrochloride, m.p. 135–6°	296
	methiodide, m.p. 188–89°	329
	acetone ketal-hydrochloride, m.p. 217–18°; free base, m.p. 113–15°	327
	cyclohexanone ketal-hydrochloride, m.p. 219–21°	328
	tripalmitate, m.p. 72–74°; trilinoleate, liquid; trioctanoate, liquid; tridecanoate, m.p. 47.5–48.5; 3,5-dipalmitate, m.p. 58–61°; 5-palmitate, m.p. 72–76°; isopropylidene-5-palmitate hydrochloride, m.p. 132.5–33.5°	332,584
	phosphonate esters	583

TABLE XIII-28. (*Continued*)

Compound	Physical properties, derivatives	Ref.
	m.p. 141.5–42°; dihydrochloride, m.p. 176–77°	290,291, 574
	R = *i*-propyl, m.p. 139°; hydrochloride, m.p. 192° R = *i*-butyl, m.p. 134°; hydrochloride, m.p. 213–14° R = phenyl, hydrochloride, m.p. 185° R = *n*-amyl, hydrochloride, m.p. 186–87° R = benzyl, hydrochloride, m.p. 202°; 3-benzylether-HCl m.p. 179–80°	369–371
	R = *i*-butyl, m.p. 42–43° R = *n*-amyl, m.p. 42–43°	370
	m.p. 239–40°	264,538
	hydrochloride, m.p. 202–203°; 4-ethyl ether, m.p. 94–95°	380
	hydrochloride, m.p. 192°	365
	m.p. 170–71°; acetone ketal-hydrochloride, m.p. 190–91°; 4-methyl ether	327,336

(*continued*)

TABLE XIII-28. (*Continued*)

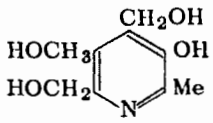
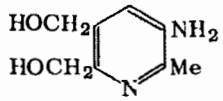
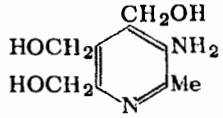
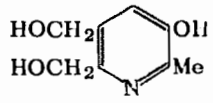
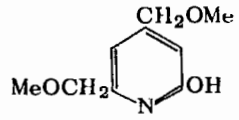
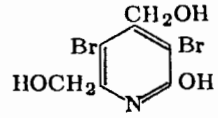
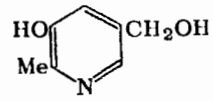
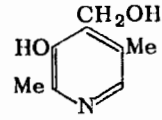
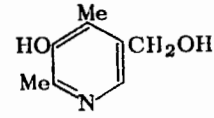
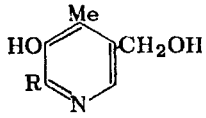
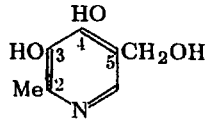
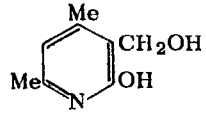
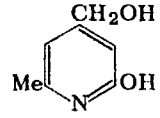
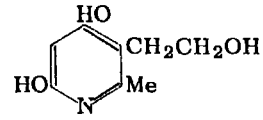
Compound	Physical properties, derivatives	Ref.
	m.p. 141–42°	386
	m.p. 154–54.5°	386
	m.p. 191–92°	386
	m.p. 145–46°; hydrochloride, m.p. 169–70°	386
	m.p. 202.5°	385
	m.p. 189–91°	221
	m.p. 174–75°; hydrochloride, m.p. 162–65°; diacetate, m.p. 125–26°	306,381
	m.p. 181–82°; hydrochloride, m.p. 143–43.5; 4-methyl ether-hydrochloride, m.p. 152–53° and picrate, m.p. 138°	379,538
	hydrochloride, m.p. 267–268°, 264°, 274°	374,375, 324,590, 588
	hydrochloride, m.p. 267–68°; dipalmitate, m.p. 59.5–61°	324,325, 332

TABLE XIII-28. (*Continued*)

Compound	Physical properties, derivatives	Ref.
	R = Et, hydrochloride, m.p. 174–76°	365
	R = *i*-butyl, hydrochloride, m.p. 163–65°	370,377
	R = *n*-amyl, hydrochloride, m.p. 125–26°; 5-dihydrogen phosphate, m.p. 251–52°; 5-acetate, hydrochloride, m.p. 180–81°; 3-dihydrogen phosphate, m.p. 205–7°; 3-dibenzyl phosphate, hydrochloride, m.p. 114–16°; 3-benzyl ether, m.p. 72–73°; 5-acetate, b.p. 160–63°/0.3 mm.	414
	m.p. 226–27°, 4-Phosphoric acid, m.p. 233–34° (dec.); 3-*p*-toluenesulfonate, 228–29°; 3,5-di-*p*-toluenesulfonate 140–41°	415
	m.p. 211–12°	384
	m.p. 184–85°; 213–14°; 4-ethyl ether, m.p. 111–12°; 4-methyl ether, m.p. 129°; 4-benzyl ether, m.p. 208–10°	75,241,244
	3-ethyl ether, m.p. 290–93°	11,13,482

(*continued*)

TABLE XIII-28. (*Continued*)

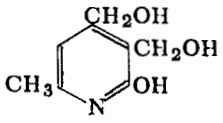
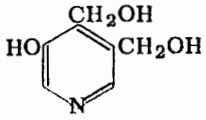
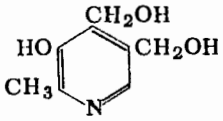
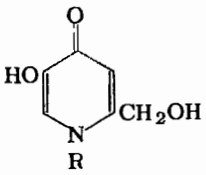
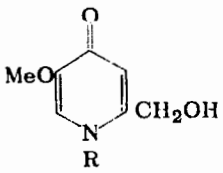
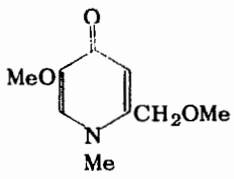
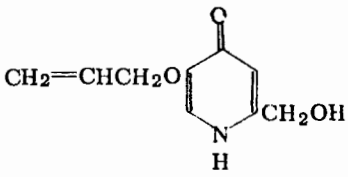
Compound	Physical properties, derivatives	Ref.
	m.p. 75–76°	593
	m.p. 130–135°	591
	m.p. 176–8°	585
	R = H, m.p. 237–38° (dec.) R = CH_2CH_2OH, m.p. 225–26°	7
	R = H, m.p. 173–74° R = Me, m.p. 203–4° R = CH_2CH_2OH, m.p. 172–73° R = $CH_2CH_2NEt_2$, m.p. 62–63° R = CH_2CO_2H, m.p. 183–84° (dec.)	6,188 7,188 7 7 7
	m.p. 57–58° (trihydrate), 113°; (anhydrous); picrate, m.p. 191°; methiodide, m.p. 116–18° (dec.)	7,188
	hydrochloride, m.p. 178.5–79°; picrate, m.p. 173–75°	8

TABLE XIII-28. (*Continued*)

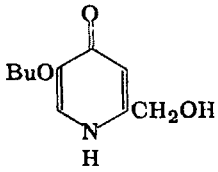
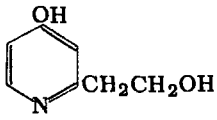
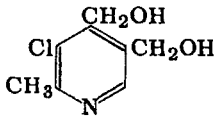
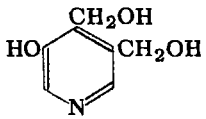
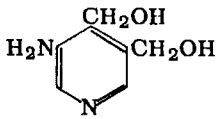
Compound	Physical properties, derivatives	Ref.
	m.p. 150–51°	239
	HCl, m.p. 128°	595
	HCl, m.p. 164–4.5°	613
	HCl, m.p. 124–6°	613
	HCl, m.p. 164–5°	613

TABLE XIII-29. Amines Related to Pyridoxamine

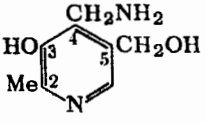
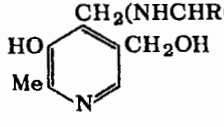
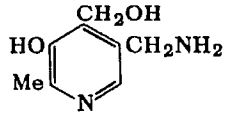
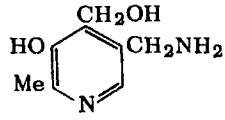
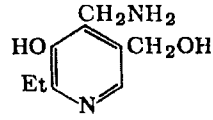
Compound	Physical properties, derivatives	Ref.
	m.p. 193–93.5°; hydrochloride, m.p. 226–27°; *N*-carbethoxy, hydrochloride, m.p. 115–18°; 5-phosphoric acid, hydrochloride, m.p. 224° (dec.); triacetate	279,336, 410, 538
Pyridoxamine	tripalmitate, m.p. 102–3°; 3,4-di-*p*-toluenesulfonate, m.p. 187–89°	332,402, 409, 413
	N-carbamide picrate, m.p. 198–203°; HCl, m.p. 205–8°; 3-acetate-HCl, m.p. 203–6°	587
	Schiff's base with pyruvic acid	569,570
Pyridoxylamino Acids	Amino Acid Residue of	
	*DL*-Phenylalanine, m.p. 233–34°; *DL*-alanine, m.p. 213–14°; *L*-tyrosine, m.p. 242–50°; glycine, m.p. 228–29°; *DL*-norleucine, m.p. 220–21°; *L*-leucine, m.p. 228–29°; *DL*-leucine, m.p. 232–33°; *DI-i*-leucine, m.p. 222–23°; *DL*-valine, m.p. 245–46°; *DL*-tryptophan, m.p. 240–41°; *DL*-threonine, m.p. 239–40°; *DL*-glutamic acid, m.p. 188–89°; *L*-glutamic acid, m.p. 181–82°; *DL*-methionine, m.p. 217–18°; *DL*-aspartic acid, m.p. 227–28°; *L*-asparagine, m.p. 209–10°; β-alanine, m.p. 212–13°; *L*-lysine, m.p. 211–13°; *L*-tyrosine butyl ester, m.p. 141–42°; *N*-benzoyl-dl-lysine, m.p. 220–21°; *DL*-serine, m.p. 217–18°; *DL*-aspartic diethyl ester hydrochloride, m.p. 168–69°; *DL*-glutamic diethyl ester hydrochloride, m.p. 155–56°; *DL*-alanine ethyl ester hydrochlo-	340,576

TABLE XIII-29. (*Continued*)

Compound	Physical properties, derivatives	Ref.
	ride, m.p. 180–81°; *DL*-alanine hydrochloride, m.p. 202–3°; *L*-leucine hydrochloride, m.p. 156–57°; *L*-valine, copper chelates	
	R = Ph hydrochloride, m.p. 230–32°	
	R = Me hydrochloride, m.p. 208–209°	
	R = Et hydrochloride, m.p. 184–86°	
	R = $CH_2CH_2CH_2Ph$ hydrochloride, m.p. 180–81°	
	R = CH_2CH_2OH m.p. 174–75°	
	R = $CH_2CHMeOH$, m.p. 194–96°	
	R = CH_2CH_2Ph hydrochloride, m.p. 227–28° (dec.)	339
	R = β-*z*-indolylethyl hydrochloride, m.p. 222–23° (dec.)	
	R = $CH_2CH_2C_6H_4OH$-*p* hydrochloride, m.p. 238–39° (dec.)	
	R = *i*-Bu hydrochloride, m.p. 204–205° (dec.)	
	R = CH_2Ph hydrochloride, m.p. 220–21° (dec.)	
	R = β-5-imidazolylethyl hydrochloride, m.p. 236–37° (dec.)	
	m.p. 176–78°; dihydrochloride, m.p. 197.5–99°; 4-methyl ether dihydrochloride, m.p. 170° (dec.); *N*,*N*-diethyl, dihydrochloride, m.p. 212–14°; dipicrate, m.p. 174°	327,336
	dihydrochloride, m.p. 214°; ethyl ether-diHCl, m.p. 127°	365,564
	dihydrochloride, m.p. 164–16°	368

(*continued*)

TABLE XIII-29. (*Continued*)

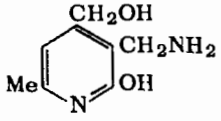
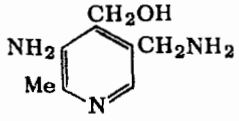
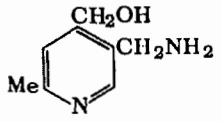
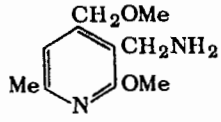
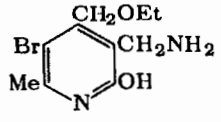
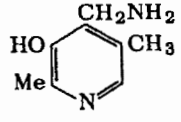
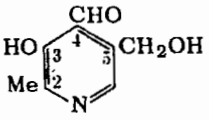
Compound	Physical properties, derivatives	Ref.
	hydrochloride, m.p. 265–67°	383
	dihydrochloride, m.p. 235–37°; ethyl ether-dipicrate, m.p. 186–87°; ethyl ether-dihydrochloride, m.p. 195°; methyl ether hydrochloride, m.p. 149°; 3-carbethoxy-phenyl ether dihydrochloride, m.p. 238°	253,255, 256, 257, 264, 289, 293
	m.p. 81–83°	380
	dihydrochloride, m.p. 270–72°; picrate, m.p. 183–84°	383
	m.p. 223°	256
	Di-HCl, m.p. 262–3°; diacetate, m.p. 176–7°; ditosyl-HCl, m.p. 194–5°	538

TABLE XIII-30. Aldehydes Related to Pyridoxal

Compound	Physical properties, derivatives	Ref.
	hydrochloride, m.p. 173–74°; (dec.); oxime, m.p. 225–26° (dec.); semicarbazone, m.p. 235° (dec.); oxime triacetate, m.p. 114.5–15°; oxime-methyl ether, m.p. 159–60°; mono-ethyl acetal, m.p. 142–43°	336,338, 403, 407, 569
Pyridoxal	monomethyl acetal, m.p. 169–70° and other acetals	404,406, 582
	nicotinoyl hydrazone, m.p. 235–36°; isonicotinoyl hydrazone, m.p. 261–62°; 3-methyl ether, m.p. 53–54°	332,361
	dipalmitate, m.p. 74°; 3-palmi-tate-hydrobromide, m.p. 132°; 3-palmitate-monoethyl acetal, m.p. 56–57°; diethyl mercap-tal, m.p. 126°; dibenzoate, m.p. 93°	413
	monobenzoate, m.p. 116–17°; ethyl cyclic acetal, acetate, b.p. 125–27°/0.005 mm.	402
Schiff's Bases	methylamine, m.p. 150–51°; ethylamine, m.p. 108–9°; 3-phenylpropylamine, m.p. 87–89°; ethanolamine, m.p. 148–49°; *i*-propanolamine, m.p. 112–14°	342
	β-phenylethylamine, m.p. 101–102°; tryptamine, m.p. 160–61°; tyramine, m.p. 168–69°; *i*-butylamine, m.p. 67–68°; pyridoxamine, m.p. 232–33°; benzylamine, m.p. 114–15°; aniline, m.p. 178–79°	341
	L-valine, copper chelates	576
	D,L-alamine and *Ni* chelate	570

(*continued*)

TABLE XIII-30. (*Continued*)

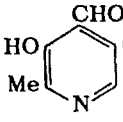
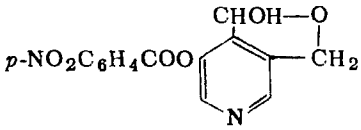
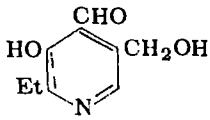
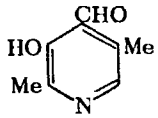
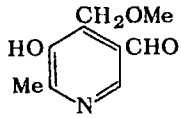
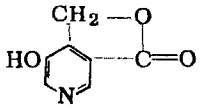
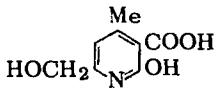
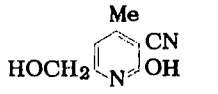
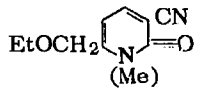
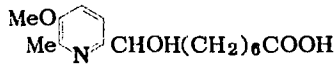
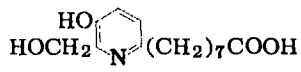
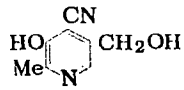
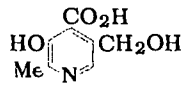
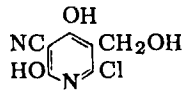
Compound	Physical properties, derivatives	Ref.
 (codecarboxylase)	oxime, m.p. 229–30° (dec.)	401,403, 407, 408
	Schiff's Bases, 575°; hydrazone, m.p. 236–37°; azine, darkens, 195–280°	586
	m.p. 210–11°; diphenylphosphate, m.p. 130–40°; *p*-nitrobenzoate, m.p. 99–102°	364
	hydrochloride, no definite m.p.; oxime, m.p. 225–36°; monoethyl acetal hydrochloride, m.p. 132–33°	368,370
	m.p. 108–109°; oxime, m.p. 239–40°; hydrochloride, m.p. 191–93°	379
	oxime, m.p. 198–99° (dec.)	336

TABLE XIII-31. Pyridine Carboxylic Acids and Derivatives with Both Nuclear and Side-Chain Hydroxyl Groups

Compound	Physical properties, derivatives	Ref.
	dec. 250°	591
	m.p. 223–24° (dec.); side-chain ethyl ether, m.p. 177–79°; side-chain methyl ether, m.p. 200–201°	241
	m.p. 224–27° (dec.); side-chain ethyl ether, m.p. 130°; side-chain methyl ether, m.p. 152°	241
	m.p. 127–28°	244
	Methyl ester, b.p. 181.5–82.5/0.7 mm.	168
	ethyl ester picrate m.p. 113–15°	238
	side-chain monacetate, m.p. 209–10°; diacetate, m.p. 63–64°	338
	m.p. 258–58.5°; lactone, m.p. 273–73.5° (dec.); hydrochloride, m.p. 252–53° (dec.)	338
	lactone, 3-methyl ether, m.p. 116–16.5°; amide, m.p. 210–11° (dec.)	336
	Salts isolated	237

(*continued*)

TABLE XIII-31. (*Continued*)

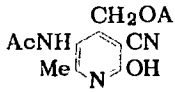
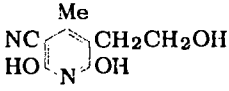
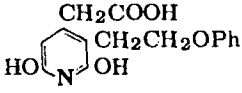
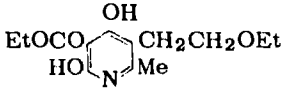
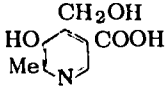
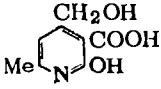
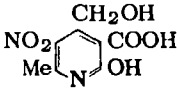
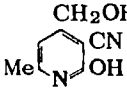
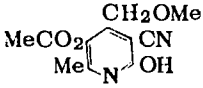
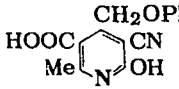
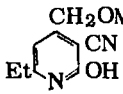
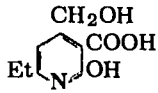
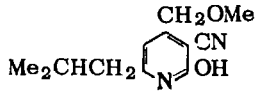
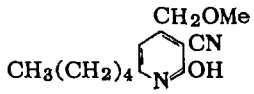
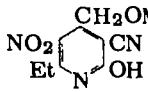
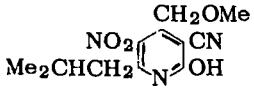
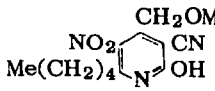
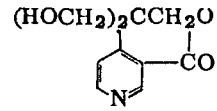
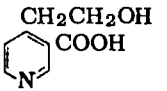
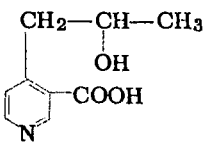
Compound	Physical properties, derivatives	Ref.
	m.p. 262–63° (dec.)	287
	Salts isolated	243
	hydrochloride, m.p. 146°	242
	m.p. 174–76°	11,13
	lactone, m.p. 280–81°; hydrochloride, 250–55° (dec.); lactone-3-methyl ether, m.p. 108–109°	247,252,259, 266, 280, 281, 496, 497
	m.p. 330° (dec.); lactone, m.p. 267–68°, > 320°; 4-monoacetate, m.p. 226°; 2-methyl ether, m.p. 163–64°; 4-ethyl ether, m.p. 182–83°; 4-ethyl ether-ethyl ester, m.p. 117–18°; 4-ethyl ether-amide, m.p. 266–67°	241,252,276, 281,383, 498
	lactone, m.p. 279–80°	252
	m.p. 202.5°; 4-methyl ether, m.p. 226°; 2,4-dimethyl ether, m.p. 56–58°; 4-ethyl ether, m.p. 209–10°; 4-benzyl ether, m.p. 208–10°	241,244,252, 253,256, 257,263, 268,281, 383
	m.p. 254–56°	286

TABLE XIII-31. (*Continued*)

Compound	Physical properties, derivatives	Ref.
	m.p. 260°	289
	m.p. 190–91°	365
	lactone, m.p. 285°	365
	m.p. 204–5°	370
	m.p. 131–32°	370
	m.p. 171–72°	365
	m.p. 167–68°	370
	m.p. 161–62°	370
	diacetate, m.p. 143–5°	601
	Lactone, m.p. 68–70°; amide, m.p. 152–4°	601
	Lactone, b.p. 150–60/3 mm.; picrate, m.p. 140°	601

I. BIBLIOGRAPHY

1. Paul and Tchelitcheff, *Bull. soc. chim. France*, **1954**, 1139.
2. Haskelberg, *Chem. and Ind.*, **54**, 261 (1935).
3. Jacobs, Craig, and Lavin, *J. Biol. Chem.*, **141**, 51 (1941).
4. Jacobs and Craig, *J. Biol. Chem.*, **139**, 277 (1941).
5. Beroza, *J. Am. Chem. Soc.*, **75**, 44 (1953).
6. Heyns and Vogelsang, *Ber.*, **87**, 13 (1954).
7. Heyns and Vogelsang, *Ber.*, **87**, 1377 (1954).
8. McLamore, Gelblum, and Bavley, *J. Am. Chem. Soc.*, **78**, 2816 (1956).
9. Oparina, *J. Russ. Phys. Chem. Soc.*, **57**, 319 (1925); *Chem Zentr.*, **1926, I**, 3336.
10. Dehnel, *Ber.*, **33**, 3498 (1900).
11. Tracy and Elderfield, *J. Org. Chem.*, **6**, 54 (1941).
12. Graf, *J. prakt. Chem.*, **133**, 19 (1932).
13. Wilson and Harris, *J. Am. Chem. Soc.*, **73**, 2388 (1951).
14. Dornow and Schacht, *Ber.*, **82**, 117 (1949).
15. Kato, *J. Pharm. Soc. Japan*, **75**, 1239 (1955).
16. Rubtsov, *Zhur. Obshcheĭ Khim.*, **25**, 1021 (1955); *C.A.*, **50**, 3432 (1956).
17. LeForge, *J. Am. Chem. Soc.*, **50**, 2484 (1928).
18. Graf, *J. prakt. Chem.*, **146**, 88 (1936).
19. Prijs, Lutz, and Erlenmeyer, *Helv. Chim. Acta*, **31**, 571 (1948).
20. Graf, *J. prakt. Chem.*, **140**, 39 (1934).
21. Wibaut and Overhoff, *Rec. trav. chim.*, **52**, 55 (1933).
22. Niemann, Lewis, and Hays, *J. Am. Chem. Soc.*, **64**, 1678 (1942).
23. Swiss patent 249,970, Hoffman-LaRoche Inc.; *C.A.*, **43**, 7973a (1949).
24. Panizzon, *Helv. Chim. Acta*, **24E**, 24 (1941).
25. Mathes, Sauermilch, and Klein, *Ber.*, **86**, 584 (1953).
26. Harries and Lenart, *Ann.*, **410**, 95 (1915).
27. Wibaut, Kooyman, and Boer, *Rec. trav. chim.*, **64**, 30 (1945).
28. Graf, *J. prakt. Chem.*, **134**, 177 (1932).
29. Graf and Laszlo, *J. prakt. Chem.*, **138**, 231 (1933).
30. Strong and McElvain, *J. Am. Chem. Soc.*, **55**, 816 (1933).
31. British patent 312,919; German patent 555,240; *Friedl.*, **19**, 1149 (1932).
32. Boekelheide and Mason, *J. Am. Chem. Soc.*, **73**, 2356 (1951).
33. Scheuing and Winterhalder, *Ann.*, **473**, 126 (1929).
34. German patent 555,240; British patent 312,919, Boehringer; *C.A.*, **24**, 862 (1930).
35. Kato, *J. Pharm. Soc. Japan*, **75**, 1228 (1955).
36. Rubtsov and Volskova, *Zhur. Obshcheĭ Khim.*, **23**, 1685, 1688 (1953); *C.A.*, **49**, 332 (1955).
37. Clemo and Hoggarth, *J. Chem. Soc.*, **1941**, 41.
38. Bachman and Micucci, *J. Am. Chem. Soc.*, **70**, 2381 (1948).
39. Davies, Kenyon, and Thaker, *J. Chem. Soc.*, **1956**, 3394.

40. Kegelman and Brown, *J. Am. Chem. Soc.*, **75**, 4649 (1953).
41. Ghigi, *Ber.*, **75**, 764 (1942).
42. Tschugaeff, *Ber.*, **39**, 3382 (1906).
43. Chichibabin, *Ber.*, **37**, 1370 (1904).
44. Engler and Bauer, *Ber.*, **24**, 2530 (1891).
45. Engler and Majmon, *Ber.*, **24**, 2536 (1891).
46. Webb and Corwin, *J. Am. Chem. Soc.*, **66**, 1456 (1944).
47. Preobrazhenskiĭ and Beer, *J. Gen. Chem.* (*U.S.S.R.*), **15**, 667 (1945); *C.A.*, **40**, 5724 (1946).
48. Benary and Psille, *Ber.*, **57**, 828 (1924).
49. Dornow and Machens, *Ber.*, **80**, 502 (1947).
50. Dornow, Ber., **73**, 156 (1940).
51. Baumgarten and Dornow, *Ber.*, **73B**, 44 (1940).
52. Baumgarten and Dornow, *Ber.*, **73**, 353 (1940).
53. Schmelkes and Joiner, *J. Am. Chem. Soc.*, **61**, 2562 (1939).
54. Burrus and Powell, *J. Am. Chem. Soc.*, **67**, 1468 (1945).
55. Dornow, Machens, and Bruncken, *Ber.*, **84**, 147 (1951).
56. Snell and McElvain, *J. Am. Chem. Soc.*, **56**, 1612 (1934).
57. Späth and Bretschneider, *Ber.*, **61**, 327 (1928).
58. Dornow and Bruncken, *Ber.*, **83**, 189 (1950); *C.A.*, **44**, 7321 (1950).
59. Rubtsov, *J. Gen. Chem.* (*U.S.S.R.*), **16**, 461 (1946); *C.A.*, **41**, 762 (1947).
60. Van der Meer, Kofman, and Veldstra, *Rec. trav. chim.*, **72**, 236 (1953).
61. Jeger, Norymberski, Szpilfogel, and Prelog, *Helv. Chim. Acta*, **29**, 684 (1946).
62. Rabe, *J. prakt. Chem.*, **151**, 65 (1938).
63. Šorm, *Collection Czechoslov. Chem. Communs.*, **13**, 57 (1948); Šorm and Šedivý, *Collection Czechoslov. Chem. Communs.*, **13**, 289 (1948).
64. British patent, 717,172, Chase, Roche Products, Ltd.; *C.A.*, **50**, 2682 (1956).
65. Mosher and Tessieri, *J. Am. Chem. Soc.*, **73**, 4925 (1951).
66. Protiva, *Chem. Listy*, **45**, 20 (1951).
67. Exner, *Collection Czechoslov. Chem. Communs.*, **19**, 1191 (1954).
68. Bohlmann and Bohlmann, *Ber.*, **86**, 1419 (1953).
69. German patent 906,332, Dornow and Petsch, Farbenfabriken Bayer A. G.; *C.A.*, **49**, 2524 (1955).
70. British patent 631,078, Cohen, Roche Products, Ltd.; *C.A.*, **44**, 5397 (1950).
71. U.S. patent 2,520,037, Cohen, 1950.
72. Winterfeld *et al.*, *Naturwissenschaften*, **41**, 230 (1954); *C.A.*, **49**, 14759 (1955).
73. Kornfeld, *J. Am. Chem. Soc.*, **77**, 4425 (1955).
74. Dornow and Hargesheimer, *Ber.*, **86**, 461 (1953).
75. Mariella and Havlick, *J. Am. Chem. Soc.*, **74**, 1915 (1952).
76. Mićović and Mihailović, *J. Org. Chem.*, **18**, 1190 (1953).
77. Ladenburg, *Ber.*, **22**, 2583 (1889).
78. Ladenburg, *Ber.*, **24**, 1619 (1891).

79. Ladenburg, *Ann.*, **301**, 117 (1898).
80. Koenigs and Hoppe, *Ber.*, **35**, 1343 (1902).
81. Lipp and Richard, *Ber.*, **37**, 737 (1904); Ladenburg, *Ber.*, **22**, 2583 (1889); Ladenburg, *Ber.*, **24**, 1619 (1891); Ladenburg, *Ann.*, **301**, 117 (1898).
82. Löffler and Grosse, *Ber.*, **40**, 1325 (1907).
83. Muller and Krauss, *Monatsh.*, **61**, 212 (1930).
84. Tullock and McElvain, *J. Am. Chem. Soc.*, **61**, 961 (1939).
85. Winterfeld and Heinen, *Ann.*, **573**, 85 (1951).
86. Meisenheimer, *Ann.*, **420**, 190 (1920).
87. Löffler and Stietzel, *Ber.*, **42**, 124 (1909).
88. Profft, *Chem. Tech. (Berlin)*, **8**, 378 (1956).
89. Koenigs, *Ber.*, **35**, 1349 (1902).
90. Prausnitz, *Ber.*, **23**, 2725 (1890).
91. Takahashi and Saikachi, *J. Pharm. Soc. Japan*, **62**, 38 (1942); *C.A.*, **45**, 620 (1951).
92. Frank, Blegen, Dearborn, Myers, and Woodward, *J. Am. Chem. Soc.*, **68**, 1368 (1946).
93. Löffler and Remmler, *Ber.*, **43**, 2048 (1909); Koenigs and Hoppe, *Ber.*, **36**, 2904 (1903); Löffler and Thiel, *Ber.*, **42**, 132 (1909).
94. Michalski and Studniarski, *Roczniki. Chem.*, **29**, 1141 (1955); *C.A.*, **50**, 12044 (1956).
95. Engels, *Ber.*, **33**, 1087 (1900).
96. Langer, *Ber.*, **38**, 3704 (1905).
97. Melichar, *Ber.*, **88**, 1208 (1955).
98. Chichibabin, *J. prakt. Chem.*, **69**, 310 (1904).
99. Löffler, *Ber.*, **37**, 161, 1879 (1904).
100. Löffler, *Ber.*, **37**, 161 (1904).
101. Meisenheimer and Mahler, *Ann.*, **462**, 308 (1929).
102. Matzdorf, *Ber.*, **23**, 2709 (1890).
103. Löffler and Plocker, *Ber.*, **40**, 1310 (1907).
104. Einhorn and Liebrecht, *Ber.*, **20**, 1592 (1887).
105. Einhorn, *Ann.*, **265**, 208 (1891).
106. Einhorn and Gilbody, *Ber.*, **26**, 1, 414 (1893).
107. Einhorn, *Ber.*, **23**, 219 (1890).
108. Feist, *Arch. Pharm.*, **240**, 178 (1902).
109. Löffler and Kaim, *Ber.*, **42**, 94 (1909).
110. Koller, *Monatsh.*, **47**, 393 (1926).
111. Winterfeld and Holschneider, *Arch. Pharm.*, **277**, 196 (1939); *Chem. Zentr.*, **1939, II**, 2431.
112. Walters, Hunt, and Fosbinder, *J. Am. Chem. Soc.*, **63**, 2771 (1941).
113. Rabe and Kindler, *Ber.*, **52**, 1842 (1919).
114. Rabe, Huntenberg, Schultze, and Volger, *Ber.*, **64**, 2487 (1931).
115. Düring, *Ber.*, **38**, 164 (1905).
116. Alberts and Bachman, *J. Am. Chem. Soc.*, **57**, 1284 (1935).

117. Kleiman and Weinhouse, *J. Org. Chem.*, **10**, 562 (1945).
118. Jones, Kornfeld, and McLaughlin, *J. Am. Chem. Soc.*, **72**, 3539 (1950).
119. Renk and Grob, *Helv. Chim. Acta*, **37**, 2119 (1954).
120. Katritsky, *J. Chem. Soc.*, **1955**, 2581.
121. Einhorn and Gilbody, *Ber.*, **26**, 1414 (1893).
122. Schubert, *Ber.*, **27**, 86 (1894).
123. Koenigs and Mengel, *Ber.*, **37**, 1322 (1904).
124. Takahashi, *J. Pharm. Soc. Japan*, **49**, 1048 (1929); *C.A.*, **24**, 1380 (1930).
125. Koenigs and Othmann, *Ber.*, **54**, 1343 (1921).
126. Gilman and Towle, *Rec. trav. chim.*, **69**, 428 (1950).
127. Walter, *Org. Syntheses*, vol. 23, p. 83, John Wiley, N. Y. (1943).
128. Norton, Seibert, Benson, and Bergstrom, *J. Am. Chem. Soc.*, **68**, 1572 (1946).
129. Japanese patent 6181 (1953); *C.A.*, **49**, 9692 (1955).
130. Prelog, Frenkiel, and Szpilfogel, *Helv. Chim. Acta*, **29**, 484 (1946).
131. Finkelstein and Elderfield, *J. Org. Chem.*, **4**, 365 (1939).
132. Chichibabin, *Bull. soc. chim.* (5) **5**, 436 (1938).
133. Prelog, Wirth, and Schönbaum, *Helv. Chim. Acta*, **29**, 1204 (1946).
134. Hey and Wibaut, *Rec. trav. chim.*, **72**, 522 (1953).
135. Edwards and Teague, *J. Am. Chem. Soc.*, **71**, 3548 (1949).
136. Profft, Schneider, and Beyer, *J. prakt. Chem.*, (4) **2**, 147 (1955).
137. Zymalkowski, *Archiv. Pharm.*, **289**, 52 (1956); *C.A.*, **50**, 13899 (1956).
138. Emmert and Asendorf, *Ber.*, **72**, 1188 (1939).
139. German patent 693,415, Emmert; *C.A.*, **35**, 4919 (1941).
140. Lochte, Kruse and Wheeler, *J. Am. Chem. Soc.*, **75**, 4477 (1953).
141. Kharasch, Schwartz, Zimmerman, and Nudenberg, *J. Org. Chem.*, **18**, 1051 (1953).
142. Dyson and Hammick, *J. Chem. Soc.*, **1937**, 1724.
143. Ashworth, Daffern, and Hammick, *J. Chem. Soc.*, **1939**, 809.
144. Mislow, *J. Am. Chem. Soc.*, **69**, 2559 (1947).
145. Cantwell and Brown, *J. Am. Chem. Soc.*, **75**, 1489 (1953).
146. Tilford, Shelton, and van Campen, *J. Am. Chem. Soc.*, **70**, 4001 (1948).
147. Doering and Weil, *J. Am. Chem. Soc.*, **69**, 2463 (1947).
148. Bullitt and Maynard, *J. Am. Chem. Soc.*, **76**, 1370 (1954).
149. Lutz, Fallot, and Erlenmeyer, *Helv. Chim. Acta*, **38**, 1114 (1955).
150. Boekelheide and Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954).
151. Okuda, *Pharm. Bull. (Tokyo)*, **3**, 316 (1955); *C.A.*, **50**, 13056. (1956).
152. Berson and Cohen, *J. Am. Chem. Soc.*, **77**, 1281 (1955).
153. Boekelheide and Harrington, *Chem. and Ind.*, **1955**, 1423.
154. Rayburn, Harlan, and Hanmer, *J. Am. Chem. Soc.*, **72**, 1721 (1950).
155. Furukawa, *Pharm. Bull. (Tokyo)*, **3**, 413 (1955); *C.A.*, **50**, 13926 (1956).
156. U.S. patent 2,735,851; *C.A.*, **50**, 14001 (1956).
157. Kato, *J. Pharm. Soc. Japan*, **75**, 1233 (1955).
158. Farley and Eliel, *J. Am. Chem. Soc.*, **78**, 3477 (1956).

159. Ginsburg and Wilson, *J. Am. Chem. Soc.*, **79**, 481 (1957).
160. Fromherz and Spiegelberg, *Helv. Physiol. et Pharmacol. Acta*, **6**, 42 (1948).
161. Calo and Bellomonte, *Farmaco (Pavia), Ed. sci.*, **10**, 755 (1955); *C.A.*, **50**, 8629 (1956).
163. Chichibabin and Knunjanz, *Ber.*, **64**, 2839 1931).
164. Kahn and Petrow, *J. Chem. Soc.*, **1945**, 858.
165. Swiss patent, 286,108, Hoffman-LaRoche and Co., H.-G.; *C.A.*, **48**, 8271 (1954).
166. Mathes and Sauermilch, *Ber.*, **89**, 1515 (1956).
167. Sugasawa and Mizukami, *Pharm. Bull. (Tokyo)*, **2**, 341 (1954); *C.A.*, **50**, 7109.
168. Rapoport and Volcheck, *J. Am. Chem. Soc.*, **78**, 2451 (1956).
169. McMillan and King, *J. Am. Chem. Soc.*, **73**, 3165 (1951).
170. Koenigs and Hoppe, *Ber.*, **36**, 2904 (1903); Löffler and Thiel, *Ber.*, **42**, 132 (1909); Löffler and Remmler, *Ber.*, **43**, 2048 (1910).
171. Knick, *Ber.*, **35**, 1162 (1902).
172. Knudsen, *Ber.*, **25**, 2985 (1892); *Ber.*, **28**, 1762 (1895).
173. Wibaut, van der Voort, and Markus, *Rec. trav. chim.*, **69**, 1048 (1950).
174. Späth, Kubiczek, and Dubensky, *Ber.*, **74B**, 873 (1941).
175. Nunn and Schofield, *J. Chem. Soc.*, **1952**, 583.
176. Oparina, *J. Russ. Phys. Chem. Soc.*, **61**, 2011 (1929); *C.A.*, **24**, 4785 (1930).
177. Lukeš and Ernest, *Collection Czechoslov. Chem. Communs.*, **15**, 107 (1950).
178. Koenigs and Bernhart, *Ber.*, **38**, 3049 (1905).
179. Heer, Sury, and Hoffmann, *Helv. Chim. Acta*, **38**, 134 (1955).
180. French and Sears, *J. Am. Chem. Soc.*, **75**, 469 (1951).
181. Karrer and Mainoni, *Helv. Chim. Acta*, **36**, 127 (1953).
182. Sury and Hoffman, *Helv. Chim. Acta*, **38**, 728 (1955).
183. Brown and Eldred, *J. Am. Chem. Soc.*, **71**, 445 (1949).
184. Beyerman and Muller, *Rec. trav. chim.*, **74**, 1568 (1955).
185. German patent 534,876.
186. McCarty, Tilford, and van Campen, *J. Am. Chem. Soc.*, **79**, 472 (1957).
187. Bockelheide and Rothchild, *J. Am. Chem. Soc.*, **70**, 864 (1948).
188. Armit and Nolan, *J. Chem. Soc.*, **1931**, 3023.
189. Yabuta, *J. Chem. Soc.*, **1924**, 575
190. Winterfeld, *Arch. Pharm.*, **268**, 308 (1930).
191. Winterfeld and Holschneider, *Ber.*, **66**, 1751 (1933).
192. Winterfeld and Holschneider, *Arch. Pharm.*, **273**, 315 (1935).
193. Prelog and Metzler, *Helv. Chim. Acta*, **29**, 1163 (1946).
194. Burtner and Brown, *J. Am. Chem. Soc.*, **69**, 630 (1947).
195. Barnden, *J. Chem. Soc.*, **1953**, 3733.
196. Vejdělek, Trčka, and Vyšatová, *Chem. Listy*, **48**, 1221 (1954).
197. Vejdělek, Trčka, Hejný, and Vyšatová, *Collection Czechoslov. Chem. Communs.*, **19**, 1274 (1954).
198. U.S. patent 2,566,376; *C.A.*, **46**, 2584 (1952).
199. Adkins, Wolff, Pavlic, and Hutchinson, *J. Am. Chem. Soc.*, **66**, 1293 (1944).

200. Borrows and Holland, *J. Chem. Soc.*, **1947**, 670.
201. Boekelheide and Ross, *J. Am. Chem. Soc.*, **77**, 5691 (1955).
202. Rubtsov and Yakhontov, *Zhur. Obshcheĭ Khim.*, **25**, 1820 (1955); *C.A.*, **50**, 7107 (1956).
203. Rubtsov and Yakhontov, *Zhur. Obshcheĭ Khim.*, **25**, 1183 (1955); *C.A.*, **50**, 3432 (1956); Copp and Timmis, *J. Chem. Soc.*, **1955**, 2021.
204. Rubtsov, Mikhlina, and Furshtatov, *Zhur. Obshcheĭ Khim.*, **26**, 445 (1956).
205. Barnes and Fales, *J. Am. Chem. Soc.*, **75**, 3830 (1953).
206. Karrer and Mainoni, *Helv. Chim. Acta*, **34**, 2151 (1951).
207. Kao and Robinson, *J. Chem. Soc.*, **1955**, 286.
208. Dubke, *Ber.*, **27**, 79 (1894).
209. Lipp and Zerngibt, *Ber.*, **39**, 1045 (1906).
210. Koenigs, *Ber.*, **35**, 1349 (1902).
211. Lukeš and Galik, *Chem. Listy*, **49**, 1832 (1955); *C.A.*, **50**, 9402 (1956).
212. Rubtsov, Nikilskaya, and Usovskoya, *Zhur. Obshcheĭ Khim.*, **25**, 2453 (1955); *C.A.*, **50**, 9401 (1956).
213. Proost and Wibaut, *Rec. trav. chim.*, **59**, 971 (1940).
214. Wibaut and Hüls, *Rec. trav. chim.*, **71**, 1021 (1952).
215. Boekelheide and Gall, *J. Am. Chem. Soc.*, **76**, 1832 (1954).
216. Wibaut and Hirschel, *Rec. trav. chim.*, **75**, 225 (1956).
217. Hurd and Holysz, *J. Am. Chem. Soc.*, **72**, 1735 (1950).
218. Ferguson and Levant, *Nature*, **167**, 817 (1951).
219. Brody and Bogert, *J. Am. Chem. Soc.*, **65**, 1075 (1943).
220. Ladenburg and Kroener, *Ber.*, **36**, 119 (1903).
221. Mariella and Belcher, *J. Am. Chem. Soc.*, **74**, 1916 (1952).
222. Allen, *J. Org. Chem.*, **15**, 435 (1950).
223. Mathes, Sauermilch, and Klein, *Ber.*, **87**, 1870 (1954).
224. Mathes, Sauermilch, and Klein, *Ber.*, **84**, 452 (1951).
225. Buchler, Addleburg, and Glenn, *J. Org. Chem.*, **20**, 1350 (1955).
226. Mathes and Sauermilch, *Ber.*, **85**, 1008 (1952).
227. Ochiai, Tsuda, and Ikuma, *Ber.*, **68**, 1551 (1935).
228. Koelsch, *J. Am. Chem. Soc.*, **65**, 2460 (1943).
229. McElvain and Johnson, *J. Am. Chem. Soc.*, **63**, 2213 (1941).
230. Rubstov and Yakhontov, *Zhur. Obshchei Khim.*, **25**, 1743 (1955); *C.A.*, **50**, 5660 (1956).
231. Biemann, *Monatsh.*, **86**, 59 (1955).
232. Knudsen, *Ber.*, **28**, 1762 (1895).
233. Clemo, Morgan, and Raper, *J. Chem. Soc.*, **1937**, 965.
234. Rosenheim and Tafel, *Ber.*, **26**, 1501 (1893).
235. Urbanski, *J. Chem. Soc.*, **1946**, 1104.
236. Urbanski, *J. Chem. Soc.*, **1947**, 132.
237. Schroeter and Finck, *Ber.*, **71**, 671 (1938).
238. Govindachari, Narasimhan, and Rajadurai, *Chem. and Ind.*, **1956**, 53.
239. Heyn and Vogelsang, *Ber.*, **87**, 1440 (1954).

240. Aso, *J. Agr. Chem. Soc. Japan*, **16**, 249 (1940); *C.A.*, **34**, 431 (1940).
241. Wenner and Plati, *J. Org. Chem.*, **11**, 751 (1946).
242. Robinson and Watt, *J. Chem. Soc.*, **1934**, 1536.
243. Stevens, Beutel, and Chamberlain, *J. Am. Chem. Soc.*, **64**, 1093 (1942).
244. Plati and Wenner, *J. Org. Chem.*, **14**, 447 (1949).
245. Lepkovsky, *Science*, **87**, 169 (1938).
246. Gyorgy, *J. Am. Chem. Soc.*, **60**, 983 (1938).
247. Kuhn and Wendt, *Ber.*, **71**, 780, 1118, 1534 (1938).
248. Keresztesy and Stevens, *J. Am. Chem. Soc.*, **60**, 1267 (1938).
249. Kuhn, Andersag, Westphal, and Wendt, *Ber.*, **72**, 309 (1939).
250. Kuhn and Wendt, *Ber.*, **72**, 305 (1939).
251. Stiller, Keresztesy, and Stevens, *J. Am. Chem. Soc.*, **61**, 1237 (1939).
252. Harris, Stiller, and Folkers, *J. Am. Chem. Soc.*, **61**, 1242 (1939).
253. Harris and Folkers, *J. Am. Chem. Soc.*, **61**, 1245 (1939).
254. Kuhn and Wendt, *Ber.*, **72**, 305 (1939).
255. Harris and Folkers, *J. Am. Chem. Soc.*, **61**, 3307 (1939).
256. Bruce and Coover, *J. Am. Chem. Soc.*, **66**, 2092 (1944); *erratum ibid.*, **67**, 2279 (1944).
257. Morii and Makino, *Enzymologia*, **7**, 385 (1939).
258. U.S. patent 2,399,347, Merck and Co.; *C.A.*, **40**, 4181 (1946).
259. U.S. patent 2,248,078, Merck and Co.; *C.A.*, **35**, 6741 (1941).
260. U.S. patent 2,382,876, Merck and Co.; *C.A.*, **40**, 6825 (1946).
261. U.S. patent 2,349,267, Merck and Co.
262. U.S. patent 2,280,831, Merck and Co.; *C.A.*, **36**, 5618 (1942).
263. U.S. patent 2,266,754, Merck and Co.; *C.A.*, **36**, 2378 (1942).
264. U.S. patent 2,272,198, Merck and Co.; *C.A.*, **36**, 3634 (1942).
265. U.S. patent 2,372,690, Merck and Co.; *C.A.*, **39**, 4199 (1945).
266. U.S. patent 2,380,478, Merck and Co.; *C.A.*, **39**, 5410 (1945).
267. British patent 2,538,000, Merck and Co.; *C.A.*, **36**, 1614 (1942).
268. U.S. patent 2,422,616, Merck and Co.
269. U.S. patent 2,422,195, Merck and Co.; *C.A.*, **41**, 5555 (1947).
270. U.S. patent 2,422,617, Merck and Co.; *C.A.*, **41**, 5554 (1947).
271. U.S. patent 2,422,618, Merck and Co.; *C.A.*, **41**, 5554 (1947).
272. U.S. patent 2,422,619, Merck and Co.; *C.A.*, **41**, 5554 (1947).
273. U.S. patent 2,422,620, Merck and Co.; *C.A.*, **41**, 5555 (1947).
274. U.S. patent 2,422,621, Merck and Co., *C.A.*, **41**, 5555 (1947).
275. U.S. patent 2,422,622, Merck and Co.; *C.A.*, **41**, 5555 (1947).
276. U.S. patent 2,325,053, Merck and Co.; *C.A.*, **38**, 2215 (1944).
278. British patent 2,557,804, Merck and Co., *C.A.*, **39**, 3398 (1945).
279. U.S. patent 2,600,676, Merck and Co.; *C.A.*, **42**, 7344 (1948).
280. U.S. patent 2,538,000, Merck and Co.; *C.A.*, **36**, 1614 (1942).
281. U.S. patent 2,534,916, Merck and Co.; *C.A.*, **36**, 1739 (1942).
282. U.S. patent 2,593,796, Merck and Co.; *C.A.*, **42**, 1710 (1948).
283. U.S. patent 2,390,593, Merck and Co.; *C.A.*, **40**, 1636 (1946).

284. U.S. patent 2,412,272, Merck and Co.; *C.A.*, **41**, 2212 (1947).
285. British patent 2,603,442, Merck and Co.; *C.A.*, **43**, 1067 (1949).
286. U.S. patent 2,481,573, Merck and Co.; *C.A.*, **44**, 668 (1950).
287. U.S. patent 2,476,464, Merck and Co.; *C.A.*, **44**, 1145 (1950).
288. U.S. patent 2,483,137, Merck and Co.; *C.A.*, **44**, 1545 (1950).
289. U.S. patent 2,389,054, Hoffer to Hoffman-LaRoche, *C.A.*, **40**, 905, 6214 (1946); also U.S. patents 2,410,938-941, *C.A.*, **41**, 1395 (1947).
290. Jones and Kornfeld, *J. Am. Chem. Soc.*, **73**, 107 (1951).
291. Jones, *J. Am. Chem. Soc.*, **73**, 5244 (1951).
292. Itiba and Emoto, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **38**, 347 (1941), *C.A.*, **35**, 6960 (1941).
293. Matsukawa and Kenzo, *J. Pharm. Soc. Japan*, **71**, 1498 (1951).
294. U.S. patent 2,349,318, Westphal to Winthrop Chem. Co.; *C.A.*, **39**, 1513 (1945).
295. Kuhn, Westphal, Wendt, and Westphal, *Naturwissenschaften*, **27**, 469 (1939).
296. German patent 707,428, Kuhn and Wendt to I. G. Farben; *C.A.*, **37**, 2745 (1943).
297. Kuhn and Wendt, *Ber.*, **72**, 311 (1939); U.S. patent 2,286,915, *C.A.*, **36**, 7242 (1942).
298. U.S. patent 2,250,396, Salzer to Winthrop Chemical Co.; *C.A.*, **35**, 7123 (1941).
299. Mowat, Pilgrim, and Carlson, *J. Am. Chem. Soc.*, **65**, 954 (1943).
300. U.S. patents 2,310,167–172, Carlson to Lederle; *C.A.*, **37**, 4207 (1943).
301. Cohen, Haworth, and Hughes, *J. Chem. Soc.*, **1952**, 4374.
302. U.S. patent 2,680,743, Stevens to General Aniline; *C.A.*, **49**, 6315 (1955).
303. U.S. patent 2,734,063, Stevens to General Aniline; *C.A.*, **50**, 13099 (1956).
304. Elming and Clauson-Kaas, *Acta Chem. Scand.*, **9**, 23 (1955).
305. Danish patent 80,971, *C.A.*, **50**, 14811 (1956). See also Kornfeld, *J. Org. Chem.*, **20**, 1135 (1955) and Williams, Kaufmann, and Mosher, *J. Org. Chem.*, **20**, 1139 (1957).
306. Perez-Medina, Mariella, and McElvain, *J. Am. Chem. Soc.*, **69**, 2574 (1947).
307. Gibbs, *J. Biol. Chem.*, **72**, 649 (1927).
308. Scudi, Koones, and Keresztesy, *Proc. Soc. Exptl. Biol. Med.*, **43**, 118 (1940).
309. Scudi, *J. Biol. Chem.*, **145**, 637 (1942).
310. Bird, Vandenbelt, and Emmett, *J. Biol. Chem.*, **142**, 317 (1942).
311. Bina, Thomas, and Brown, *J. Biol. Chem.*, **148**, 111 (1943).
312. Hochberg, Melnick, and Oser, *J. Biol. Chem.*, **155**, 119 (1944).
313. Melnick, Hochberg, Himes, and Oser, *J. Biol. Chem.*, **160**, 1 (1945).
314. Waisman and Elvehjem, *Ind. Eng. Chem.*, **13**, 221 (1941).
315. Brown, Bina, and Thomas, *J. Biol. Chem.*, **158**, 455 (1945).
316. Swaminathan, *Nature*, **145**, 780 (1940).
317. Kuhn and Löw, *Ber.*, **72**, 1453 (1939).
318. Sarma, Snell, and Elvehjem, *J. Biol. Chem.*, **165**, 55 (1946).

319. Hopkins and Pennington, *Biochem. J.*, **41**, 110 (1947).
320. Hochberg, Melnick, and Oser, *J. Biol. Chem.*, **155**, 129 (1944).
321. Unna and Antopol, *Proc. Soc. Exptl. Biol. Med.*, **43**, 116 (1940).
322. Huff and Perlzweig, *J. Biol. Chem.*, **155**, 345 (1944).
323. Johnson, Hamilton, and Mitchell, *J. Biol. Chem.*, **158**, 619 (1945).
324. Harris, *J. Am. Chem. Soc.*, **62**, 3203 (1940).
325. Moller, *Naturwissenschaften*, **27**, 288 (1939).
326. Harris, *J. Am. Chem. Soc.*, **63**, 3363 (1941).
327. Cohen and Hughes, *J. Chem. Soc.*, **1952**, 4384.
328. British patent, 715,212; *C.A.*, **49**, 13300 (1955).
329. Harris, Webb, and Folkers, *J. Am. Chem. Soc.*, **62**, 3198 (1940).
330. Itiba and Miti, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **35**, 73 (1938); *C.A.*, **33**, 3430 (1939).
331. Sakuragi and Kummerow, *J. Am. Chem. Soc.*, **78**, 838 (1956).
332. Sakuragi and Kummerow, *J. Am. Chem. Soc.*, **78**, 839 (1956).
333. Snell, Gutard, and Williams, *J. Biol. Chem.*, **143**, 519 (1942).
334. Snell, *J. Am. Chem. Soc.*, **66**, 2082 (1944).
335. Snell, *J. Biol. Chem.*, **154**, 313 (1944).
336. Harris, Heyl, and Folkers, *J. Am. Chem. Soc.*, **66**, 2088 (1944).
337. Harris, Heyl, and Folkers, *J. Biol. Chem.*, **154**, 315 (1944).
338. Heyl, *J. Am. Chem. Soc.*, **70**, 3434 (1948).
339. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **70**, 1670 (1948).
340. Heyl, Harris, and Folkers, *J. Am. Chem. Soc.*, **70**, 3429 (1948).
341. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **70**, 3669 (1948).
342. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **74**, 414 (1952).
343. U.S. patent 2,695,297; *C.A.*, **49**, 13297 (1955).
344. U.S. patent, 2,683,716; *C.A.*, **49**, 10383 (1955).
345. Eichorn and Dawes, *J. Am. Chem. Soc.*, **76**, 5663 (1954).
346. Metzler, *J. Am. Chem. Soc.*, **79**, 485 (1957).
347. Baddiley, *Nature*, **170**, 711 (1952).
348. McCullough, Piligian and Daniel, *J. Am. Chem. Soc.*, **79**, 628 (1957).
349. Longnecker and Snell, *J. Am. Chem. Soc.*, **79**, 142 (1957).
350. Cennamo, Carafoli, and Bonetti, *J. Am. Chem. Soc.*, **78**, 3523 (1956).
351. Snell and Rabinowitz, *J. Am. Chem. Soc.*, **70**, 3432 (1948).
352. Metzler and Snell, *J. Am. Chem. Soc.*, **74**, 979 (1952).
353. Snell and Rabinowitz, *J. Am. Chem. Soc.*, **75**, 998 (1953).
354. Metzler, Longnecker, and Snell, *J. Am. Chem. Soc.*, **76**, 639 (1954).
355. Metzler, Olivard, and Snell, *J. Am. Chem. Soc.*, **76**, 644 (1954).
356. Metzler, Ikawa, and Snell, *J. Am. Chem. Soc.*, **76**, 648 (1954).
357. Puztai, *Acta Physiol. Acad. Sci. Hung.*, **9**, 381 (1956); *C.A.*, **50**, 16890 (1956).
358. Schwartzman and Fisher, *J. Biol. Chem.*, **167**, 345 (1947).
359. Snell and Rannefeld, *J. Biol. Chem.*, **157**, 475 (1945).
360. Snell, *J. Biol. Chem.*, **157**, 491 (1945).
361. Sah, *J. Am. Chem. Soc.*, **76**, 300 (1954).

362. Emoto, *J. Sci. Research Inst. (Tokyo)*, **47**, 37 (1953); *C.A.*, **48**, 12095 (1954).
363. Wiegand, *J. Am. Chem. Soc.*, **78**, 5307 (1956).
364. Viscontini, Ebnöther, and Karrer, *Helv. Chim. Acta*, **34**, 2438 (1951).
365. Harris and Wilson, *J. Am. Chem. Soc.*, **63**, 2526 (1941).
366. U.S. patent 2,480,649; *C.A.*, **44**, 1144.
367. Rabinowitz and Snell, *Arch. Biochem. Biophys.*, **43**, 399, 408 (1953).
368. Ikawa and Snell, *J. Am. Chem. Soc.*, **76**, 637 (1954).
369. Davoll and Kipping, *J. Chem. Soc.*, **1953**, 1395.
370. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **75**, 4079 (1953).
371. Cohen and Silk, *J. Chem. Soc.*, **1952**, 4386.
372. Rabinowitz and Snell, *Arch. Biochem. Biophys.*, **43**, 399 (1953).
373. Ott, *Proc. Exptl. Biol. Med.*, **61**, 125 (1946).
374. Van Wagtendonk and Wibaut, *Rec. trav. chim.*, **61**, 728 (1942).
375. Moller, Zima, Jung, and Moll, *Naturwissenschaften*, **27**, 228 (1939).
376. Cravens and Snell, *J. Am. Chem. Soc.*, **71**, 73 (1949).
377. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **75**, 4080 (1953).
378. Rabinowitz and Snell, *Arch. Biochem. Biophys.*, **43**, 408 (1953).
379. Heyl, Harris, and Folkers, *J. Am. Chem. Soc.*, **75**, 653 (1953).
380. Ichiba, Michi, and Emoto, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **39**, 126 (1941); *C.A.*, **41**, 6246 (1947).
381. Perez-Medina, Mariella, and McElvain, *J. Am. Chem. Soc.*, **69**, 2574 (1947).
382. Mariella and Leech, *J. Am. Chem. Soc.*, **71**, 331 (1949).
383. Mariella and Belcher, *J. Am. Chem. Soc.*, **74**, 4049 (1952).
384. Mariella and Belcher, *J. Am. Chem. Soc.*, **73**, 2616 (1951).
385. Mariella and Havlik, *J. Am. Chem. Soc.*, **73**, 1864 (1951).
386. Jones, *J. Am. Chem. Soc.*, **74**, 1489 (1952).
387. Ott, *Proc. Soc. Exptl. Biol. Med.*, **66**, 215 (1947).
388. Williams, Eakin, Bierstecher, and Shive, *Biochemistry of B Vitamins*, Reinhold, N. Y., 1950, p. 652.
389. Unna, *Proc. Soc. Exptl. Biol. Med.*, **43**, 122 (1940).
390. Umbreit and Gunsalus, *J. Biol. Chem.*, **179**, 279 (1949).
391. Umbreit and Waddell, *Proc. Soc. Exptl. Biol. Med.*, **70**, 293 (1949).
392. Bellamy, Umbreit, and Gunsalus, *J. Biol. Chem.*, **160**, 461 (1945).
393. O'Kane and Gunsalus, *J. Biol. Chem.*, **170**, 425 (1942).
394. Umbreit, Bellamy, and Gunsalus, *Arch. Biochem.*, **7**, 185 (1945).
395. Wood, Gunsalus, and Umbreit, *J. Biol. Chem.*, **170**, 313 (1947).
396. Wood and Gunsalus, *J. Biol. Chem.*, **190**, 403 (1951).
397. Gunsalus, Bellamy, and Umbreit, *J. Biol. Chem.*, **155**, 685 (1944).
398. Gunsalus, Umbreit, Bellamy, and Faust, *J. Biol. Chem.*, **161**, 743 (1945).
399. Viscontini and Karrer, *Helv. Chim. Acta*, **34**, 2435 (1951).
400. Lichstein, Gunsalus, and Umbreit, *J. Biol. Chem.*, **161**, 311 (1945).
401. Karrer and Viscontini, *Helv. Chim. Acta*, **30**, 52, 524 (1947).
402. Karrer, Viscontini, and Forster, *Helv. Chim. Acta*, **31**, 1004 (1948).
403. Wilson and Harris, *J. Am. Chem. Soc.*, **73**, 4693 (1951).

404. Heyl and Harris, *J. Am. Chem. Soc.*, **73**, 3434 (1951).
405. Baddiley, Thain, and Rodwell, *Nature*, **167**, 556 (1951).
406. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **73**, 3430 (1951).
407. Viscontini, Ebnother, and Karrer, *Helv. Chim. Acta*, **34**, 1834 (1951).
408. Baddiley and Mathias, *J. Chem. Soc.*, **1952**, 2583.
409. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **73**, 3436 (1951).
410. British patent 715,183, Roche Products Ltd.; *C.A.*, **49**, 13299 (1955).
411. Viscontini, Ebnother, and Karrer, *Helv. Chim. Acta*, **34**, 2198 (1951).
412. Viscontini and Karrer, *Helv. Chim. Acta*, **35**, 1924 (1952).
413. Peterson and Sober, *J. Am. Chem. Soc.*, **76**, 169 (1954).
414. Long and Morrison, *J. Chem. Soc.*, **1954**, 3854.
415. Heyl, Luz, and Harris, *J. Am. Chem. Soc.*, **73**, 3437 (1951).
416. Räth, *Ber.*, **33**, 3476 (1900).
417. Bach, *Ber.*, **34**, 2223 (1901).
418. Löffler and Grunnert, *Ber.*, **40**, 1342 (1907).
419. Räth, *Ber.*, **57**, 840 (1924).
420. Shaw and Wagstaff, *J. Chem. Soc.*, **1933**, 77.
421. Bach, *Ber.*, **34**, 1893 (1901).
422. Räth and Lehmann, *Ber.*, **58**, 342 (1925).
423. Klein, *Ber.*, **23**, 2693 (1890).
424. Stanek and Zvěřina, *C.A.*, **47**, 9971 (1953).
425. Staněk, Hebký, and Zvěřina, *Chem. Listy*, **46**, 735 (1952); *C.A.*, **47**, 12378 (1953).
426. Werner, *Ber.*, **36**, 1683 (1903); Castner, *Ber.*, **34**, 1897 (1901).
427. Dierig, *Ber.*, **35**, 2774 (1902); Knick, *Ber.*, **35**, 2790 (1902).
428. Thorausch, *Ber.*, **35**, 415 (1902).
429. Ollendorf, *Ber.*, **35**, 2782 (1902).
430. Diels and Alder, *Ann.*, **505**, 103 (1933).
431. Winterfeld and Holschneider, *Arch. Pharm.*, **273**, 305 (1935); *Chem. Zentr.*, **1935, II**, 1180.
432. Sperber, Papa, Schwenk, and Sherlock, *J. Am. Chem. Soc.*, **71**, 887 (1949).
433. Czechoslovakian patent 85411, Protiva and Borovicka; *C.A.*, **50**, 10798 (1956).
434. Hurd and Webb, *J. Am. Chem. Soc.*, **49**, 554 (1919).
435. Villani, King, and Papa, *J. Org. Chem.*, **17**, 249 (1952).
436. Chichibabin, *J. prakt. Chem.*, **75**, 526 (1907).
437. Chichibabin, *Ber.*, **61**, 547 (1928).
438. Schofield, *J. Chem. Soc.*, **1949**, 2408.
439. Nunn and Schofield, *J. Chem. Soc.*, **1952**, 589.
440. Dejonge, den Hertog, and Wibaut, *Rec. trav. chim.*, **70**, 989 (1951).
441. Sobecki, *Ber.*, **41**, 4103 (1908).
442. Lyle and Lyle, *J. Am. Chem. Soc.*, **76**, 3536 (1954).
443. Emmert and Pirot, *Ber.*, **74**, 714 (1941).
444. Lochte, Thomas, and Truitt, *J. Am. Chem. Soc.*, **66**, 550 (1944).

445. Sperber, Papa, Schwenk, and Sherlock, *J. Am. Chem. Soc.*, **73**, 3856 (1951).
446. Brown, *J. Chem. Soc.*, **1949**, 2577.
447. Itai and Ogura, *J. Pharm. Soc. Japan*, **75**, 296 (1955); *C.A.*, **50**, 1810 (1956).
448. Shono, Yasumura, and Oda, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **57**, 902 (1954); *C.A.*, **50**, 999 (1956).
449. Iddles, Lang, and Gregg, *J. Am. Chem. Soc.*, **59**, 1945 (1937).
450. Arens, van Dorp, and van Dijk, *Rec. trav. chim.*, **69**, 287 (1950).
451. Kloppenburg and Wibaut, *Rec. trav. chim.*, **65**, 393 (1946).
452. British patent 687,288.
453. U.S. patent 2,663,711, Bullitt.
454. Gilman and Spatz, *J. Org. Chem.*, **16**, 1485 (1951).
455. Overhoff and Proost, *Rec. trav. chim.*, **57**, 179 (1938).
456. Knott, Ciric, and Breckenridge, *Can. J. Chem.*, **31**, 615 (1953).
457. Wibaut, Wallingford, Rang, and Kettenes, *Rec. trav. chim.*, **74**, 1049 (1953).
458. French and Sears, *J. Am. Chem. Soc.*, **73**, 469 (1951).
459. Wibaut, de Jonge, van der Voort, and Otto, *Rec. trav. chim.*, **70**, 1054 (1951).
460. Nunn and Schofield, *J. Chem. Soc.*, **1953**, 716.
461. Wibaut and Heeringa, *Rec. trav. chim.*, **74**, 1003 (1955).
462. Tilford and van Campen, *J. Am. Chem. Soc.*, **76**, 2431 (1954).
463. Bergmann and Rosenthal, *J. prakt. Chem.*, **135**, 267 (1932).
464. Beyerman, Eveleens, and Muller, *Rec. trav. chim.*, **75**, 63 (1956).
465. Profft and Schneider, *J. prakt. Chem.*, (4) **2**, 315 (1955).
466. Goldberg, Barkley, and Levine, *J. Am. Chem. Soc.*, **73**, 4301 (1951).
467. Chichibabin, *Rec. trav. chim.*, **57**, 582 (1938).
468. Löffler and Stretzel, *Ber.*, **20**, 1208 (1887).
469. Sperber, Papa, Schwenk, Sherlock, and Fricano, *J. Am. Chem. Soc.*, **73**, 5752 (1951).
470. Rubtsov and Mikhlina, *Zhur. Obshchel Khim.*, **25**, 2303 (1955).
471. Beckett, Kerridge, Clarke, and Smith, *J. Pharm. and Pharmacol.*, **7**, 717 (1955).
472. Beets, *Chem. Weekblad*, **39**, 187 (1942).
473. Beets, *Rec. trav. chim.*, **63**, 120 (1944).
474. Wibaut, Kloppenburg, and Beets, *Rec. trav. chim.*, **63**, 134 (1940).
475. Wibaut and van der Voort, *Rec. trav. chim.*, **71**, 798 (1952).
476. Berger, Ziering, and Lee, *J. Org. Chem.*, **12**, 904 (1947).
477. Osuch and Levine, *J. Org. Chem.*, **21**, 1099 (1956).
478. Berger, Ziering, and Lee, *J. Org. Chem.*, **12**, 905 (1947).
479. German patent 834,407, Arens, Van Dorp, and Herloff; *C.A.*, **50**, 2684 (1956).
480. Prelog and Geyer, *Helv. Chim. Acta*, **29**, 1595 (1946).
481. Wilson and Harris, *J. Am. Chem. Soc.*, **73**, 2388 (1951).
482. Raffauf, *Helv. Chim. Acta*, **33**, 102 (1950).

483. Adams and Billinghurst, *J. Chem. Soc.*, **1950**, 1039.
484. British patent, 689,234, *C.A.*, **48**, 4007 (1954).
485. British patent 718,276, *C.A.*, **50**, 1090 (1956).
486. British patent, 682,160, *C.A.*, **48**, 184 (1954).
487. Chichibabin and Knunjanz, *Ber.*, **62**, 3048 (1929).
488. Von Braun and Weisbach, *Ber.*, **63B**, 2018 (1930).
489. U.S. patent 2,657,212. *C.A.*, **49**, 5533 (1955); British patent 700,757, *C.A.*, **49**, 10382 (1955).
490. Swiss patent, 220,214; *C.A.*, **42**, 6860 (1948).
491. British patent, 550,889; *C.A.*, **38**, 1850 (1944).
492. Kuhn and Wendt, *Ber.*, **71**, 1534 (1938).
493. Itiba and Miti, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **35**, 73 (1938); *C.A.*, **33**, 3430 (1939).
494. Baker and McEvoy, *J. Org. Chem.*, **20**, 136 (1955).
495. Hardegger and Mikles, *Helv. Chim. Acta*, **39**, 505 (1956).
496. Velluz and Amiard, *Bull. soc. chim. France*, **1947**, 136.
497. Scott, Norris, Heuser, and Bruce, *J. Am. Chem. Soc.*, **67**, 157 (1945).
498. U.S. patent 2,384,136, Schnider; *C.A.*, **40**, 611 (1946).
499. Lehmann, *Chim. and Ind. (Paris)*, **63, No. 3 bis**, 474 (1950); *C.A.*, **47**, 6891 (1953).
500. Belgian patent 486,234, Morren; *C.A.*, **49**, 4023 (1955).
501. Schmelkes and Joiner, *J. Am. Chem. Soc.*, **61**, 2562 (1939).
502. Rabe, Huntenburg, Schultze, and Volger, *Ber.*, **64**, 2487 (1931).
503. Norton, Skinner, and Shive, *J. Org. Chem.*, **26**, 1495 (1961).
504. Armit and Nolan, *J. Chem. Soc.*, **1931**, 3023.
505. Thomas and Marxer, *Helv. Chim. Acta*, **43**, 464 (1960).
506. Elming and Clauson-Kaas, U.S. patent 2,944,059, July 5, 1960, *C.A.*, **54**, 24812 (1960).
507. Yoshida and Kumagae, *Nippon Kaguku Zasshi*, **80**, 1315 (1959); *C.A.*, **55**, 4496 (1961); *Kogyo Kaguku Zasshi*, **59**, 196 (1956).
508. Walker, *J. Org. Chem.*, **25**, 1047 (1960).
509. Hamana and Umezawa, *Chem. Pharm. Bull. (Tokyo)*, **8**, 692 (1960); *C.A.*, **55**, 18723 (1961).
510. Kost, Terentev, and Zavanda, *Doklady Akad. Nauk S.S.S.R.*, **130**, 326 (1960); *C.A.*, **54**, 11015 (1960).
511. Godar and Mariella, *J. Org. Chem.*, **25**, 557 (1960).
512. Smith and Holley, *J. Am. Chem. Soc.*, **80**, 3714 (1958).
513. Mathes and Sauermilch, *Ber.*, **93**, 286 (1960).
514. U.S. patent 2,966,494, Allen and Bencze, Ciba Pharm. Prod., Inc.; *C.A.*, **55**, 7442 (1961).
515. Yoshida and Kumagae, *Nippon Kagaku Zasshi*, **81**, 345 (1960); *C.A.*, **55**, 6477 (1961).
516. Nakashima and Endo, *Nippon Kagaku Zasshi*, **81**, 816 (1960); *C.A.*, **56**, 5923 (1962).

517. Bobbitt and Scola, *J. Org. Chem.*, **25**, 560 (1960).
518. Sato, Iwashige, and Miyadera, *Chem. Pharm. Bull. (Tokyo)*, **8**, 427 (1960).
519. Miller and Levine, *J. Org. Chem.*, **24**, 1364 (1959).
520. Zymalkowski, *Arch. Pharm.*, **291**, 12 (1958).
521. Merz and Stolte, *Arch. Pharm.*, **292**, 496 (1959).
522. Robertson, *J. Org. Chem.*, **25**, 374 (1960).
523. Dornow and Boberg, *Ann.*, **578**, 101 (1952).
524. Bolhme and Koo, *J. Org. Chem.*, **26**, 3589 (1961).
525. Boekelheide and Lehn, *J. Org. Chem.*, **26**, 428 (1961).
526. Sato, Iwashige, and Miyadera, *Chem. Pharm. Bull. (Tokyo)*, **8**, 427 (1960).
527. Endo and Nakashima, *Yakugaku Zasshi*, **80**, 875 (1960); *C.A.*, **54**, 24705 (1960).
528. Hamana and Yamazaki, *Yakugaku Zasshi*, **81**, 612 (1961); *C.A.*, **55**, 24742 (1961).
529. Furukawa, *Yakugaku Zasshi*, **59**, 478, 492 (1959); *C.A.*, **53**, 18028 (1959).
530. Biland, Lohse, and Hardegger, *Helv. Chim Acta*, **43**, 1436 (1960).
531. Nishimoto and Nakashima, *Yakugaku Zasshi*, **81**, 88 (1961); *C.A.*, **55**, 13420 (1961).
532. Traynelis and Martello, *J. Am. Chem. Soc.*, **80**, 6590 (1958).
533. Oae, Kutuo, and Ktooka, *Chem. Ind.*, **1961**, 515.
534. Nakamoto and Martell, *J. Am. Chem. Soc.*, **81**, 5857 (1959).
535. Profft and Linke, *Chem. Ber.*, **93**, 2591 (1960).
536. Jerchel and Heck, *Ann.*, **613**, 171, 180 (1958).
537. Duncan and Scales, *Biochem. J.*, **80**, 1p (1961).
538. Naito and Veno, *Yakugaku Zasshi*, **79**, 1277 (1959); *C.A.*, **54**, 4566 (1960).
539. Miller and Levine, *J. Org. Chem.*, **24**, 1364 (1959).
540. Benington, Morin, and Clarke, *J. Org. Chem.*, **25**, 1912 (1960).
541. Freifelder, Robinson, and Stone, *J. Org. Chem.*, **27**, 284 (1962).
542. Lavagino, Chauvette, Cannon, and Kornfeld, *J. Am. Chem. Soc.*, **82**, 2609 (1960).
543. Zymalkowski and Koppe, *Arch. Pharm.*, **294**, 453 (1961).
544. Furst and Haug, *J. prakt. chem.*, **10**, 343 (1960).
545. Schneider, German patent 1,046,055, Dec. 11, 1958; *C.A.*, **55**, 5537 (1961).
546. Vejdělek, Trčka, Hejný, and Vyšatová, *Collection Czechoslov. Chem. Communs.*, **19**, 1274 (1954).
547. Vejdělek, Trčka, and Vyšatová, *Chem. Listy*, **48**, 1221 (1954).
548. Berson and Eviett, *Chem. & Ind. (London)*, **1959**, 901.
549. Huebner, Ciba Pharm. Prod. Inc., U.S. patent 2,970,149.
550. Bencze and Allen, U.S. patent 2,923,710; *C.A.*, **54**, 9963 (1960).
551. Profft and Linke, *Ber.*, **93**, 2591 (1960).
552. Galbraith, Small, Barnes, and Boekelheide, *J. Am. Chem. Soc.*, **83**, 453 (1961).
553. Zymalkowski and Koppe, *Arch. Pharm.*, **294**, 453 (1961).

554. Rubinstein and Christiansen, *Acta Chem. Scand.*, **12**, 1274 (1958).
555. Allen, Pierson, and Siragusa, *J. Chem. Soc.*, **1961**, 2081.
556. Zymalkowski and Koppe, *Naturwissenschaften*, **47**, 203 (1960).
557. Allen, Pierson, and Siragusa, *J. Chem. Soc.*, **1961**, 757.
558. Raschig, G. m. b. h., British patent 824,554, Dec. 2, 1959; *C.A.*, **54**, 8860 (1960).
559. Allen and Bencze, Ciba Pharm. Prod., Inc., U.S. patent 2,966,493; *C.A.*, **55**, 7442 (1961).
560. Klosa, *J. prakt. chem.*, **10**, 335 (1960).
561. DeFazi, Carboni, and Marsili, *Gazz. Chim. Ital.*, **89**, 1701, 1709 (1959).
562. Wuest, Bigot, DeBoer, vander Wal, and Wibaut, *Rec. trav. chim.*, **78**, 226 (1959).
563. Ichiba and Emoto, *J. Sci. Research Inst. (Tokyo)*, **43**, 30 (1948); *C.A.*, **43**, 4670 (1949).
564. Kon'kova and Petrova, *Tr. Vses. Nauchn. Issled. Vitamin. Inst.*, **6**, 10 (1959); *C.A.*, **55**, 12399 (1961).
565. Pollack, Merck and Co., U.S. patent 2,904,551; *C.A.*, **55**, 572 (1960).
566. Merck & Co., British patent 834,451; *C.A.*, **55**, 17657 (1961).
567. McCasland, Gottwald, and Furst, *J. Org. Chem.*, **26**, 3541 (1961).
568. Clauson-Kaas and Elming, U.S. patent 2,875,207; *C.A.*, **54**, 569 (1960).
569. Manoušek, *Collection Czechoslov. Chem. Communs.*, **25**, 2250 (1960).
570. Banks, Diamantis, and Vernon, *J. Chem. Soc.*, **1961**, 4235.
571. Mowat and Webb to Am. Cyan. Co., U.S. patent 2,918,471; *C.A.*, **54**, 8855 (1960).
572. British patent 804,236; *C.A.*, **54**, 7743 (1960).
573. British patent 839,583, Pfizer, 1960; *C.A.*, **55**, 1662 (1961).
574. vander Wal, DeBoer, and Huisman, *Rec. trav. chem.*, **80**, 228 (1961).
575. Buell and Hansen, *J. Am. Chem. Soc.*, **82**, 6042 (1960).
576. Christensen, *J. Am. Chem. Soc.*, **81**, 6495 (1959).
577. Cennamo, *Boll. Soc. Ital. Biol. Spec.*, **37**, 183 (1961); *C.A.*, **56**, 1725 (1962).
578. Cennamo, *Boll. Soc. Ital. Biol. Spec.*, **37**, 187 (1961); *C.A.*, **56**, 1725 (1962).
579. Volke, *Chem. Listy*, **55**, 26 (1961); *C.A.*, **55**, 6480 (1961).
580. Hemert, Univ. Microfilms, L. C. card No. MIC 59-6177; *Dist. Abst.*, **20**, 2563 (1960); *C.A.*, **54**, 8814 (1960).
581. Kreisky, *Monatsh.*, **90**, 417 (1959).
582. British patent 852,398; *C.A.*, **55**, 10477 (1961).
583. Bennett, Burger, and Umbreit, *J. Med. Pharm. Chem.*, **1**, 213 (1959).
584. U.S. patent 2,955,155; *C.A.*, **55**, 5539 (1961).
585. Schmidt and Giesselmann, *Angew. Chem.*, **72**, 709 (1960).
586. Curry and Bulen, *J. Org. Chem.*, **25**, 209 (1960).
587. McCosland, Blanz, and Furst, *J. Org. Chem.*, **24**, 1000 (1959).
588. Taborsky, *J. Org. Chem.*, **26**, 596 (1961).
589. Wagtendonk and Wibaut, *Rec. trav. chim.*, **61**, 728 (1942).

590. Wibaut, Uhlenbroek, Kooyman and Kettenes, *Rec. trav. chim.*, **79**, 481 (1960).
591. vander Wal, DeBoer, and Huisman, *Rec. trav. chim.*, **80**, 203 (1961).
592. Pol, Klein, and Bink, *Rec. trav. chim.*, **80**, 217 (1961).
593. vander Wal, DeBoer, and Huisman, *Rec. trav. chim.*, **80**, 221 (1961).
594. Profft and Busse, *Z. Chem.*, **1**, 19 (1961).
595. Profft and Richter, *Wiss. Z. Tech. Hochsch. Chem. Leuna-Merseburg*, **2**, 85 (1959–60); *C.A.*, **54**, 11019 (1960).
596. Lukes, Galik, and Jizba, *Collection Czechoslov. Chem. Communs.*, **26**, 2727 (1961); *C.A.*, **56**, 5924 (1962).
597. Profft, *Chem. Ber.*, **91**, 957 (1958).
598. Bodalski and Micbolski, *Bull. Acad. Polon. Sci., Ser. Sci. Chem.*, **8**, 217 (1960); *C.A.*, **55**, 18721 (1961).
599. Farberov, Uslavshchelsov, Kut'en, Vernova, and Yarosh, *Izuest. Uysshykh Uchev. Zavedenii, Khim. i Khim. Tekhnol.*, 1958, No. 5, 92.
600. Ikekowa, *Chem. Pharm. Bull. (Tokyo)*, **6**, 263 (1958); *C.A.*, **53**, 371 (1959).
601. Ikekowa, *Chem. Pharm. Bull. (Tokyo)*, **6**, 269 (1958); *C.A.*, **53**, 372 (1959).
602. Cale, McGinnis, and Teague, *J. Org. Chem.*, **25**, 1507 (1960).
603. Villani, U.S. patent 2,898,338 to Schering Corp.; *C.A.*, **54**, 580 (1960).
604. Kyte, Jeffery, and Vogel, *J. Chem. Soc.*, **1960**, 4454.
605. Wibaut and Otto, *Rec. trav. chim.*, **77**, 1048 (1958).
606. British patent 834,336; *C.A.*, **55**, 3621 (1961).
607. Gautier, Miocque, and Lafontaine, *Bull. Soc. Chim., France*, **1960**, 1121.
608. Gautier, Miocque, and Lafontaine, *Bull. Soc. Chim., France*, **1960**, 1117.
609. U.S. patent 3,007,934, Bencze, Ciba Pharm. Prod., Inc.
610. Tissier, *C. R. Acad. Sci.*, **252**, 2301, 2308 (1961).
611. Lüttringhaus and Berrer, *Tetrahedron Letters*, No. 10, 10–12 (1959).
612. Büchi, Kracher, and Schmidt, *Helv. Chim. Acta*, **45**, 729 (1962).
613. Gadekar, Frederick, and DeRenso, *J. Med. Pharm. Chem.*, **5**, 531 (1962).
614. Terent'ev, Kost, Shehegoler, and Terent'ev, *Doklady Nauk. S.S.S.R.*, **141**, 110 (1961); *C.A.*, **56**, 11564 (1962).
615. Ravenna, *Farmaco (Pavia) Ed. Sci.*, **14**, 483 (1959); *C.A.*, **55**, 9925 (1961).
616. Miocque, *Bull. soc. chim. France*, **1960**, 330.
617. Papa, Villani, and Ginsberg, *J. Am. Chem. Soc.*, **76**, 4446 (1954).
618. Arata and Asai, *Yakugaku Zasshi*, **79**, 1442 (1959); *C.A.*, **54**, 6712 (1960).
619. Kobayashi and Furukawa, *Pharm. Bull. (Tokyo)*, **1**, 347 (1953); *C.A.*, **49**, 10948 (1955).
620. British patent 850,299; *C.A.*, **55**, 10474 (1961).
621. Sauermilch and Wolf, *Arch. Pharm.*, **292**, 38 (1959).
622. Boyer and Wolford, *J. Org. Chem.*, **23**, 1053 (1958).
623. Davies, Kenyon, and Thaker, *J. Chem. Soc.*, **1956**, 3394.
624. Michalski and Studniarski, *Chem. Tech. (Berlin)*, **9**, 96 (1957); *C.A.*, **51**, 10530 (1957).

625. McLean and Schnizer, U.S. patent 2,754,300; *C.A.*, **51**, 2878 (1957).
626. Ivashchenko and Gepshtein, U.S.S.R. patent 105,851; *C.A.*, **51**, 14829 (1957).
627. Lukes and Galik, *Chem. Listy*, **51**, 2319 (1957); *C.A.*, **52**, 6347 (1958).
628. Swain, U.S. patent 2,800,485 to McNeil Lab., Inc.
629. Bachman, Hamer, Dunning, and Schisla, *J. Org. Chem.*, **22**, 1296 (1957).
630. Elming, *Acta Chem. Scand.*, **11**, 1496 (1957).
631. Long and Morrison, U.S. patent 2,777,851 to Hoffman-LaRoche, Inc.; *C.A.*, **51**, 12984 (1957).
632. Micovic and Mikailovic, *Rec. trav. chem.*, **71**, 972 (1952).
633. U.S. patent 2,763,658, Reilly Tar and Chemical Co.; *C.A.*, **51**, 3670 (1957).
634. Bellemonte, Calo and Cardini, *Farmaco (Pavia) Ed. Sci.*, **12**, 722 (1957); *C.A.*, **52**, 11832 (1958).
635. Cavallini, Ravenna, and Grassu, *Farmaco (Pavia) Ed. Sci.*, **12**, 887 (1957); *C.A.*, **52**, 11848 (1958).
636. Suzuki, *Pharm. Bull. (Tokyo)*, **4**, 211, 479 (1956); *C.A.*, **51**, 7372, 13862 (1957).
637. Sauermilch, *Ber.*, **90**, 833 (1957).
638. Zymalkowski and Schauer, *Arch. Pharm.*, **290**, 267 (1957).
639. Elming and Clauson-Kaas, *Acta Chem. Scand.*, **9**, 23 (1955).
640. Heinert and Martell, *Tetrahedron*, **3**, 49 (1958).
641. Christenson, *J. Am. Chem. Soc.*, **79**, 4073 (1957).
642. Sakuragi and Kummerow, *J. Org. Chem.*, **24**, 1032 (1959).
643. Cislak to Reilly Tar and Chem. Corp., U.S. patent 2,789,982; *C.A.*, **51**, 12985 (1957).
644. Cislak to Reilly Tar and Chem. Corp., U.S. patent 2,750,392; *C.A.*, **51**, 491 (1957).
645. Bader and Oroshnik, *J. Am. Chem. Soc.*, **79**, 5686 (1957).
646. Cislak and McGill to Reilly Tar and Chem. Corp., U.S. patent 2,759,946; *C.A.*, **51**, 2058 (1957).
647. Marékov, *Compt. rend. acad. bulgare sci.*, **9**, 35 (1956); *C.A.*, **52**, 18418 (1958).
648. Jerchel and Heider, *Angew. Chem.*, **70**, 189 (1958).
649. Lüttringhaus and Berrer, *Angew. Chem.*, **70**, 139 (1958).
650. Zymalkowski and Schauer, *Arch. Pharm.*, **290**, 218 (1957).

CHAPTER XIV

Pyridine Aldehydes and Ketones

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The first pyridine aldehyde was prepared about forty years ago. It has only been in the last decade or so, however, that this class of compounds has experienced rapid development. Early syntheses involved such reactions as the ozonolysis of stilbazoles and cleavage of the ozonides, and condensation of activated picolines with aryl nitroso compounds and subsequent cleavage. These reactions were cumbersome, generally giving poor yields, and frequently were not amenable to quantity production. Recent developments, among these the catalyzed gas phase oxidation of methylated pyridines, have made many of the pyridine aldehydes more readily available. The direct formylation of pyridine is of interest; this gives picolinaldehyde in low yield (*278*).

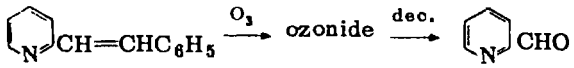
Pyridine ketones, both simple and complex, have been known for many years, and a variety of methods exists for their synthesis. The older synthetic methods include the preparation from aliphatic compounds and ammonia, the dry distillation of mixed calcium salts of pyridine and aliphatic carboxylic acids, mixed ester condensations, and the Friedel-Crafts reaction of pyridine acid chlorides and aromatic hydrocarbons. The extensive development which has occurred in recent years includes a variety of preparative methods which will be discussed in the text.

A. PYRIDINE ALDEHYDES

1. Preparation

a. Oxidation of Unsaturated Compounds or Alcohols

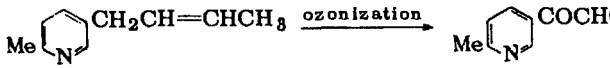
Lenart (*231*) and Harries and Lenart (*135*) described the preparation of picolinaldehyde by ozonolysis of 2-stilbazole and reduction of the ozonide. Other workers have employed this method with varying degrees of success. Hart (*138*), for example, reported the conversion of α-stilbazole to picolinaldehyde in 57 per cent yield by modification of the ozonide decomposition; results were less satisfactory, however, when the process was attempted on anything but a small scale (XIV-1). Wibaut and collaborators (*401*) applied this



(XIV-1)

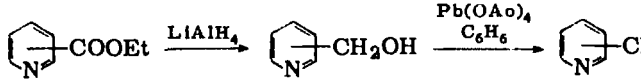
method to the preparation of isonicotinaldehyde, which was isolated in unspecified yield. More recently, Callighan and Wilt (*63*) have prepared a number of pyridine aldehydes in 50 to 80 per cent yields by ozonolysis of the related vinyl pyridine in methanol at – 40°C.

The ozonolysis of 5-(2-butenyl)-2-picoline affords 6-methyl-3-pyridylglyoxal (XIV-2) (*148*), and application of this process to ethyl 6-styrylnicotinate gives ethyl 6-formylnicotinate (*314*).



(XIV-2)

Micovic and Mihailovic (*273*) have prepared pyridine 2-, 3-, and 4-aldehydes by a convenient route. The related carboxylic acid ester undergoes reduction with lithium aluminum hydride to the carbinol, which then gives the aldehyde by selenium dioxide oxidation in good yield. Furakawa and Kurowia (*129*) have prepared pyridine aldehydes in high yields from the alcohols by a similar process (XIV-3).



(XIV-3)

b. Oxidation of Methylpyridines

The oxidation of picolines in solution gives variable yields of aldehydes. The products obtained by oxidation with selenium dioxide in amyl alcohol at 125°C. are for the most part carboxylic acids (*169*); 2-picoline, however, is converted in low yield to picolinaldehyde (*44*). 3-Nitro-4-picoline, on the other hand, gives high yields of 3-nitroisonicotinaldehyde (*21*). While α- and γ-picolines are oxidized readily by this method, β-picoline is apparently unreactive (*434*).

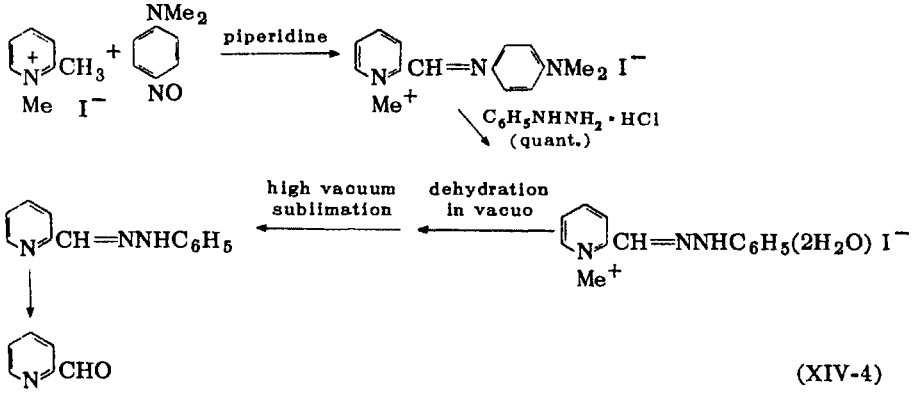
The catalyzed gas-phase oxidation of methylated pyridines has been investigated extensively during recent years. A variety of pyridine aldehydes can be obtained in this way, and some are produced on a commercial scale. The method requires a vanadium pentoxide-molybdenum oxide catalyst supported on silica gel. An aqueous solution of the methylated pyridine is passed over the catalyst at elevated temperatures, usually around 400°C., with carefully controlled quantities of air. 2-Picoline gives picolinaldehyde or α-pyridoin, depending on the air-to-picoline ratio (*268*). Isonicotinaldehyde is formed similarly from 4-picoline. Although 3-picoline is more resistant to oxidation, its conversion to nicotinaldehyde has been indicated.

Polymethylated pyridines give a variety of oxidation products under these conditions. 2,4-Lutidine thus yields 2-methylisonicotinaldehyde, 4-methylpicolinaldehyde, and pyridine-2,4-dialdehyde (*264, 267*). 2,6-Lutidine affords 6-methylpicolinaldehyde and dipicolinaldehyde, and aldehyde collidine (5-ethyl-2-picoline) gives 5-ethylpicolinaldehyde (*259*) under similar conditions. Oxidation of 2,4,6-collidine results in the formation of all possible mono- and dialdehydes: 6-methylpyridine-2,4-dialdehyde, 4-methylpyridine-2,6-dialdehyde, 4,6-dimethylpicolinaldehyde and 2,6-dimethylisonicotinaldehyde. The corresponding trialdehyde, however, has not been reported (*265*).

c. From Picoline Methiodide and p-Nitrosodimethylaniline

The first recorded preparation of picolinaldehyde, that of Kaufmann and Valette (*199*), proceeds by condensation of *p*-nitrosodimethylaniline with 2-picoline methiodide, then conversion to the

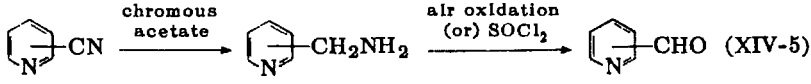
phenylhydrazone and subsequent cleavage to the aldehyde. Although the phenylhydrazone is produced in good yield, the over-all efficiency of the reaction is not stated (XIV-4).



(XIV-4)

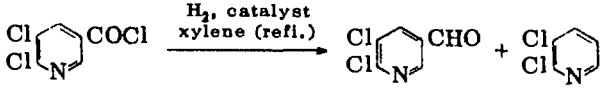
d. Reduction of Pyridinecarboxylic Acid Derivatives

Reductive methods have received extensive application. Graf (*150*) reduced various pyridine nitriles with chromous acetate to the corresponding picolylamines, which yielded the related aldehydes by treatment with nitrosobenzene or thionyl chloride. Air oxidation of the amines proceeds slowly and incompletely to the aldehydes (XIV-5).



(XIV-5)

The Rosenmund reduction of pyridine acid chlorides has also been employed. Graf and associates (*149,151*) prepared a number of chlorinated pyridine aldehydes in moderate yields by this method. Decarbonylation occurs as a side reaction in some cases (XIV-6).

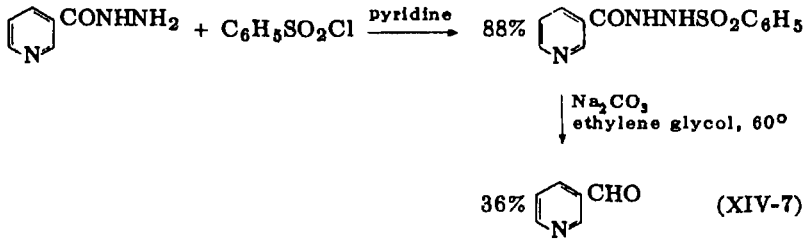


(XIV-6)

Several acid chlorides yielded intensely colored dyes which coated the catalyst and stopped the reaction; this occurred with isonicotin-

oyl, 4-chloropicolinoyl, isocinchomeronoyl, and dipicolinoyl chlorides. Earlier attempts by Rojann and Schulten (*335*) failed, possibly because of impure starting materials. Levelt and Wibaut (*233*) similarly were unsuccessful in the reduction of 2,6-dichloroisonicotinoyl chloride and 2,6-dibromoisonicotinoyl chloride.

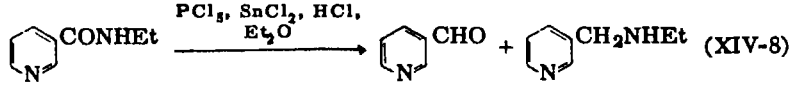
Panizzon (*307*) applied the MacFadyen-Stevens reaction to the synthesis of nicotinaldehyde in low yield from nicotinic hydrazide (XIV-7). Niemann, Lewis, and Hays (*290*) applied the reaction to



(XIV-7)

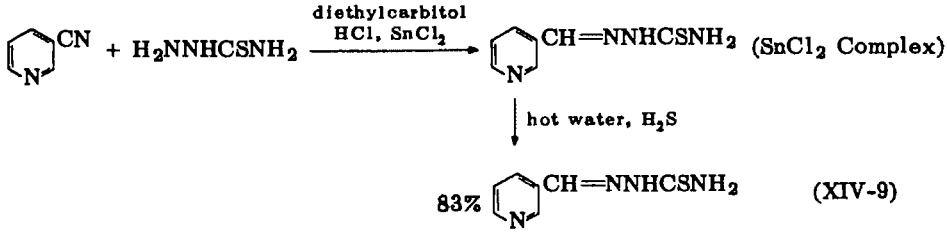
picolinic and nicotinic hydrazides, with similar results. 2-Methylnicotinaldehyde is obtained in 31 per cent yield by this reaction (*95*).

Work (*419*) applied the Sonn-Müller reaction to the synthesis of nicotinaldehyde (XIV-8).



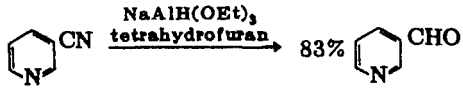
(XIV-8)

Gardner, Smith, Wenis, and Lee (*132*) attributed the low yields of various pyridine aldehydes to their destruction during the reaction. The Stephen reaction of nicotinonitrile in the presence of thiosemicarbazide gives nicotinaldehyde thiosemicarbazone in high yield (XIV-9). The corresponding guanylhydrazone is formed by substi-



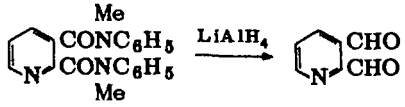
(XIV-9)

tuting aminoguanidine for thiosemicarbazide. The reduction of nicotinonitrile with sodium triethoxyaluminum hydride, however, gives the aldehyde directly and in good yields (XIV-10) (*171*).



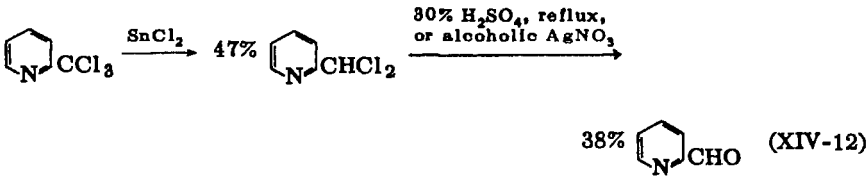
(XIV-10)

Weygand (*394*) has reported the synthesis of two pyridine dialdehydes by reduction of the bis(*N*-methyl)anilides with lithium aluminum hydride (XIV-11). Experimental details, however, are lacking.



(XIV-11)

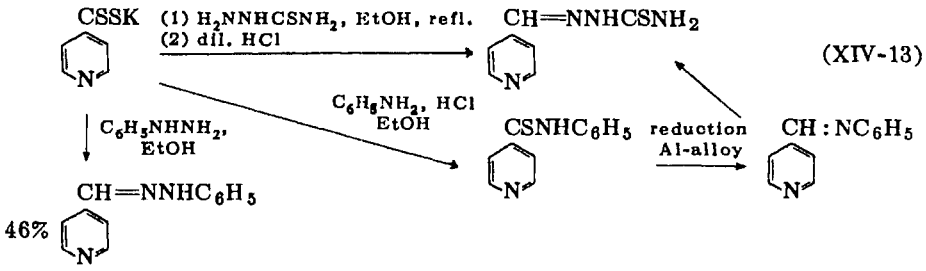
Dyson and Hammick (*99*) reported the preparation of picolinaldehyde from 2-dichloromethylpyridine. The latter substance cannot be obtained by direct chlorination of 2-picoline, which invariably leads to complete halogenation of the side chain; instead, it is obtained by careful reduction of 2-trichloromethylpyridine (XIV-12).



(XIV-12)

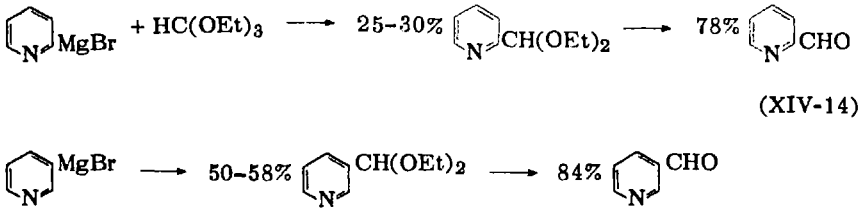
4-Trichloromethylpyridine reacts readily with thiosemicarbazide in refluxing pyridine to give isonicotinaldehyde thiosemicarbazone in 60% yield (*216*).

Dithioisonicotinic acid gives isonicotinaldehyde thiosemicarbazone in low yield by reaction with thiosemicarbazide; with phenylhydrazine the conversion to the phenylhydrazone is moderately successful (*216*). The anil results on reduction of the anilide of this acid, and this gives the aldehyde thiosemicarbazone (XIV-13).



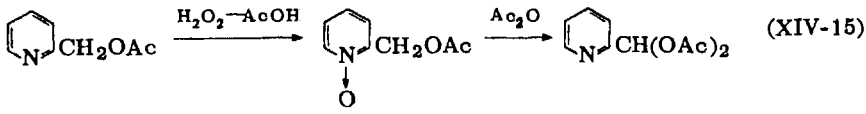
e. From Pyridine Grignard Reagents and Orthoformic Esters

2-, 3-, and 4-Pyridylmagnesium bromides react readily with ethyl orthoformate to afford the corresponding pyridine aldehydes (*165, 397,402,403,441*). Yields were only moderate (XIV-14). (*Cf.* Chapter VII, p. 461).



f. Acetylation of Pyridine-1-Oxides

2-Picoline 1-oxide rearranges on refluxing with acetic anhydride to give 2-acetoxymethyl-pyridine. Repetition of this reaction with 2-acetoxymethylpyridine 1-oxide gives picolinaldehyde diacetate in moderate yield (*40*) (XIV-15). The method is useful in the synthesis of 3-ethylisonicotinaldehyde (*315*). Oxidation occurs preferentially at the 2 position when 2- and 4-methyl groups are available; 2,4-lutidine, for example, gives 4-methylpicolinaldehyde (*291*). 4-Benzyl-2,6-lutidine, however, is oxidized at the 4 position (*213*).



g. Sommelet Reaction

3-Picolylamine reacts with hexamethylenetetramine under conditions of the Sommelet reaction to give a 57% yield of nicotinaldehyde. Gardner, Smith, Wenis, and Lee (*132*) prepared 2-methyl-3-hydroxy-4,5-pyridinedialdehyde dithiosemicarbazone by a modification of this reaction (XIV-16). Similarly, the synthesis of 4,6-dimethyl-5-hydroxy-

(XIV-16)

nicotinaldehyde thiosemicarbazone proceeds from 5-chloromethyl-2,4-dimethyl-3-pyridinol under Sommelet conditions.

h. From Aliphatic Components

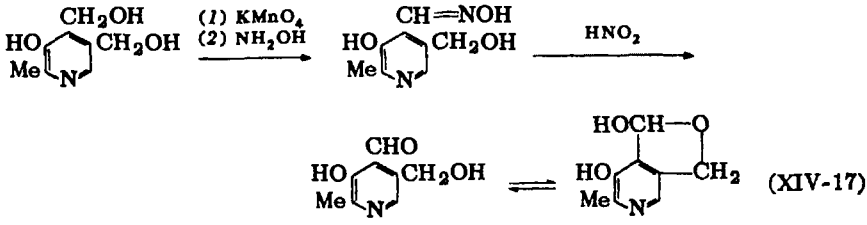
The synthesis of nicotinaldehyde from 2-(dimethylaminomethylene)-3-pentenedial and ammonium chloride has been reported to take place in good yield (*12*).

i. From Picolyllithium and Haloacetals

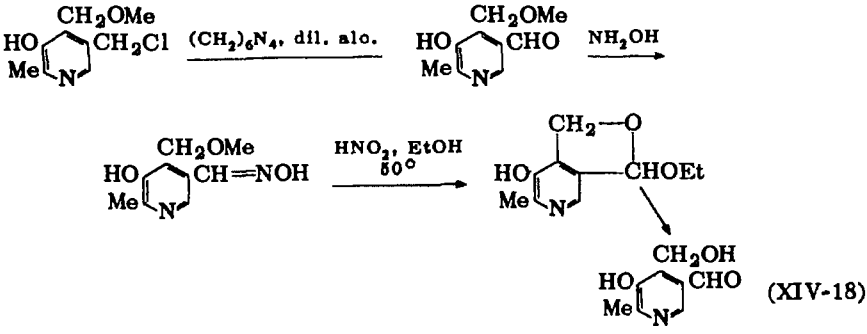
The alkylation of 2-picolyllithium with bromoacetaldehyde diethylacetal gives 2-pyridinepropionaldehyde diethylacetal. This product alone is obtained with phenyllithium as the metallating agent (XIV-22, page 134); the use of propyllithium or butyllithium, however, leads to further alkylation of the methylpyridine as a side reaction (XIV-24 and XIV-25, page 134) (*363*). The corresponding aldehydes are then obtained by hydrolysis.

2. Synthesis of Biologically Important Pyridine Aldehydes (Pyridoxal and Codecarboxylase)

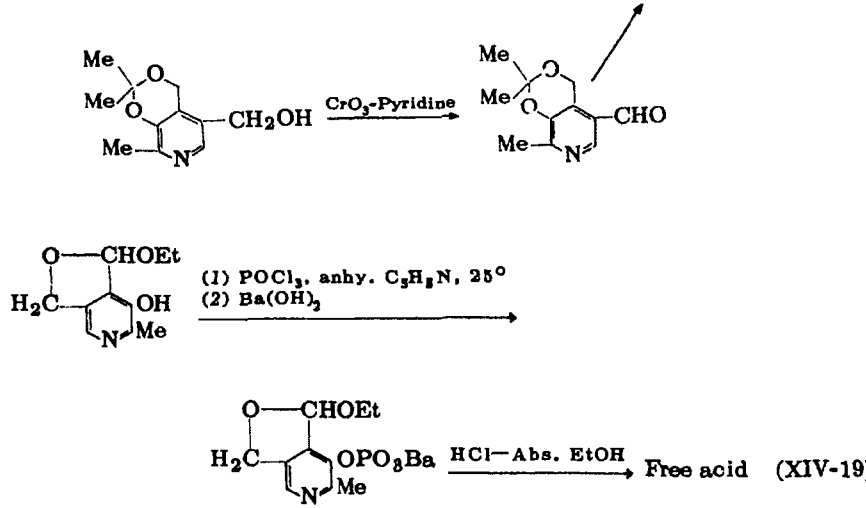
Snell and co-workers (*357*) first demonstrated the existence of a physiologically active metabolite of pyridoxine which was also produced by oxidation of this substance. Harris and co-workers (*161, 162,173*) elucidated the structure of this product (3-hydroxy-5-hydroxymethyl-2-methylisonicotinaldehyde $\rightleftharpoons$ hemiacetal) and synthesized it (XIV-17). The isomeric aldehyde (5-hydroxy-4-hydroxymethyl-6-methylnicotinaldehyde $\rightleftharpoons$ acetal) was also prepared (XIV-18); it possesses no growth-promoting properties (*161*) and is a metabolite of pyridoxine with certain bacteria (*217,333*).



(XIV-17)



(XIV-18)

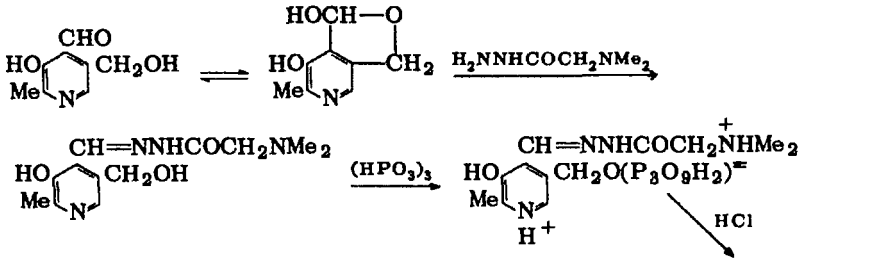


(XIV-19)

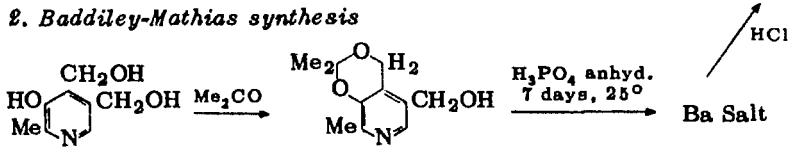
Codecarboxylase (XIV-21) is widely distributed in nature; it functions as the coenzyme of tyrosine decarboxylase and in transaminations. It was first prepared by action of adenosine triphosphate

on pyridoxal and is a phosphorylated derivative of the latter substance. Swiss workers (*196,389*) considered the coenzyme to be phosphorylated in the 3 position; this derivative was prepared and found to differ from the naturally occurring substance (XIV-19). Heyl, Luz, Harris, and Folkers (*174*) demonstrated conclusively that the coenzyme is phosphorylated in the 5 position. A number of syntheses have been devised: (*cf.* Chapter XIII, p.24).

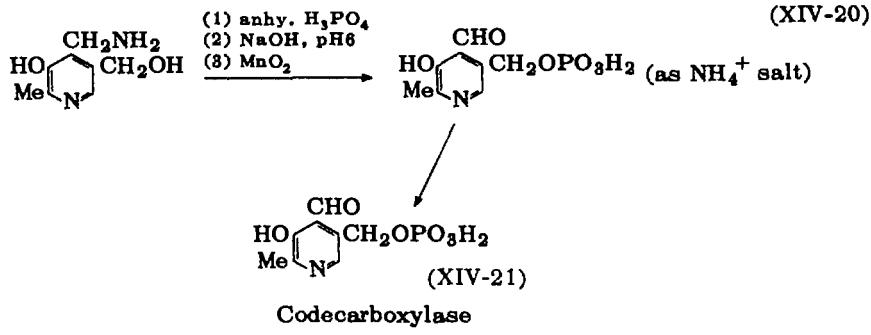
1. Visconti-Ebnöther-Karrer synthesis

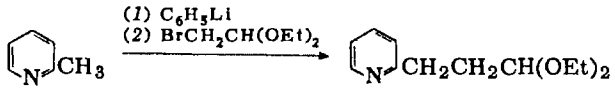


2. Baddiley-Mathias synthesis



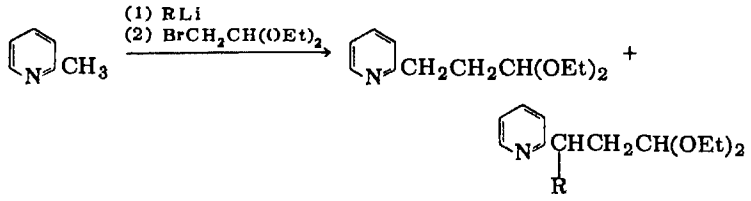
3. Wilson-Harris synthesis





(XIV-22)

(XIV-23)



R = butyl: 5.7% (XIV-24)
R = propyl: 6.8% (XIV-25)

3. Reactions

Pyridine aldehydes are typical aromatic aldehydes in most respects. They give normal carbonyl addition reactions with hydroxylamine, semicarbazide, phenylhydrazine, and other reagents; some of these reactions are discussed below. They react with Grignard reagents to give the expected secondary alcohols (*230,328*) (*cf.* Chapter XIII, p. 28). The 2-and4-isomers undergo aldol condensation with nitromethane; the products are dehydrated readily to pyridylnitroethylenes (*421*). An aldol-like condensation has been reported with diethyl phosphite (*56*). Chapter XI, Table 10 (pp. 384 ff.) summarizes the Perkin condensation and Table 25 (pp. 431 ff.) the Knoevenagel reaction.

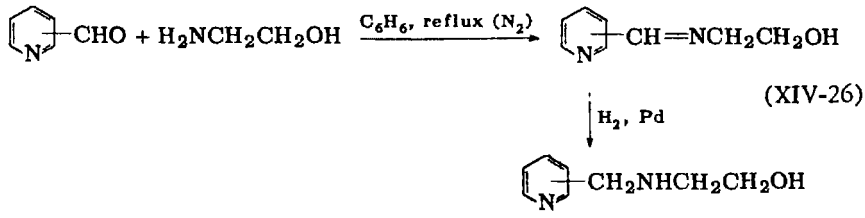
Oxidation to the corresponding acids occurs with great ease. Picolinaldehyde discolors rapidly in air and is oxidized by hydrogen peroxide. Nicotinaldehyde is even more labile. The oxidation of isonicotinaldehyde with dilute hydrogen peroxide gives isonicotinic acid. In like manner, dipicolinaldehyde and 6-carbomethoxypicolinaldehyde afford dipicolinic acid and its monomethyl ester respectively (*261,265,267*).

Pyridine aldehydes react with carbethoxymethyl triphenylphosphonium bromide under conditions of the Wittig reaction to give β-pyridylacrylic esters in almost quantitative yields (*372*).

Picolinaldehyde undergoes decarbonylation to pyridine by heating with palladium on carbon at 180° (*166*). This behavior is similar to that of benzene aldehydes.

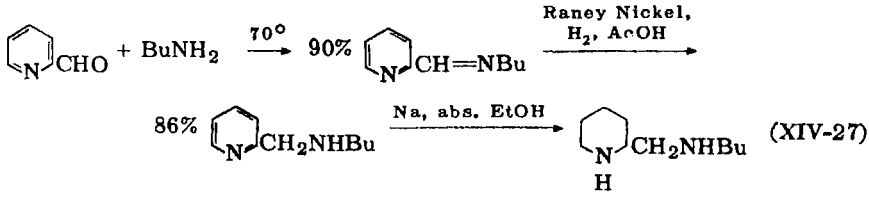
a. Formation and Reduction of Imines

The pyridine aldehydes react with primary amines to form azomethines, which give the expected secondary amines by reduction. This process has been applied to the condensation of pyridine 2-, 3-, and 4-aldehydes with 2-hydroxyethylamine; catalytic reduction of the azomethines (XIV-26) gives the amines (*106*). Profft (*332*) con-



(XIV-26)

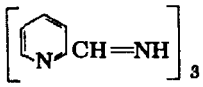
densed butylamine with picolinaldehyde in high yield. Hydrogenation of the azomethine with Raney nickel afforded the secondary amine, and further reduction with sodium and ethanol yields pipecolylbutylamine (XIV-27). Azomethines of this type can be reduced conveniently with sodium borohydride (*281*).



(XIV-27)

The condensation of pyridinealdehydes with chloramine gives the expected *N*-chloroazomethines in moderate to good yields. The product from chloramine and isonicotinaldehyde affords isonicotinonitrile in high yield on dehydrohalogenation with triethylamine (*317*).

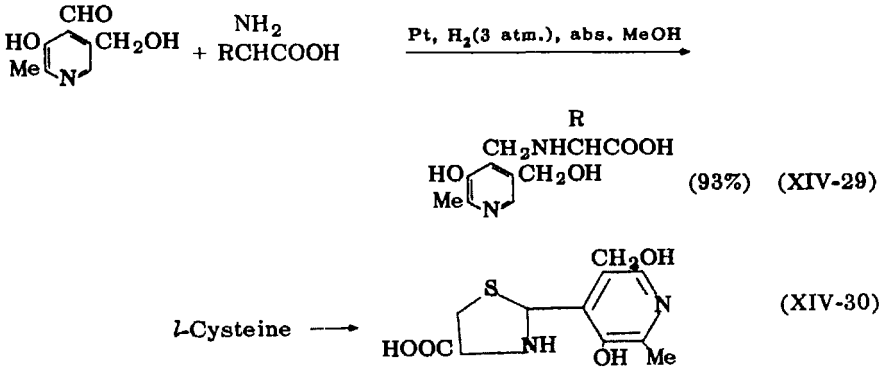
Various condensation products have been obtained from pyridine aldehydes and ammonia. Harries and Lenart (*160*) described the formation of a trimeric aldehyde-ammonia in the reaction of picolinaldehyde with a fourfold excess of concentrated aqueous ammonia (XIV-28); the product is a yellow solid, m.p. 126° (dec.). Nicotin-



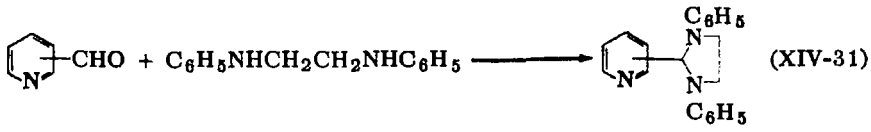
(XIV-28)

aldehyde forms an analogous condensation product, m.p. ~ 115°, which decomposes readily into its components.

Pyridoxal undergoes reductive condensation with a number of amino acids (XIV-29). Cyclic products result in certain instances (XIV-30) (*448*).

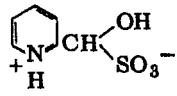


Pyridine aldehydes condense with dianilinoethane and similar compounds to give tetrahydroimidazoles; these *gem*-diamines split readily on treatment with acids (*182,265*) (XIV-31).



b. Addition of Bisulfite

Picolinaldehyde reacts readily with sodium bisulfite to give a normal addition compound (*99,160,257*). The free acid possesses exceptional stability and probably exists as a betaine (XIV-32); it

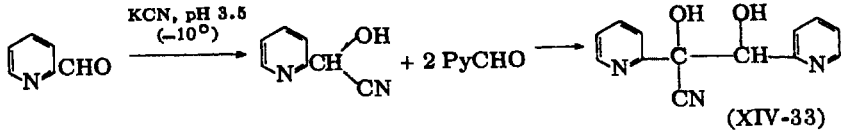


(XIV-32)

forms in high yield, sublimes readily, and is difficultly soluble in water. The free hydroxysulfonic acid is formed also by treating a cold aqueous solution of the aldehyde with sulfur dioxide (*257*). Isonicotinaldehyde and 6-methylpicolinaldehyde also form stable hydroxysulfonic acids. Nicotinaldehyde gives a sodium bisulfite addition compound (*307*); the free acid apparently was not prepared.

c. Cyanhydrin and Pyridoin Formation

Picolinaldehyde reacts at low temperature and controlled pH to give a normal cyanhydrin. At ordinary temperatures, however, a benzoin condensation occurs, giving the cyanhydrin of α-pyridoin (XIV-33). 5-Ethylpicolinaldehyde yields the bimolecular compound

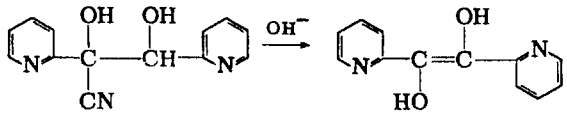


(XIV-33)

exclusively, while nicotinaldehyde and the 4-methyl, 6-methyl, and 4,6-dimethyl homologs of picolinaldehyde form only the normal cyanhydrins. Isonicotinaldehyde forms the pyridoin cyanhydrin very readily, and only gives the simple compound by treatment of the anhydrous aldehyde with excess hydrogen cyanide (*258*).

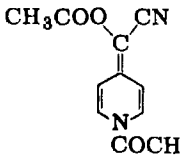
The cyanhydrins are hydrolyzed by warm water or alkali to the corresponding pyridoins (XIV-34). Isonicotinaldehyde cyanhydrin

gives a diacetyl derivative which has been formulated as (XIV-35).



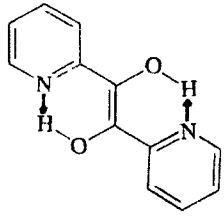
(XIV-34)

(Enediol form)



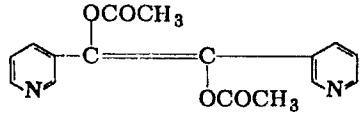
(XIV-35)

The direct conversion of picolinaldehyde to 2-pyridoin occurs with potassium cyanide, acetic acid, or merely by heating (*53,168*), while boron trifluoride and boron trichloride give a mixture of 2-pyridoin and 2-pyridil (*252*). 2-Pyridoin is a remarkably stable substance, and considerable evidence exists in support of a chelated *trans* enediol structure (XIV-36).



(XIV-36)

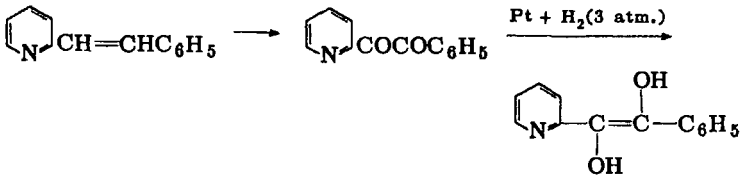
Nicotinaldehyde yields the enediol diacetate (XIV-37) in acetic anhydride solution. A yellow color is produced by reaction with potassium cyanide in aqueous solution, but no pyridoin has been isolated (*255*). Isonicotinaldehyde, in contrast, yields isonicotinic acid and 1,2-bis(4-pyridyl)glycol (*185,263*), the result of a Cannizzaro-



(XIV-37)

like reaction. No intramolecular stabilization of an enediol structure is possible in these two cases.

Buehler and associates (*53*) prepared several ethenediols of mixed structure by indirect means (XIV-38) and found the following order of stability to exist: 2-pyridoin > 1-phenyl-2-(2-pyridyl)-1,2-ethenediol > 1-phenyl-2-(4-pyridyl)-1,2-ethenediol. Chelation evidently tends to stabilize 2-pyridoin.

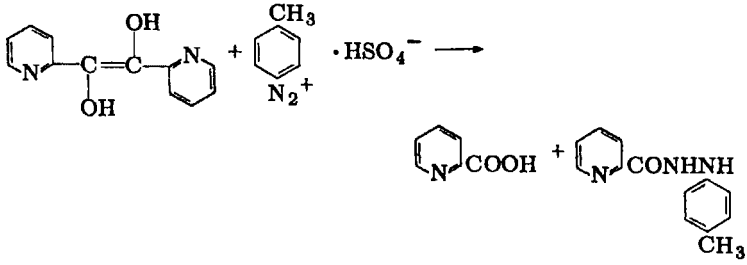


(XIV-38)

2-Pyridoin reacts as rapidly as the aldehyde with Tollens reagent and also with 2,6-dichlorobenzenone-indophenol. It yields either a mono- or diacetate according to conditions; reaction of the dipotassium salt of the enediol with benzoyl chloride gives the dibenzoate (*51,86,100*). Urea and acetic acid give an oxazolone (*86*).

2-Pyridoin monophenylhydrazone results from phenylhydrazine and the enediol in equimolar amounts. A threefold excess of phenylhydrazine, however, gives the bis-phenylhydrazone of 2-pyridil (*86*). This suggests a mechanism similar to that of osazone formation.

Solid 2-pyridoin reacts with aryl isocyanates to form bis-arylcarbamate esters which are unstable and cleave in solution to the monocarbamate and the aryl isocyanate (*100*). The enediol cannot be methylated with diazomethane or methyl iodide in the presence of basic reagents, while a monomethiodide forms with methyl iodide in acetic acid (*53,86,100*). Reaction of 2-pyridoin with *p*-toluene diazonium sulfate in aqueous solution gives picolinic acid and its *p*-tolylhydrazide (*101*) (XIV-39).

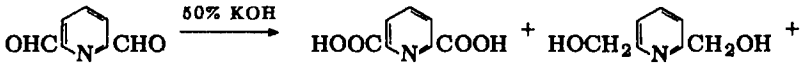


(XIV-39)

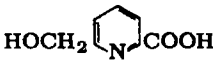
2-Pyridoin is oxidized readily by air or concentrated nitric acid to 2-pyridil (*381*), which enters normally into the benzilic acid rearrangement (*207*), and reacts with tosylhydrazine to give a pyridotriazole (*50, 103*).

d. Cannizzaro Reaction

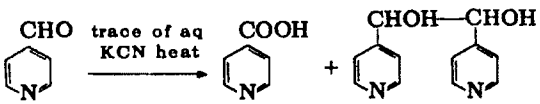
The simple pyridine aldehydes give the expected products in the Cannizzaro reaction, and pyridine 2,6-dialdehyde (XIV-40) reacts normally (*149,151,160,267*) (XIV-41). Isonicotinaldehyde apparently undergoes a similar reaction with catalytic amounts of aqueous potassium cyanide (*263*) (XIV-42).



(XIV-40)



(XIV-41)

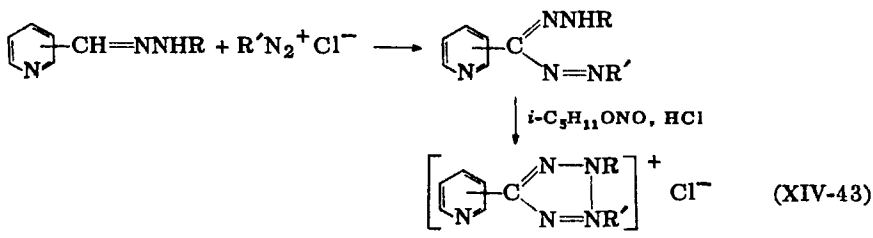


(XIV-42)

e. Reactions of Functional Derivatives

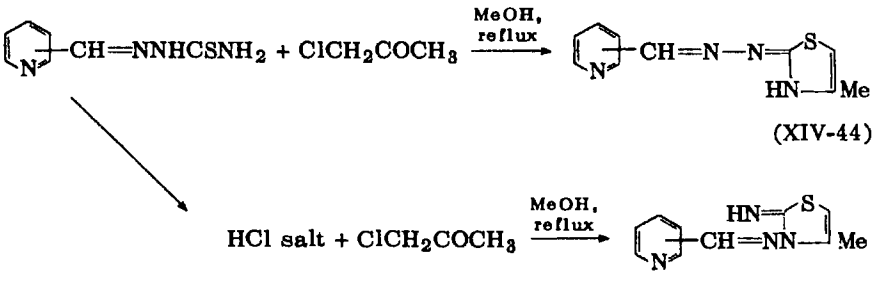
Ried and co-workers (*331,332*) and Seyhan (*353*) have prepared a series of formazans and tetrazolium salts from substituted phenylhydrazones of pyridine 2- and 4-aldehydes (XIV-43).

The pyridine aldehyde thiosemicarbazones react with α-haloketones to give thiazolines. Two types of products are formed according to conditions of acidity (XIV-44). Nicotinaldehyde thiosemi-



(XIV-43)

carbazone gives 2-amino-5-(3-pyridyl)-1,3,4-thiadiazole by oxidation with aqueous ferric chloride (*133*).



(XIV-44)

f. Condensation Reactions with Ketones

Pyridine aldehydes condense with a variety of aliphatic and aromatic ketones and β-ketoesters to give pyridyl-(hydroxyethyl) and unsaturated pyridyl ketones and ketoesters. The usual catalyst is aqueous base, although the resin Amberlite IRA 400 (OH^-) has effected the condensation in moderate yields (*38,60,62,102,253,324*).

The preparation and properties of pyridine aldehydes are summarized in Table XIV-1 (p. 175 ff.).

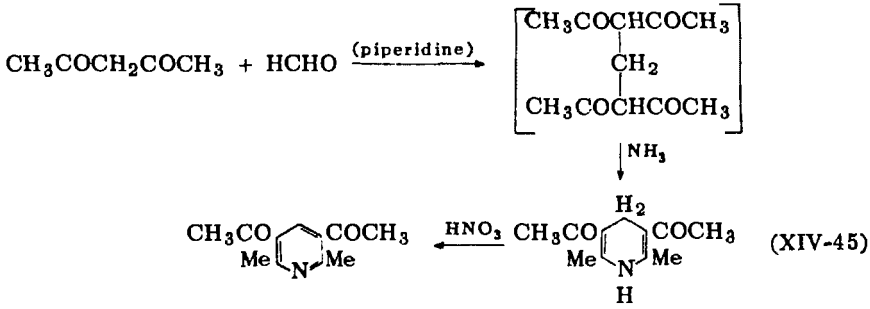
B. PYRIDINE KETONES

1. Preparation

a. Ring Closure Methods

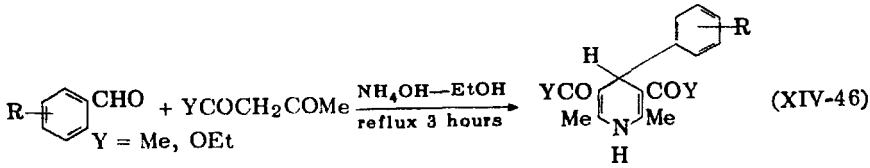
A number of pyridine ketones result by ring closure reactions of aliphatic components and ammonia. Scholtz (*208,345*) and others

have applied a modified Hantzsch synthesis to the preparation of pyridine ketones. The reaction of acetylacetone, formaldehyde, and ammonia gives a dihydropyridine which is oxidized with nitric acid to 3,5-diacetyl-2,6-lutidine (XIV-45). The yields in the reaction of



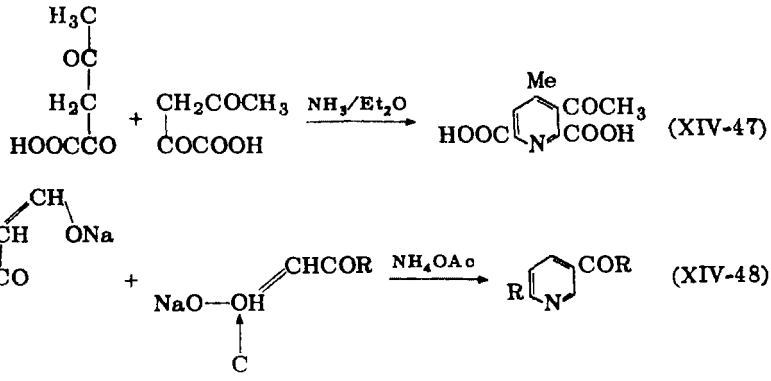
(XIV-45)

aromatic aldehydes, acetylacetone, and ammonia are affected by the substituents on the aromatic ring. Benzaldehyde, for example, gives the lowest yield (32%) and *m*-dimethylaminobenzaldehyde methiodide the highest (100%). Acetoacetic ester can serve as the ketonic component (*313*) (XIV-46). Acetylpyruvic acid and ammonia



(XIV-46)

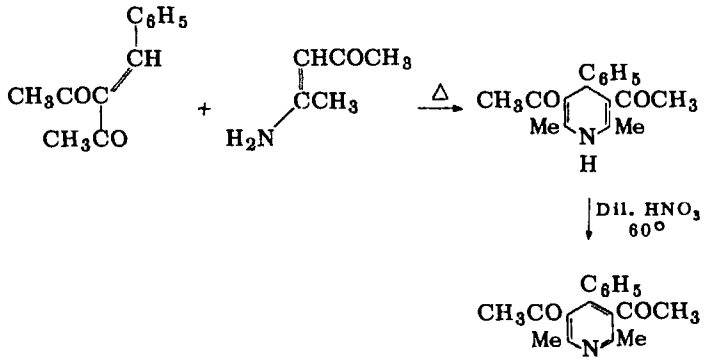
undergo an analogous reaction in ether solution to afford 3-acetyl-4-methyldipicolinic acid (*285*) (XIV-47). Ketoaldehyde derivatives react with ammonium acetate by a similar process to give pyridine ketones in low yields (XIV-48).



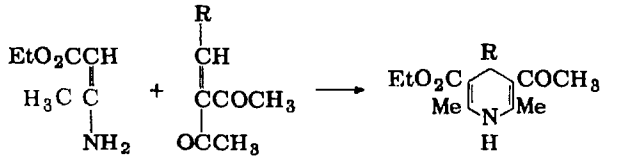
(XIV-47)

(XIV-48)

Appropriate aminoketones can be employed in the synthesis, thereby obviating the need for ammonia or ammonium salts. Ring formation occurs here at the 1–2 bond. For example, benzalacetylacetone and iminoacetylacetone (or 2-amino-2-penten-4-one) give a dihydropyridine which yields 3,5-diacetyl-4-phenyl-2,6-lutidine by oxidation with dilute nitric acid (XIV-49). β-Aminocrotonic ester and appropriate acetylacetone derivatives behave in a similar manner (*208*) (XIV-50).

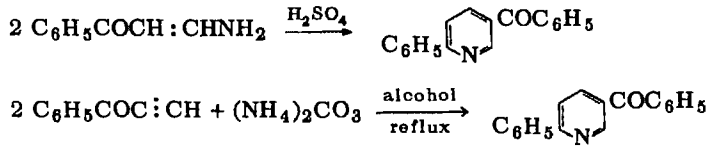


(XIV-49)



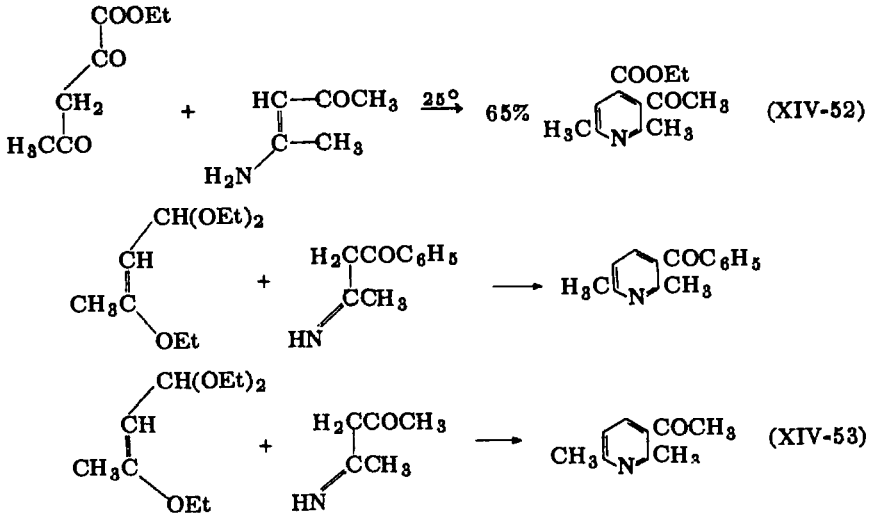
(XIV-50)

The bimolecular condensation of phenyl 2-aminovinyl ketone with acid catalysis affords 3-benzoyl-6-phenylpyridine (*28*); benzoylacetylene and ammonium carbonate react to give the same product (*49*) (XIV-51). A similar ring closure occurs in the reaction of



(XIV-51)

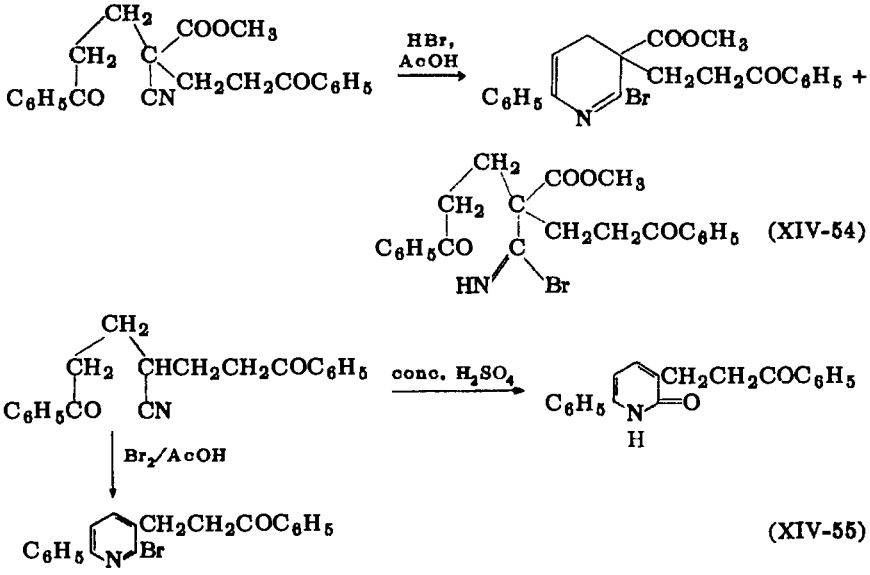
1-amino-1-hexene-3-one and 1-chloro-1-hexene-3-one to give 5-butyryl-2-propylpyridine (*158*). In other modifications of the reaction the syntheses of 3-acetyl-2,6-dimethylisonicotinic ester (*294*) (XIV-52) and 3-acetyl-2,6-lutidine (*92*) (XIV-53) may be noted.



(XIV-52)

(XIV-53)

Ring closure of methyl bis(benzoylethyl)cyanoacetate occurs under acidic conditions to give a dihydropyridine (*8*) (XIV-54). 1,5-Dibenzoyl-3-cyanopentane undergoes a similar ring closure to 3-benzoylethyl-6-phenyl-2(1*H*)-pyridone with sulfuric acid and to 3-benzoylethyl-2-bromo-6-phenyl-pyridine with bromine and acetic acid (XIV-55).

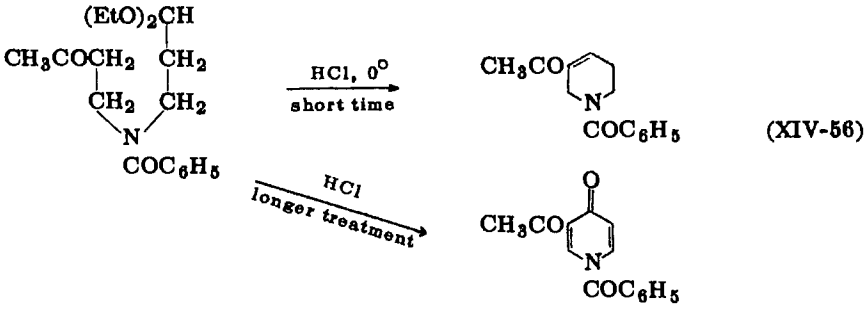


(XIV-54)

(XIV-55)

Ring formation at other sites, as in the synthesis of Albers, Kallischnegg, and Schmidt (*5*), gives dihydro- and tetrahydropyridine ketones (XIV-56).

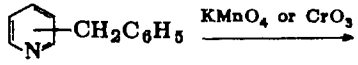
A more complete discussion of ring closure methods is found in Chapter II (pp. 272 ff.).



(XIV-56)

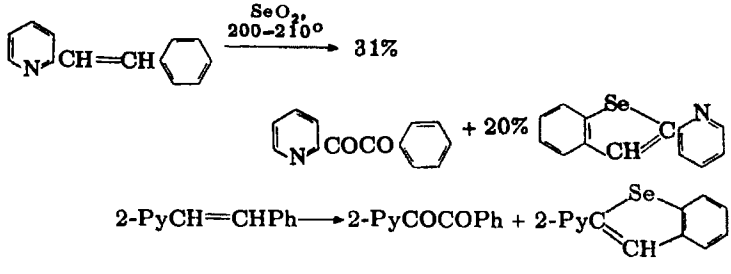
b. Side-Chain Oxidation

The oxidation of 2- and 4-benzylpyridines with potassium permanganate or chromic acid, first accomplished by Chichibabin, gives the corresponding ketones in high yields (*68*) (XIV-57). The method has since received wide application in the synthesis of diverse aroylpyridines (*28,52,74,87,359,378,388*). Selenium dioxide has been used with success (*242*). 2-Benzylpyridine gives the ketone by irradiation with a quartz mercury lamp (*284*).



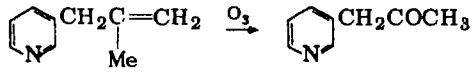
(XIV-57)

The oxidation of α-stilbazole with selenium dioxide at elevated temperatures gives a mixture of phenyl-2-pyridylglyoxal and 2-(2-pyridyl)selenonaphthene (*54*) (XIV-58). 4-Vinylpyridine gives the selenonaphthene exclusively.



(XIV-58)

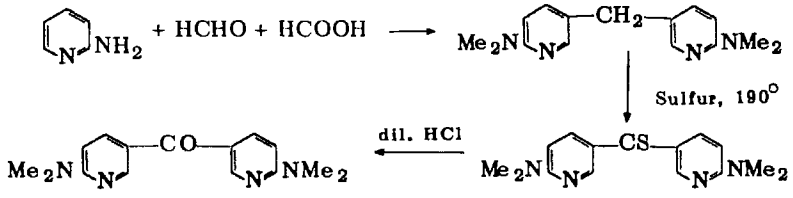
The ozonization of 5-(2-butenyl)-2-picoline to give 2-methyl-5-pyridylglyoxal has been mentioned earlier (p. 125). This reaction gives 3-pyridylacetone from 3-(β-methallyl)pyridine (XIV-59) (*148*).



(XIV-59)

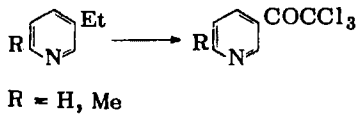
Pyridine ketones can be prepared from the corresponding alcohols by oxidation with permanganate (*67,381*), chromic acid (*209, 210,211*), or *N-bromosuccinimide* (*391*), and by palladium black dehydrogenation (*365*).

Bis(6-dimethylamino-3-pyridyl)methane, prepared by the reductive methylation of 2-aminopyridine with formaldehyde and formic acid, gives a low yield of thioketone on heating with sulfur. Dilute hydrochloric acid converts this compound to bis(6-dimethylamino-3-pyridyl) ketone (*73*) (XIV-60).



(XIV-60)

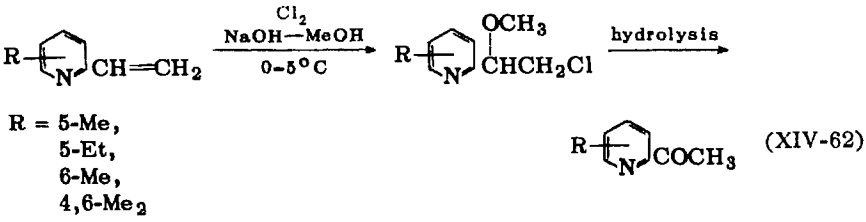
3-Ethylpyridine is converted by side-chain chlorination and hydrolysis to 3-trichloroacetyl pyridine. Application of this reaction to 5-ethyl-2-picoline gives 5-trichloroacetyl-2-picoline (*425*) (XIV-61).



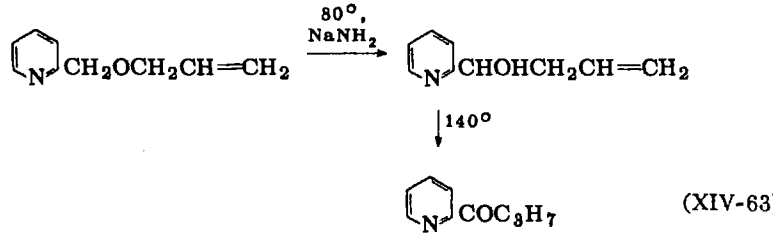
(XIV-61)

R = H, Me

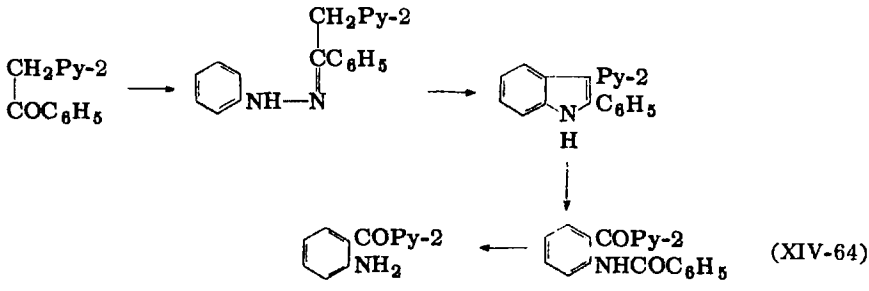
2-Vinylpyridine undergoes low temperature chlorination in methanolic sodium hydroxide to afford 2-(α-methoxy-β-chloroethyl)pyridine, which gives 2-acetylpyridine on hydrolysis (*424*) (XIV-62).



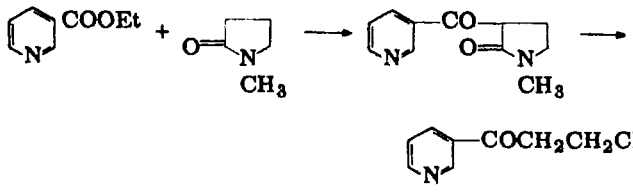
Suzuki (*374*) has described an interesting base-catalyzed rearrangement of 2-picolyl allyl ether. At 80° the product is allyl-(2-pyridyl)-carbinol; an internal oxidation-reduction ensues at 140° to give 2-butyrylpyridine (XIV-63). 4-Picolyl allyl ether rearranges in like manner, although the reaction stops at the carbinol stage.



Ockenden and Schofield (*300*) have prepared 2-(*o*-aminobenzoyl)-pyridine by an indirect route. 2-Phenacylpyridine reacts under conditions of the Fischer indole synthesis to give 2-phenyl-3-(2-pyridyl)-indole, which then yields *o*-benzamidophenyl 2-pyridyl ketone by ozonolysis of the indole 2,3-bond. The aminophenyl ketone follows by hydrolysis (XIV-64).



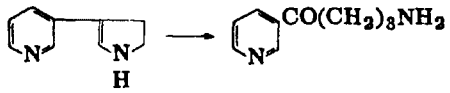
The fermentation of tobacco yields, among other substances, 3-acetylpyridine, 3-nicotinoylpropionic acid and pseudooxynicotine. Pinner and Wolfenstein prepared the last-named compound by oxidation of nicotine with hydrogen peroxide and cleavage of the resulting oxynicotine. The synthesis of Haines and Eisner (*155*) constitutes a structure proof of pseudooxynicotine (XIV-65).



(XIV-65)

(Pseudooxynicotine)

Derivatives of 3-(γ-aminobutyryl)pyridine result by reaction of myosmine with carbonyl reagents (*156*) (XIV-66). *N*-Methylmyosmine, however, is resistant to such treatment.



(XIV-66)

Myosmine

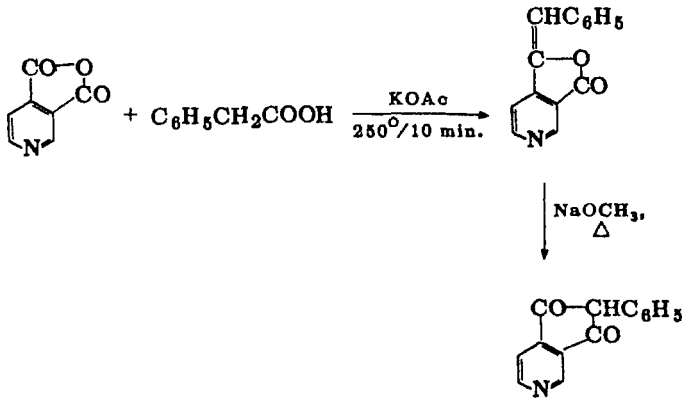
c. From Carboxylic Acids and Salts

Ketones can be prepared by dry distillation of mixed calcium salts of aliphatic and pyridinecarboxylic acids. The process, however, is of little practical importance. Calcium nicotinate, for example, reacts with calcium acetate, propionate and butyrate to give, respectively, 3-acetyl, propionyl, and butyryl pyridines (*108*). Similar conversions result with calcium picolinate and aliphatic acid salts, although in unsatisfactory yields (*109,112,113*). Thermal decomposition of calcium nicotinate gives low yields of bis(3-pyridyl) ketone (*229,239*). Bis(2,6-diphenyl-4-pyridyl) ketone, however, forms in a satisfactory manner by pyrolysis of calcium 2,6-diphenylnicotinate in high vacuum (*351*).

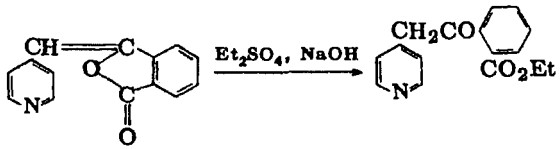
The passage of mixtures of pyridyl and aliphatic acid esters over heated catalysts also furnishes acylpyridines. For example, ethyl

nicotinate and acetic acid over thoria give 3-acetylpyridine in modest yield (*393*).

The condensation of cinchomeronic anhydride with phenylacetic acid gives a lactone which rearranges with sodium methoxide to 2-phenyl-6-aza-1,3-indandione (*117*) (XIV-67). Cleavage of 4-pyridophthalone with sodium hydroxide and diethylsulfate yields 4-(2-carbethoxyphenacyl)pyridine (*422*) (XIV-68).



(XIV-67)



(XIV-68)

d. Ester Condensation

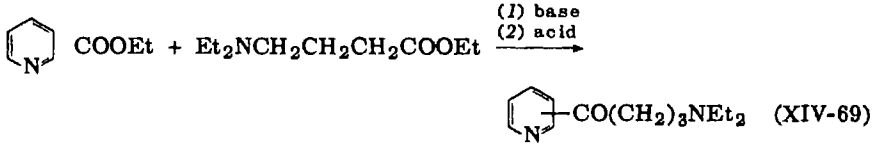
The Claisen ester condensation with its modifications is simple and widely applicable for the preparation of pyridine ketones, usually in satisfactory yields. *Cf.* Chapter XI, pp. 388 ff.

Ethyl picolinate and ethyl acetate react readily under ordinary conditions to give the β-ketoester, which then affords 2-acetylpyridine by hydrolysis (*59,79,215,229,254,269,309*). Ring-alkylated homologs of picolinic ester give equally satisfactory results (*321,360*).

Ester condensation likewise affords 3-pyridyl β-ketoesters and ketones in satisfactory yields (*78,96,180,215,229,302,325,353,370*). Webb

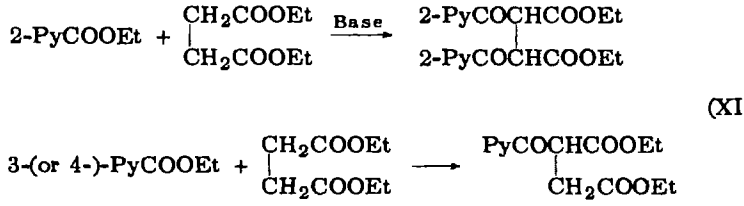
and Corwin (*392*) prepared 3-acetyl-4-picoline by means of acid catalysis. 4-Acetylpyridine results from the normal base-catalyzed condensation (*197,215,229*), the homologous 4-propionylpyridine in poor yield (*223*).

Pyridine esters and α-(diethylamino)butyric ester give the aminopropyl ketones (*36*) (XIV-69).



(XIV-69)

Ethyl picolinate gives a dicondensation product with diethyl succinate, while ethyl nicotinate and ethyl isonicotinate react in a 1:1 ratio (*64,353,360*) (XIV-70). Diethyl glutarate condenses similarly with nicotinic ester (*353*).

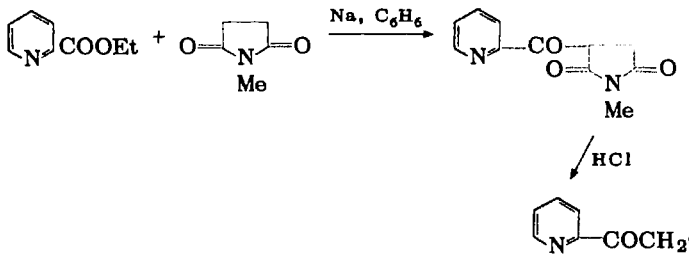


(XIV-70)

Nicotinic acid esters give pyridyl-β-diketones with alkyl and aryl methyl ketones (*78,224*) in yields ranging from 42 to 72%. Ethyl isonicotinate reacts with acetophenone in an analogous manner (*382*).

The condensation of ethyl nicotinate and *N*-methyl-2-pyrrolidone affords 3-nicotinoyl-1-methyl-2-pyrrolidone, which undergoes hydrolysis to 3-(γ-methylaminopropionyl)pyridine (*364*). An analogous reaction between ethyl picolinate and 2-pyrrolidone gives 3-picolinoyl-2-pyrrolidone and 2-(γ-aminopropionyl)pyridine (*364*); *N*-methylsuccinimide reacts to give 1-methyl-3-picolinoylsuccinimide and the γ-keto acid (XIV-71).

Ethyl nicotinate and γ-butyrolactone give the ketolactone, which is converted to γ-picolinoylpropanol in poor yield (*413*). Substituted butyrolactones react similarly (*414*).



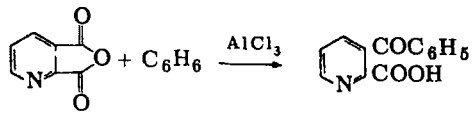
(XIV-71)

e. Friedel-Crafts Synthesis

The pyridine ring cannot be acylated by means of the Friedel-Crafts reaction (*113,392,418*). Pyridine acid chlorides and anhydrides are useful acylating agents, however, and afford a variety of pyridyl aryl ketones.

Picolinoyl chloride reacts with aromatic hydrocarbons in the presence of aluminum chloride to give 2-aroylpyridines in unspecified yields (*112,418*). Nicotinoyl chloride also affords ketones; with naphthalene, substitution occurs in the β position. Isonicotinoyl chloride has apparently not been employed. Dipicolinoyl chloride and isocinchomeronyl chloride react with benzene to give the expected disubstitution products (*418*).

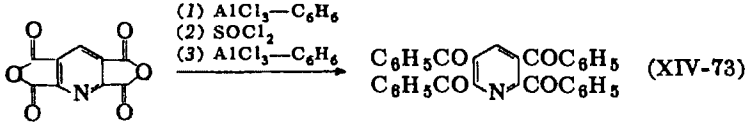
The anhydrides of the pyridine dicarboxylic acids are of special interest in regard to orientation effects. Quinolinic anhydride, for example, reacts with benzene in the presence of aluminum chloride to give 3-benzoylpicolinic acid; the more aromatic ring position thus provides the ketone-forming group (XIV-72). Numerous examples proceed in the direction shown (*125,157,183,184,188,203,214*). The isomeric cinchomeronic acid was reported by Freund (*123*) to give 3-benzoylisonicotinic acid. Fulda (*124*) re-examined the product and



(XIV-72)

assigned the isomeric structure 4-benzoylnicotinic acid; this corresponds to the findings of Philips (*312*). Kirpal (*202*), however, demonstrated the presence of both isomers and proved their structures by synthesis. The inductive effect of the hetero atom is much more pronounced with quinolinic than with cinchomeronic anhydride.

The dianhydride of 2,3,5,6-pyridinetetracarboxylic acid reacts with benzene to give a mixture of dibenzoyl dicarboxylic acids; the corresponding diacid chloride gives 2,3,5,6-tetrabenzoylpyridine (XIV-73) (*245*).

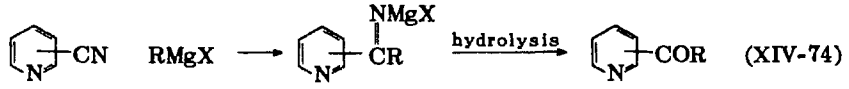


(XIV-73)

These reactions are also discussed in Chapter X (pp. 216 and 240 ff.).

f. From Organometallic Compounds and Pyridine Nitriles or Acid Chlorides

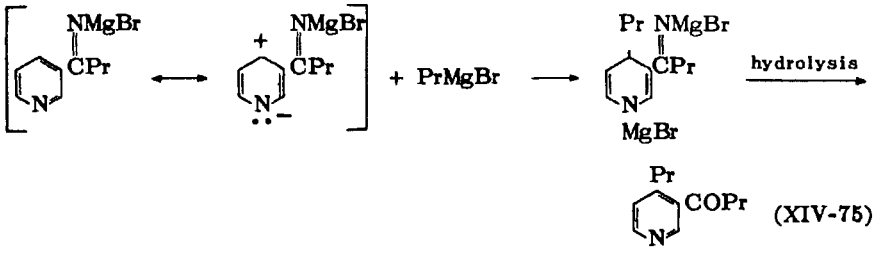
Pyridine nitriles react with alkyl and aryl Grignard reagents to give the corresponding ketones. The α-pyridine nitriles generally react more readily than the β-isomers. Räth and co-workers (*327, 329*) first applied this method to the synthesis of 3-acetylpyridine and 6-chloro-3-acetylpyridine in yields of about 30 to 35%. Preparation of the former compound, however, is more successful by the procedure of La Forge (*227*). Homologous ketones can be obtained in the same way (XIV-74).



(XIV-74)

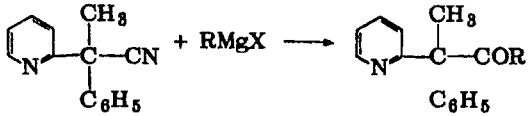
Frank and Weatherbee (*120*) reported an interesting reaction between nicotinonitrile and excess propylmagnesium bromide; with

4 moles of Grignard reagent the product is 4-propyl-3-propionylpyridine. A possible mechanism is shown (XIV-75), although the process is not entirely clear.



(XIV-75)

3-Benzoylpyridine forms in essentially quantitative yield from phenylmagnesium bromide and nicotinonitrile (*228*). 2-Acylpyridines are produced from picolinonitrile and alkylmagnesium halides (*379*). Ketones also result from highly hindered 2-pyridineacetonitriles (XIV-76).



(XIV-76)

Alkylcadmium halides react with pyridinecarboxylic acid chlorides to give 3-acyl and 2,6-diacyl pyridines. Yields are somewhat inferior to those of the normal Grignard reaction (*14,120*).

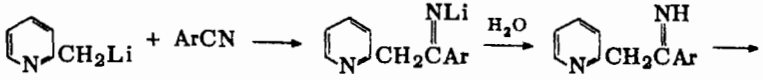
These reactions are also discussed in Chapter X; see pp. 217 and 236.

g. Acylation of Metallopyridine Derivatives

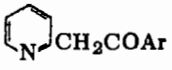
Metallopyridine derivatives, such as pyridylmagnesium bromide, pyridyllithium, and picolyllithium, react with various reagents to give pyridine ketones. The process is not altogether free of side reactions, and in many cases the yield of ketone is low (*24,206,398,400*). Acylating agents include nitriles, esters, anhydrides and acid chlorides (*30,143,206,223,398,420*).

The reaction of aromatic nitriles with 2-picolyllithium (XIV-77) gives ketimines isolable by careful hydrolysis of the primary reaction

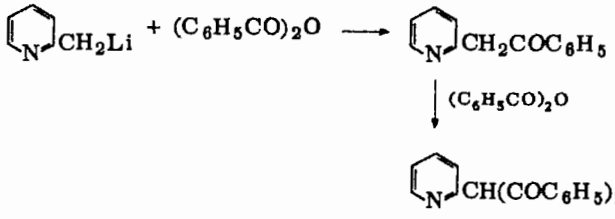
products (XIV-78). An analogous reaction of aromatic esters and anhydrides with 2-picolyllithium gives 2-phenacylpyridines; the use of excess anhydride, however, may lead to diketone formation (*143,206,420*) (XIV-79).



(XIV-77)

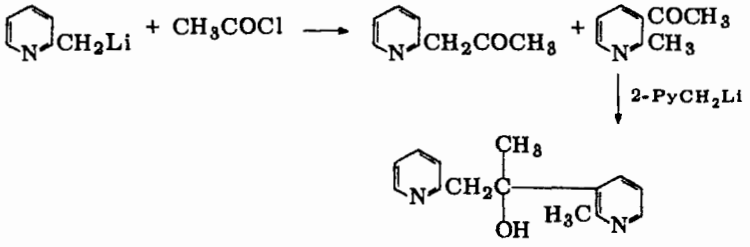


(XIV-78)



(XIV-79)

Gilman and Towle (*139*) have reported an interesting side reaction which occurs in the acylation of 2-picolyllithium (XIV-80). The mechanism of β-acylation of the pyridine ring has not been established.



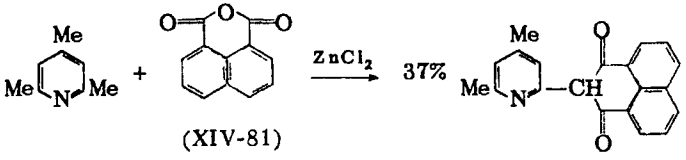
(XIV-80)

The reader is referred to Chapter VII for further discussion.

h. Acylation of Picolines

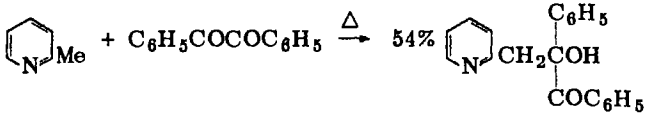
2-Picoline undergoes an uncatalyzed acylation with benzoic anhydride at elevated temperatures to give a mixture of mono- and di-

benzoyl derivatives (*5*). The zinc chloride-catalyzed condensation of 2-picoline and homologs yields diketones (*157,160*). Naphthalic anhydride (XIV-81), reacts with 2,4,6-collidine to form a cyclic β-diketone (XIV-82). The reaction of phthalic anhydride and 2-and 4-picolines is of special interest (*cf.* Chapter V, p. 196).



(XIV-81) (XIV-82)

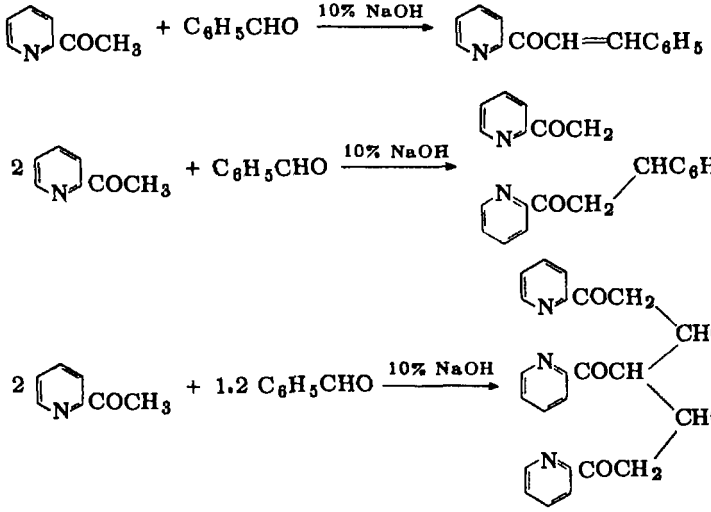
The uncatalyzed condensation of diketones, ketoesters, and ketoamides with 2-picoline occurs with ease by addition of $PyCH_2$-H to a ketonic group. Benzil, for example, reacts with 2-picoline to give 2-hydroxy-1,2-diphenyl-3-(2-pyridyl)-1-propanone (*244*) (XIV-83).



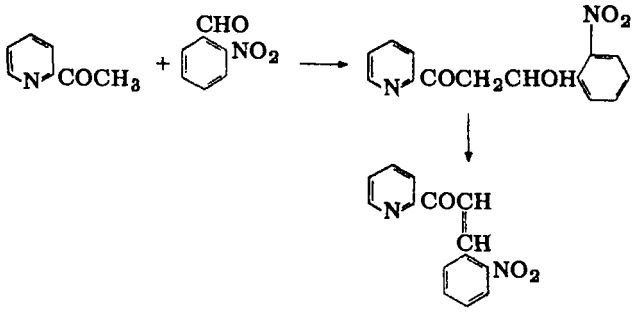
(XIV-83)

3-Picoline is less active than the 2- and 4-isomers and might be expected to resist acylation at the methyl group. Levine and coworkers (*277,330*) have shown, however, that it can be acylated with a variety of esters in the presence of strong bases. Sodium diisopropylamide is probably the most effective agent. The method affords a number of 3-picolyl ketones in good yields; 4-picoline gives comparable yields. 3-Pyridineacetonitrile, which possesses an activated methylene group, condenses with ethyl acetate as expected (*57*). 3-Pyridineacetic acid gives 3-pyridylacetone by reaction with acetic anhydride and sodium acetate.

The reaction of 2-acetylpyridine with benzaldehyde gives a number of products according to the conditions (XIV-84). 2-Acetylpyridine and *o*-nitrobenzaldehyde give a hydroxyketone which undergoes dehydration with base to a chalcone isostere (*110*) (XIV-85).



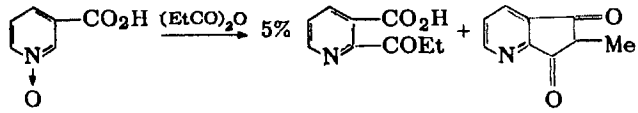
(XIV-84)



(XIV-85)

The acylation reaction of Boekelheide and Linn has been extended to the production of pyridine ketones. In an interesting example, 4-benzyl-2,6-lutidine-1-oxide gives 4-benzoyl-2,6-lutidine (*213*). Treatment of 4-benzoyl-2,6-lutidine-1-oxide with acetic anhydride affords 4-benzoyl-3-hydroxy-2,6-lutidine.

Nicotinic acid 1-oxide gives 2-acetylnicotinic acid 1-oxide on refluxing with acetic anhydride. A similar reaction with propionic anhydride, however, gives only small amounts of the expected ketone; instead, a ring closure occurs to yield 2-methyl-7-aza-1,3-indanedione (*17*) (XIV-85a). Similar reactions with isonicotinic acid 1-oxide and cinchomeronic acid 1-oxide were unsuccessful.

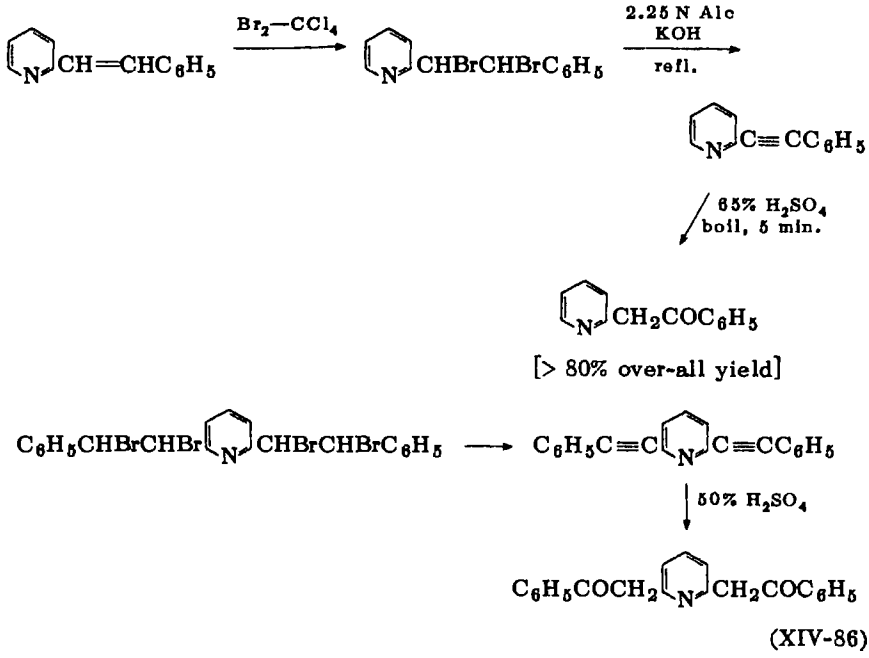


(XIV-85a)

2-Picoline 1-oxide reacts with ketene under acid catalysis to give 2-pyridylacetone in 50% yield (*190*).

i. Hydration of Acetylenes

The hydration of acetylenes constitutes an effective method for the preparation of phenacylpyridines (*34,250,279,356*). 2-(Phenylethynyl)pyridine, for example, which is prepared readily from the corresponding stilbazole, gives a high yield of 2-phenacylpyridine. 2,6-Diphenacylpyridine results in high yield by a similar process (XIV-86). The hydration evidently proceeds in only one direction (*343, 433*).

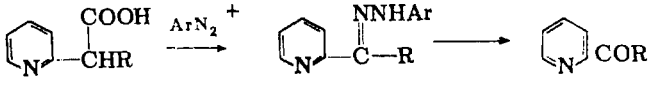


(XIV-86)

j. Japp-Klingemann Reaction

This is the reaction of a diazonium salt with a carboxylic acid to form an arylhydrazone of an aldehyde or ketone with the elimination

of carbon dioxide. Frank and Phillips (*119*) have prepared several pyridine ketones by this method (XIV-87).

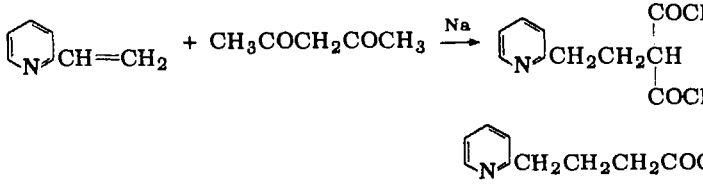


(XIV-87)

k. Addition Reactions of Vinylpyridines

β-(2-Pyridyl)alkyl ketones form by Michael addition of ketones to 2-vinylpyridine. A variety of ketonic compounds have been used (*6,39,237,407,426*). Sodium and "Triton B" are effective basic catalysts.

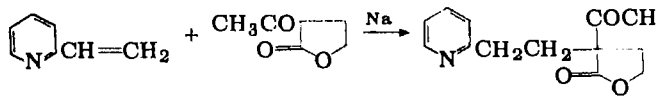
Certain side reactions occur in these condensations. Acetylacetone and 2-vinylpyridine react in the presence of sodium, for example, to give both the normal addition product and 5-(2-pyridyl)-2-pentanone by cleavage (*6*) (XIV-88). Ethyl acetoacetate gives the normal compound which can be hydrolyzed to the same substance



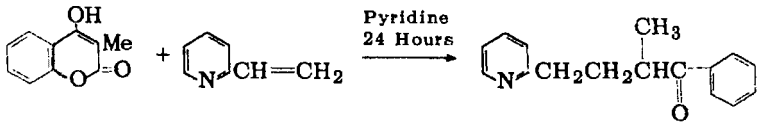
(XIV-88)

(*91*). Another common side reaction involves the introduction of more than one pyridylethyl group into the carbonyl compound. This occurs frequently with sodium and to a lesser extent with Triton B catalysis.

The formation of α-acetyl-α-(2-pyridyl)ethylbutyrolactone from α-acetylbutyrolactone and 2-vinylpyridine occurs in 40% yield (*39*) (XIV-89). An open chain ketone is obtained exclusively in the reaction of 2-vinylpyridine with 3-methyl-4-hydroxycoumarin (XIV-90).

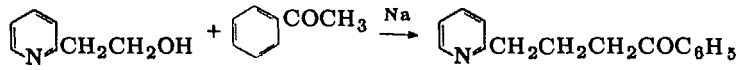


(XIV-89)



(XIV-90)

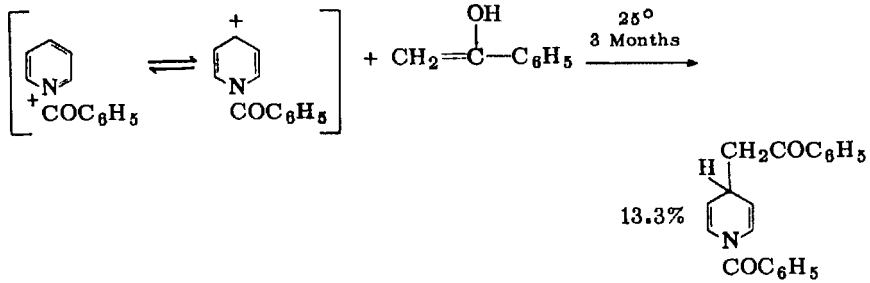
2-Pyridineethanol has been employed as a source of 2-vinylpyridine in reactions with substituted acetophenone; yields are low, however (*349*) (XIV-91).



(XIV-91)

l. From Acylpyridinium Salts and Acyldihydropyridine Derivatives

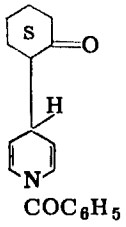
Claisen and Haase (*76*) obtained a yellow crystalline compound by interaction of pyridine, acetophenone, and benzoyl chloride at ordinary temperatures. Doering and McEwen (*90*) considered the product to be 1-benzoyl-4-phenacyl-1,4-dihydropyridine (XIV-92).



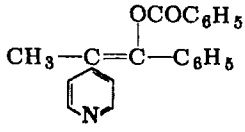
(XIV-92)

Cyclohexanone reacts in a similar way; the product (XIV-93) gives 2-(4-pyridyl)cyclohexanone by oxidation with iodine. Propiophenone gives the pyridine (XIV-94) directly.

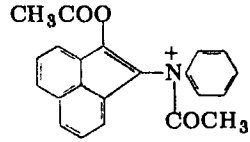
The reaction product of acetic anhydride, pyridine, and acenaphthenone was assigned structure (XIV-95) by Ghigi (*135,136*), but



(XIV-93)

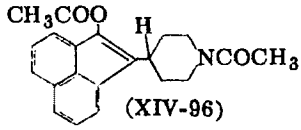


(XIV-94)



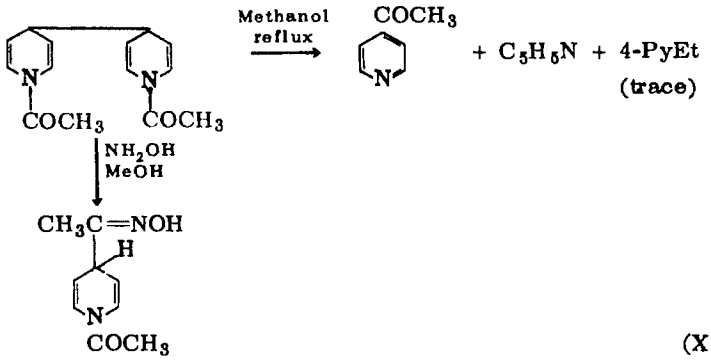
(XIV-95)

Doering and McEwen (*90*) showed that the product is the 1-acetyl-4-substituted tetrahydropyridine (XIV-96).



(XIV-96)

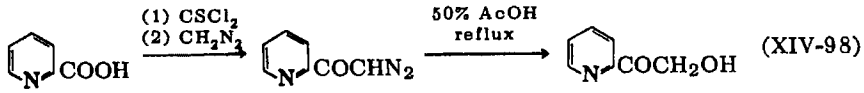
4,4′-Bis(1-acetyltetrahydropyridine) undergoes cleavage and rearrangement on prolonged boiling with methanol to give 4-acetylpyridine. Cleavage results also by treatment with methanolic hydroxylamine, but the product instead is a dihydropyridine (XIV-97) (*107*).



(XIV-97)

m. Diazoketones and Halomethyl Ketones

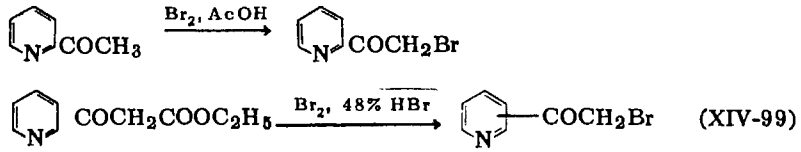
Pyridine diazoketones can be prepared by conventional means from the acid chlorides and diazomethane and are useful intermediates for the preparation of diverse substituted ketones. 2-Diazoacetylpyridine, for example, gives the corresponding hydroxymethyl ketone by hydrolysis with 50% acetic acid (*93,94,416*) (XIV-98). The



(XIV-98)

3-diazomethyl isomer is prepared in low yield by a similar procedure; treatment with hydrogen chloride yields 3-chloroacetylpyridine. Addition of diazomethane to the acid chloride (reverse addition) gives the chloroketone directly. 2-Aminonicotinoyl chloride and 2-carbomethoxynicotinoyl chloride afford the corresponding diazoketones in good yields (*189,274*).

α-Bromoalkyl pyridyl ketones are readily available by direct bromination. 2-Bromoacetylpyridine, thus, is formed from 2-acetylpyridine (*80*); it is available, however, in much better yield by bromination and hydrolysis of 2-carbethoxyacetylpyridine (*417*). A similar procedure affords 3-bromoacetyl- and 4-bromoacetylpyridine (XIV-99).

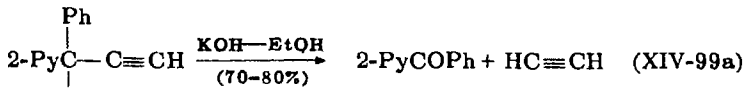


(XIV-99)

n. Other Methods

Bachman and Schisla (*15*) have effected the direct acylation of pyridine with *N,N*-dimethylbenzamide in the presence of magnesium-mercuric chloride. The mixed benzoylpyridines, which amount to about 55%, consist of the 2- and 4-isomers in a 9 : 1 ratio. Less satisfactory results are obtained with an aluminum amalgam catalyst and ethyl benzoate.

An interesting conversion is found in the reaction of α-phenyl-α-(2-pyridyl)propynol with ethanolic potassium hydroxide to give 2-benzoylpyridine and acetylene (*131*) (XIV-99a).



(XIV-99a)

α-Pyridoin reacts with *p*-toluenesulfonyl chloride in pyridine to give α-pyridil. Mixed diketones of this type may be obtained by

other methods. For example, selenium dioxide treatment of 2-picolyl phenyl ketone gives the diketone, and isonicotinoyl-4-pyridylcarbinol affords γ-pyridil (*301*).

2. Properties and Reactions

The preparation and properties of nuclear pyridine ketones are summarized in Tables XIV-2–4 (pp. 206 ff.); side-chain ketones are found in Tables XIV-5 and XIV-6 (pp. 272 ff.). Table XIV-7 (p. 310) covers di- and polyketones, and Table XIV-8 (p. 324) covers ketones with a hydrogenated pyridine nucleus.

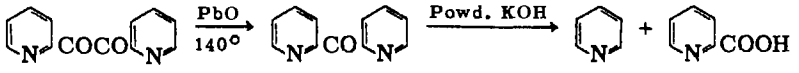
Pyridine ketones give the expected reactions. Thus, they condense with the usual carbonyl reagents to give well-defined derivatives. The β-ketoesters, β-ketoaldehydes and β-diketones form pyrazoles with hydrazines and pyrimidines with amidines. Numerous reactions have been reported with Grignard reagents to give tertiary carbinols or their dehydration products. (*Cf.* Chapter XIII.) Hydantoins form readily and in good yield, while the Leuckart reaction gives the expected amines in variable yields. 3-Acetylpyridine reacts with ethylene glycol and ethylene dithiol to give the cyclic ketal and thioketal (*371*). The Elbs reaction, on the other hand, has been unsuccessful with various pyridine ketones (*16*). The Wittig reaction with (carbethoxymethyl)triphenylphosphonium bromide gives high yields of acrylic esters (*372*).

a. Oxidation and Hydrolysis

Pyridine ketones generally exhibit ordinary behavior on oxidative treatment. 2-Acetylpyridine, for example, undergoes the normal iodoform reaction (*296*). Oxidation of sodium phenyl-(4-pyridyl)-pyruvate with hydrogen peroxide gives the corresponding acetic acid (*354*). The Willgerodt reaction generally gives good yields of products.

Mathes and Sauermilch (*264*) have found α-pyridil to undergo decarbonylation on heating with lead oxide. The product, bis(2-pyridyl) ketone, gives pyridine and picolinic acid on cleavage with powdered potassium hydroxide (XIV-100).

The alcoholysis of aryl pyridyl and alkyl pyridyl β-diketones



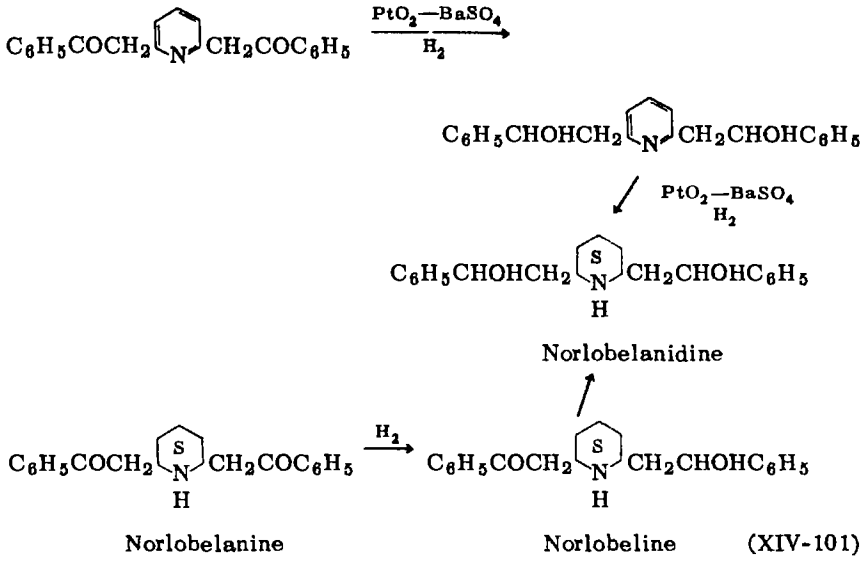
(XIV-100)

occurs on both sides of the methylene group to give all possible products (*224*).

b. Catalytic Hydrogenation

Pyridine ketones can be reduced conveniently with hydrogen and noble metal catalysts; the products are pyridine carbinols, piperidine ketones, or piperidine carbinols according to the conditions employed. 3-Acetylpyridine, for example, gives α-methyl-3-pyridinemethanol with hydrogen and platinum; in the presence of hydrochloric acid the product is the 3-piperidyl carbinol (*370*).

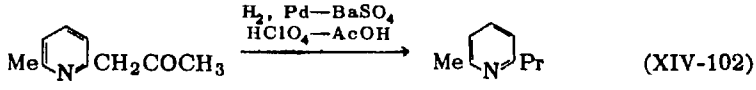
Scheuing and Winterhalder examined the reduction of 2,6-diphenacylpyridine in synthetic studies pertaining to the lobelia alkaloids. Hydrogenation proceeds stepwise; the pyridine dialcohol, initially obtained, is transformed on further reduction to the piperidine dialcohol norlobelanidine. Norlobeline, derived from norlobelanine, yields the same product on hydrogenation (XIV-101). Bachmann and Jenkins (*14*) prepared a series of 2,6-diacylpyridines



(XIV-101)

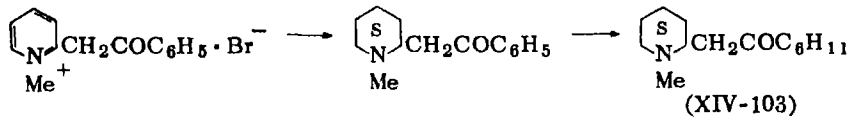
which undergo catalytic reduction to the piperidine dialcohols. 1-(3-Pyridyl)-4-dimethylamino-2-butanone gives the pyridine alcohol, with some reduction of the ring (*358*).

The addition of acids does not always lead to reduction of the pyridine ring. Graef, Fredericksen, and Burger (*146*) found, for example, that hydrogenation of 6-methyl-2-pyridylacetone in the presence of perchloric acid affects the side chain alone (XIV-102).



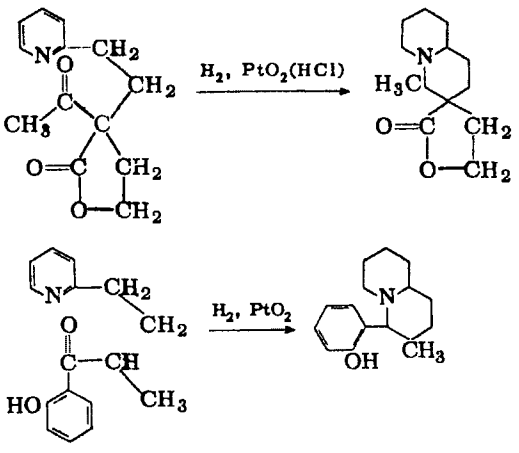
(XIV-102)

The hydrogenation of 2-phenacylpyridine and its methobromide is of interest. The base gives the carbinol in the presence of platinum oxide or nickel. The methobromide, however, is transformed first to 2-phenacyl-1-methylpiperidine and then to cyclohexyl 1-methylpipecolyl ketone (XIV-103) (*177*).



(XIV-103)

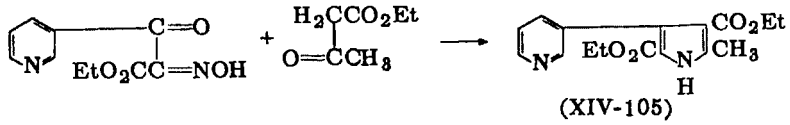
Certain γ-(2-pyridyl)alkyl ketones are of value in the formation of bicyclic systems, since hydrogenation is almost invariably accompanied by cyclization (XIV-104). For example, phenyl γ-(2-pyridyl)-propyl ketone yields the corresponding phenylquinolizidine. Reduc-



(XIV-104)

tion with lithium aluminum hydride, however, gives the pyridylphenylcarbinol.

Reductive cyclizations of a somewhat different type have been effected by Ochiai (*298*). In one example, hydrogenation of isonitrosonicotinoylacetic ester and acetoacetic ester over a palladium catalyst gives a 3-pyridylpyrrole derivative (XIV-105). This also occurs with zinc and acetic acid.



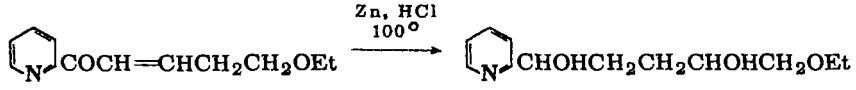
(XIV-105)

Kuick and Adkins (*224*) have shown that hydrogenation of 3-pyridyl-β-diketones with nickel invariably gives piperidine derivatives; the pyridinecarbonyl bond is susceptible to cleavage.

c. Chemical Reduction

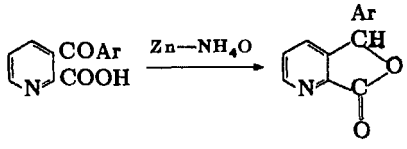
Chemical reductions generally proceed in a normal manner, although some examples of anomalous behavior have been noted.

3-Benzoyl-6-phenylpyridine gives quantitative yields of the corresponding carbinol by reduction with zinc in neutral alcohol solution (*28*). Treatment of XIV-106 with zinc and hydrochloric acid causes hydration as well as reduction (*414*). Reduction with zinc and acid sometimes converts the ketone to a methylene group (*293,360*).



(XIV-106)

The reduction of 3-aroylpicolinic and 2-aroylnicotinic acids with zinc and ammonia proceeds much as in the benzene series; thus, alcohols are formed which undergo lactone formation with ease (XIV-107).



(XIV-107)

The Clemmensen reduction has been employed in the reduction of pyridine ketones. 2-Acetylpyridine, for example, gives 2-ethylpyridine as expected. The reduction of 3-(acetoxyacetyl)pyridine, on the other hand, gives α-methyl-3-pyridinemethanol (*20*).

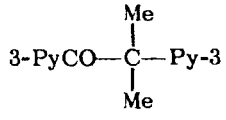
Reduction with sodium or sodium amalgam affords either monomolecular or bimolecular reduction products according to the nature of the ketone employed. Bis(6-dimethylamino-3-pyridyl) ketone gives quantitative yields of the carbinol with sodium amalgam. 2-Benzoylpyridine and 3-benzoylpyridine yield simple carbinols, while the 4-isomer gives the corresponding pinacol (*200*) with sodium amalgam. A further example of the variability of the reaction is found in the reduction of 2-propionylpyridine. Sodium and amyl alcohol reduction gives the carbinol, and sodium-ethanol reduction the pinacol (*109,112*).

The Meerwein-Ponndorf reaction has not been much employed in the pyridine series; 4-acetylpyridine gives the carbinol (*77*).

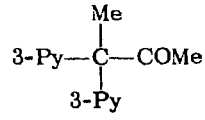
The Wolff-Kishner reaction has found rather extensive use in the reduction of pyridine ketones (*116,120,156,167,321,325,420*). The conversions are effected in moderate yields and without unusual behavior.

d. Bimolecular Reduction and Pinacol Rearrangement

Acetylpyridines undergo bimolecular reduction to the corresponding pinacols under controlled conditions of electrolysis or ultraviolet irradiation (*29*). Pinacol rearrangement gives a variety of products. 3-Acetylpyridine, for example, gives two isomers, XIV-107a and XIV-107b, the former predominating.



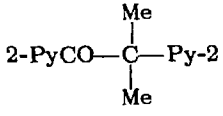
(XIV-107a)



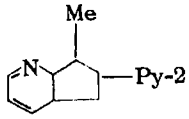
(XIV-107b)

2-Acetylpyridine gives the pinacol in normal fashion. Rearrangement gives a complex mixture which yields three substances on

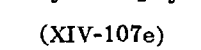
chromatographic separation: 1,2-bis(2-pyridyl)-2-methyl-1-propanone (XIV-107c), 6-(2-pyridyl)-7-methyl-5H-1-pyrindene (XIV-107d), and 2-pyridyl 2-picolyl ketone (XIV-107e).



(XIV-107c)

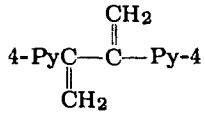


(XIV-107d)

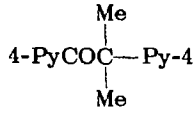


(XIV-107e)

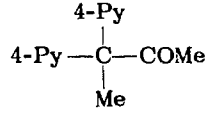
Rearrangement of the pinacol derived from 4-acetylpyridine gives three products: 2,3-bis(4-pyridyl)-1,3-butadiene (XIV-107f), 1,2-bis(4-pyridyl)-2-methyl-1-propanone (XIV-107g), and 3,3-bis(4-pyridyl)-2-butanone (XIV-107h).



(XIV-107f)



(XIV-107g)

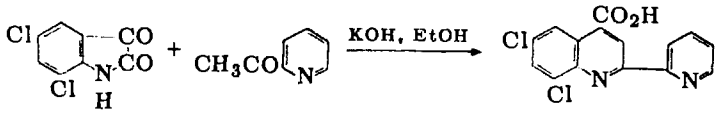


(XIV-107h)

The major isomer resulting from rearrangement of 1,4-bis(3-pyridyl)-2,3-butanediol possesses profound biological effects on the adrenal cortex. It is a potent inhibitor of 11-β-hydroxylation of steroids in man, and interferes with the synthesis and secretion of cortisol, corticosterone, and aldosterone (*82*).

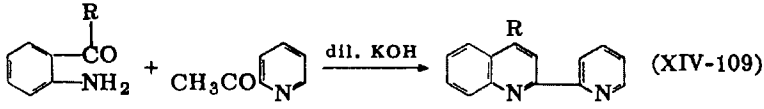
e. Carbonyl-Activated Condensations

Pyridine ketones which possess an α-methyl or methylene group undergo the usual base-catalyzed condensation. Among these, 2-acetylpyridine reacts with isatin and substituted isatins in the Pfitzinger reaction to afford quinoline derivatives (XIV-108) (*21,254*). Other

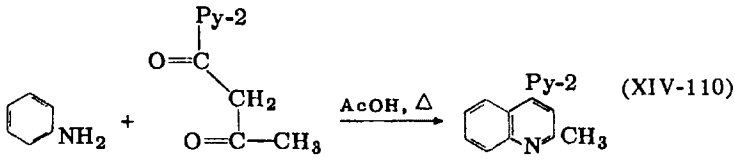


(XIV-108)

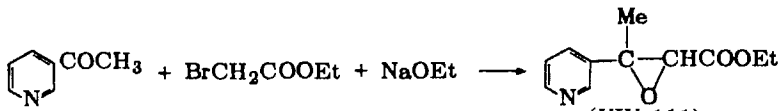
examples of bimolecular base-catalyzed reactions are found in the condensation of aromatic *o*-aminoaldehydes and pyridine ketones (XIV-109), and in the reaction of aniline and pyridine β-diketones to give quinoline derivatives (*172*) (XIV-110). Still another illustration is found in the formation of glycidic ester (XIV-111) from 3-acetylpyridine (*201*).



(XIV-109)



(XIV-110)

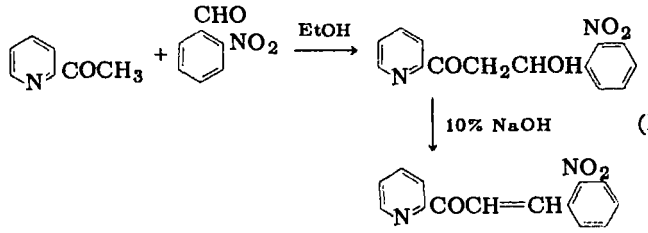


(XIV-111)

Phenacylpyridines undergo either C- or O-alkylation or acylation according to reaction conditions. Methyl iodide and benzyl chloride, for example, give C-alkylation with basic catalysts in toluene solution. Higher alkyl halides react similarly in media of high dielectric constants. Beckett and Kerridge (*22*) reported that dimethylaminoethyl chloride gives O-alkylation. Sperber, Fricano, and Papa (*361*), however, found that C-alkylation also occurred. Acetic anhydride gives O-acetylation, while benzoic anhydride gives C-benzoylation.

The condensation of 2-acetylpyridine with aromatic aldehydes leads to various products. *o*-Nitrobenzaldehyde, for example, reacts with 2-acetylpyridine to give the hydroxy ketone, which undergoes dehydration with aqueous alkali to the unsaturated ketone (*110*) (XIV-112). The reaction of benzaldehyde with 2-acetylpyridine yields a variety of products (XIV-84).

Acylpyridines participate in the Mannich reaction to give mono- and di-(aminoalkyl) ketones (*88,358*).

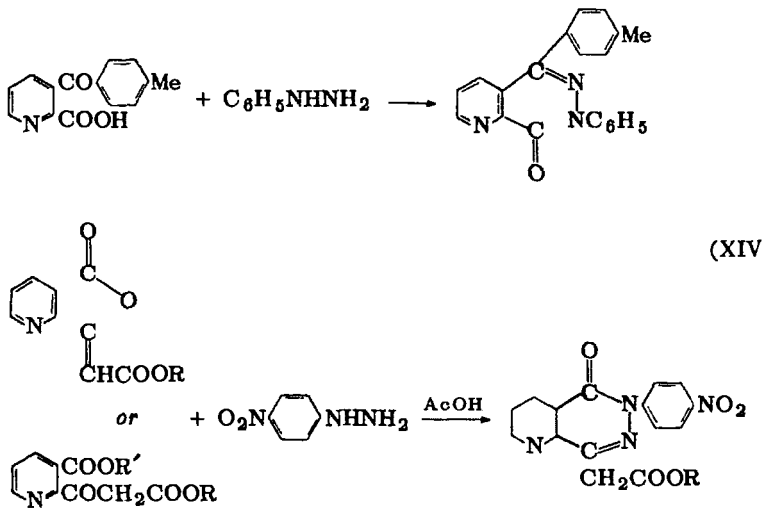


(XIV-112)

Pyridine ketones and β-ketoesters react with nitrous acid to give isonitroso derivatives which are useful intermediates in the preparation of α-aminoketones (*298,299*).

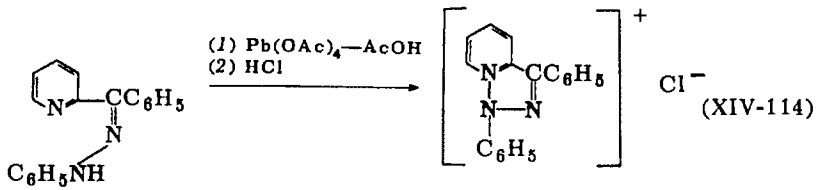
f. Cyclization Reactions of Substituted Ketones

Structurally suitable pyridine ketoacids and derivatives react with phenylhydrazine to give quinazolones (*188,296*) (XIV-113).



(XIV-113)

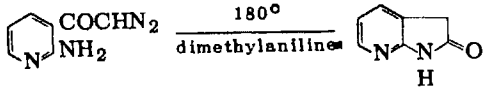
Kuhn and Muenzing (*225*) have described an interesting cyclization reaction of 2-benzoylpyridine phenylhydrazone. The *syn* (higher-melting) modification undergoes oxidative conversion to a bicyclic triazolium salt; the *anti* form, however, does not react (XIV-114). A similar transformation occurs with 2-acetylpyridine phenylhydrazone.



(XIV-114)

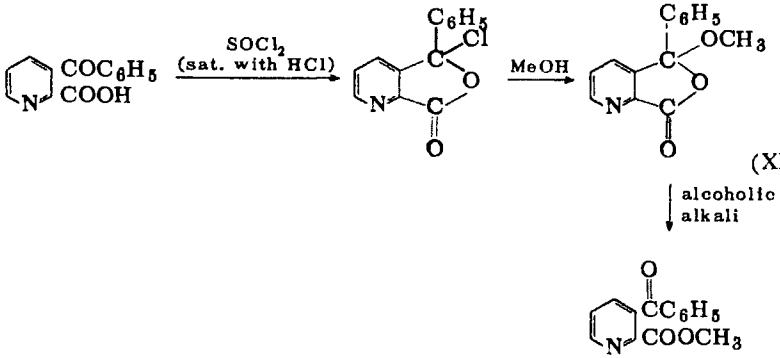
The Fischer indole synthesis with γ-nicotinoylpropylamine phenylhydrazone affords 3-(γ-aminopropyl)-2-(3-pyridyl)indole (*156*). 3-Acetylpyridine *o*-nitrophenylhydrazone does not undergo this reaction, however (*178*). Other examples of this reaction in the pyridine series are known (*194*).

Kägi has reported an interesting extension of the Arndt-Eistert reaction which leads to 8-azaoxindole (*189*) (XIV-115).



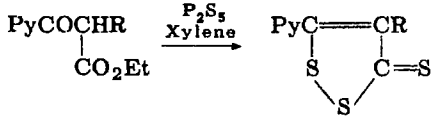
(XIV-115)

3-Benzoylpicolinic acid reacts with thionyl chloride to give a chlorolactone which yields methyl 3-benzoylpicolinate on reaction with methanol and isomerization with alcoholic alkali (*204*) (XIV-116).



(XIV-116)

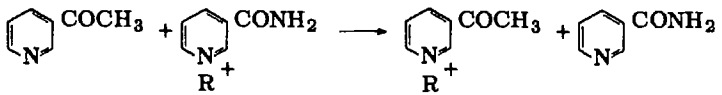
The reaction of a number of pyridyl β-ketoesters with phosphorus pentasulfide in xylene gives cyclic dithiolethiones (XIV-117) (*232*).



(XIV-117)

g. Biological Transformations

3-Acetylpyridine has been reported to produce nicotinamide deficiencies in animals, although without growth effects. Kaplan and Ciotti (*195*) demonstrated the synthesis of the 3-acetylpyridine analog of DPN. This analog is cleaved by pig-brain DPNase at the same rate as DPN; neurospora DPNase cannot effect this transformation, while crystalline yeast alcohol dehydrogenase reacts at only 1/20 of the rate of pig-brain DPNase (XIV-118).



(XIV-118)

R = Adenosine diphosphate moiety

3. Ketoximes and Their Reactions

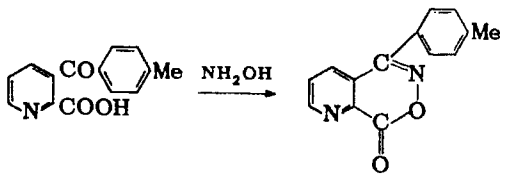
Pyridine ketones form oximes readily under ordinary conditions; in many cases both *syn* and *anti* forms can be isolated and their structures proved by Beckmann rearrangement. Thus, Nienburg (*290a*) showed that 3-benzoyl-6-phenylpyridine forms a mixture of oximes. The α-form, m.p. 160°, undergoes partial transformation into the other isomer during the Beckmann reaction. The β-oxime, m.p. 183–184°, rearranges with phosphorus pentachloride to aniline and 6-phenylnicotinic acid; the α-isomer yields the latter product, benzoic acid and 3-amino-6-phenylpyridine. The configuration of the α-oxime, therefore, is *syn*-phenyl, and that of the β-isomer, *anti*-phenyl.

The oxime of 2-phenacylpyridine and the dioxime of 2,6-diphenacylpyridine undergo the Beckmann rearrangement to give

2-pyridineacetic acid and 2,6-pyridinediacetic acid; both oximes, therefore, must have the *anti*-phenyl configuration (*304*).

Chichibabin first prepared the oxime of 2-benzoylpyridine as a mixture of two forms: (a) m.p. 150–152° and (b) m.p. 165–167°. Tschugaeff (*382a*) showed that only the lower-melting isomer formed complexes with metal salts and, on this basis, surmised that it was the *syn*-pyridyl modification. Huntress and Walter (*179*) investigated the structures of these isomers by means of the Beckmann reaction. The lower-melting form proved to be the *anti*-pyridyl and the high-melting (noncomplexing) form, the *syn*-pyridyl. The assumption of Tschugaeff thus was erroneous.

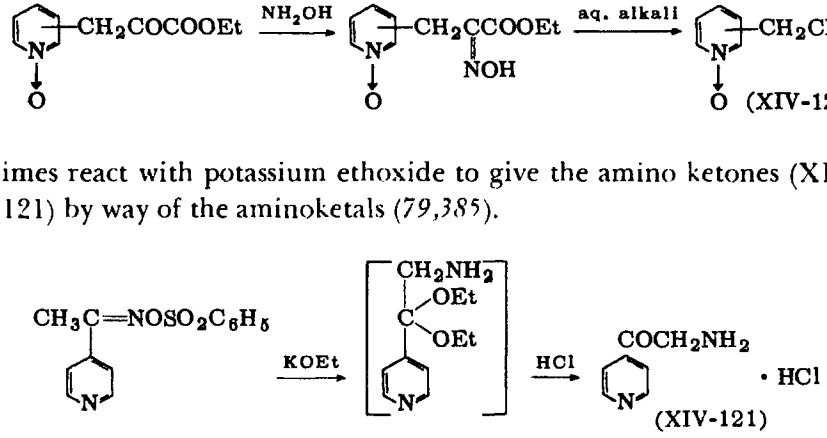
3-*p*-Toluylpicolinic acid reacts with hydroxylamine to form the cyclic oxime anhydride (*188,309*) (XIV-119).



(XIV-119)

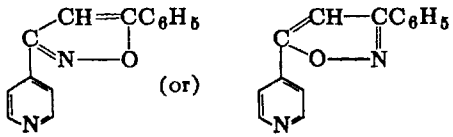
Adams and Miyano (*1*) prepared the oximes of various pyridinepyruvic ester 1-oxides and converted these products to the corresponding pyridineacetonitrile 1-oxides (XIV-120) with aqueous alkali.

The benzenesulfonyl esters of 2-, 3-, and 4-acetylpyridine ketoximes react with potassium ethoxide to give the amino ketones (XIV-121) by way of the aminoketals (*79,385*).



(XIV-121)

4-Benzoylacetylpyridine, which is prepared easily by reaction of acetophenone with ethyl isonicotinate, does not form an oxime. Instead, the reaction product with hydroxylamine hydrochloride is an isoxazole (*382*) (XIV-122).



(XIV-122)

4. Quaternary Pyridinium Aldoximes and Ketoximes

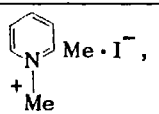
Many organophosphorus compounds are powerful inhibitors of acetylcholinesterase; among these may be found dialkylphosphofluoridates, tetraalkylpyrophosphates, and *p*-nitrophenylphosphates. Examples of exceedingly toxic compounds are isopropylmethylphosphorofluoridate (GB), *N,N*-dimethyl-O-ethylphosphonamidocyanidate (GA) and tetraethylpyrophosphate. The mode of action of these substances, which is noncompetitive and not readily reversible, is believed to be phosphorylation of a vital group at the active center of the enzyme. Childs and co-workers (*75*) studied the effects of isonitro compounds, which are moderately strong acids, and oximes in this connection. Wilson and Ginsburg (*405*) found the pyridine 2- and 4-aldoxime methiodides to be among the most active compounds. The quaternary aldoximes, for example, were about one million times more active than the simple aldoximes.

Considerable work has since been done in the field of quaternary pyridinium aldoximes and ketoximes. 2- and 4-Pyridine aldoxime quaternary salts are, for example, much more active than the corresponding 3-isomers. Alkylene-bis-pyridinium aldoximes are among the most potent reactivators of phosphorylated acetocholinesterase (*176,316*).

Certain quaternary pyridinium ketoximes likewise possess acetylcholinesterase reactivating properties, for example, α-pyridil dioxime dimethiodide (*cf.* Table XIV-9, p. 328).

The pyridine aldoximes and aldazines are capable of complexing with metals such as iron, platinum, palladium, nickel, cobalt, and copper (*158,218,240,350,368*).

TABLE XIV-1. Pyridine Aldehydes.

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
Picolinaldehyde	 (1) Me_2N⟨⟩NO, piperidine (2) $PhNHNH_2$ (3) high vacuum sublimation (4) HCl		b.p. 210°/725 mm. anil with Me_2N⟨⟩NH_2 m.p. 185° (dec.) phenylhydrazone, m.p. 180–82° phenylhydrazone-HCl, m.p. 188° (dec.) phenylhydrazone-MeI, m.p. 244° (dec.)	199
	2-PyCH=CHPy-2, (1) O_3 (2) Heat	27%	b.p. 62–63°/13-14 mm.; 180°/750 mm. phenylhydrazone, m.p. 173–76° oxime, m.p. 113.5° semicarbazone, m.p. 195–96° $D_4^{18.5} = 1.1255$ $n_D^{18.5} = 1.53886$	231
	2-$PyCHCl_2$, 30% H_2SO_4 or $AgNO_3$	38%	b.p. 181°/760 mm. 2,4-dinitrophenylhydrazone, m.p. 213° *p*-nitrophenylhydrazone, m.p. 245°	79,99

(continued)

TABLE XIV-1. (*Continued*)

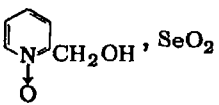
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			$NaHSO_3$ addition compd., sublimes 160°	
			methiodide, m.p. 180–183° (dec.)	369
			ethyl hemiacetal methiodide, m.p. 62–70°	
			methyl hemiacetal methiodide, m.p. 104°	
	catalyzed gas phase oxidation of 2-picoline		b.p. 70–71° 16 mm.; 181°/760 mm.	259,268
			2-pyridoin, m.p. 156°	
			2-pyridoin-HCl, m.p. 211–12°	
2-$PyCH_2OAc$,	(1) H_2O_2—AcOH (2) AC_2O	46% as diacetate	$D_4^{18} = 1.126$	44,66,85, 258,265, 373
			picrate, m.p. 102°	
			hydrochloride, m.p. 103–07°	
			semicarbazone, m.p. 196°	
			thiosemicarbazone, m.p. 209°; 227° (dec.) 2,4-dinitrophenylhydrazone, m.p. 239–40°	

		oxime, m.p. 113.5°	
		phenylhydrazone, m.p. 179°	
		cyanhydrin, m.p. 88°	
		1,3-diphenyltetrahydroimidazole, m.p. 176°	
		diacetyl deriv., b.p. 160–62.5°/15 mm.; n_D^{20} = 1.4872	
2-PyCONHNHSO$_2$C$_6$H$_5$, Na_2CO_3, glycerine, 160°	20%	phenylhydrazone hydrochloride, m.p. 194.5–97°	290
2-PyMgBr, HC(OEt)$_3$, dil. HCl	78% as acetal	diethylacetal, b.p. 112–13°/12 mm.	257,397
		2,4-dinitrophenylhydrazone, m.p. 249°	
		p-nitrophenylhydrazone, m.p. 257°	
		$NaHSO_3$ addition compd., sublimes ca. 200°; free acid, m.p. 205° (sealed tube).	
2-PyMe,SeO_2, amyl alc., 125°	small amt.	phenylhydrazone, m.p. 175°	169
		anti-phenylhydrazone, m.p. 176°	347

(*continued*)

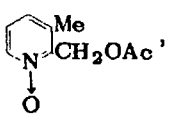
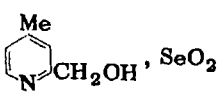
TABLE XIV-1. (*Continued*)

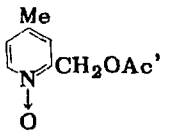
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			syn-phenylhydrazone, m.p. 86°	347
	2-PyCH=CHC$_6$H$_5$, O$_3$, HCl		b.p. 62–3°/13–14 mm.; 70–71°/16–17 mm.; 181°/760 mm. rhodanine der., m.p. 243–5°; 253–8° hydrochloride, m.p. 103–07° picrate, m.p. 101–02° aldehyde-ammonia, m.p. 126° (dec.) azine, m.p. 149°; m.p. 151–52° anil, b.p. 165°/13 mm. *p*-nitrophenylhydrazone, m.p. ca. 235° phenylhydrazone-MeI, m.p. 239–40° diethylacetal, b.p. 95–105°/14 mm.	7,160,
	2-PyCH$_2$OH, SeO$_2$	86–95%	b.p. 63–5°/13 mm. phenylhydrazone, m.p. 180–82°; m.p. 175°	129,352

		thiosemicarbazone, m.p. 210–12°	
	low	oxime, m.p. 112–13°	128
		4-phenylthiosemicarbazone, m.p. 191–92°; picrate, m.p. 192°	324
		picolylhydrazone, m.p. 160–61°	
		acethydrazone, m.p. 123–25°; picrate, m.p. 215–16°	
		salicyloylhydrazone, m.p. 219°	
pyridine, *N*-methylformanilide, $POCl_3$, 60–70°	low	phenylhydrazone, m.p. 180–82°	278
		phenylhydrazone-HCl, m.p. 196°	
		thiosemicarbazone, m.p. 204–5°	
		syn-oxime, m.p. 114°; acetyl deriv., m.p. 51–3°	140

(*continued*)

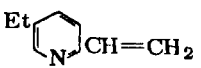
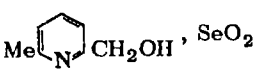
TABLE XIV-1. *(Continued)*

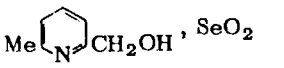
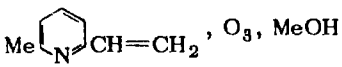
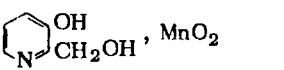
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	2-PyCH=CH_2, O_3, MeOH (−40°)	65%	b.p. 181°/760 mm. oxime, m.p. 111–13° $n_D^{18.5}$ = 1.5389 sp. gr. = 1.126	63
3-Methylpicolinaldehyde			m.p. 8° b.p. 52–4°/0.2 mm. pyridoin, m.p. 107° 1,3-diphenyltetrahydroimidazole, m.p. 161.5° oxime, m.p. 151° semicarbazone, m.p. 197° thiosemicarbazone, m.p. 209° phenylhydrazone, m.p. 160°	261,262
	 (1) AC_2O (2) HCl		b.p. 83–84°/12 mm. oxime, m.p. 152–4°	140,262
4-Methylpicolinaldehyde	 SeO_2	76–92%	b.p. 94–97°/15 mm. *p*-nitrophenylhydrazone, m.p. 243–5°	129

		semicarbazone, m.p. 204–6° thiosemicarbazone, m.p. 194–6°	
	 (1) Ac_2O (2) HCl	b.p. 65–68°/8 mm. semicarbazone, m.p. 198–200°	291
	catalyzed gas phase oxidation of 2,4-lutidine	b.p. 41°/0.5 mm.; 82–84/10 mm. pyridoin, m.p. 190° 1,3-diphenyltetrahydroimidazole, m.p. 121° cyanhydrin, m.p. 102°; acetyl deriv., m.p. 68.5°	258,259, 261
5-Methylpicolinaldehyde	catalyzed gas phase oxidation of 2,5-lutidine	m.p. 41.5° b.p. 70–72°/0.7 mm. pyridoin, m.p. 126° 1,3-diphenyltetrahydroimidazole, m.p. 153° oxime, m.p. 158.5° semicarbazone, m.p. 209° thiosemicarbazone, m.p. 221°	261,262

(*continued*)

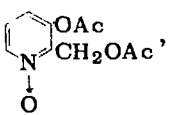
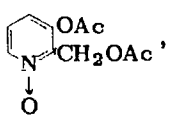
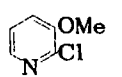
TABLE XIV-1. (*Continued*)

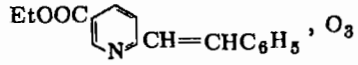
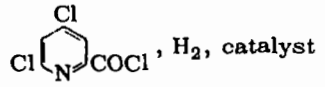
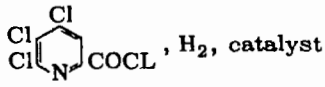
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			phenylhydrazone, m.p. 160°	
			cyanhydrin, m.p. 66°	
5-Ethylpicolinaldehyde	catalyzed gas phase oxidation of 5-ethyl-2-picoline		b.p. 84°/5 mm.	258,259,
			pyridoin, m.p. 140°	261,
			1,3-diphenyltetrahydroimidazole, m.p. 143°	265
			oxime, m.p. 150°	
			thiosemicarbazone, m.p. 186°	
			phenylhydrazone, m.p. 126°	
		63%	b.p. 84°/5 mm.	63
			oxime, m.p. 147–48°	
6-Methylpicolinaldehyde	catalyzed gas phase oxidation of 2,6-lutidine		m.p. 33°	152,258,
			b.p. 77–78°/12 mm.	259,
			hydrochloride, m.p. 147°	261,265
			pyridoin, m.p. 198° (dec.)	267, 268,
			1,3-diphenyltetrahydroimidazole, m.p. 114°	341
			cyanhydrin, m.p. 134°	
		81–92%	phenylhydrazone, m.p. 203–5°	129,152

			thiosemicarbazone, m.p. 203–4°	
		low	b.p. 100°/5 mm. semicarbazone, m.p. 211–13° 1-oxide (also formed), m.p. 82–83°	128
	 (−40°)	80%	m.p. 33° oxime, m.p. 168–169.5° *syn* oxime, m.p. 170–171°; acetyl deriv., m.p. 58–60°	63,140
4,6-Dimethylpicolinaldehyde	catalyzed gas phase oxidation of *s*-collidine		m.p. 12.5° b.p. 75°/3 mm.; 74–77°/5 mm. 1,3-diphenyltetrahydroimidazole, m.p. 119° phenylhydrazone, m.p. 179° cyanhydrin, m.p. 130°; acetyl deriv., m.p. 50.5°	258,259 261, 265
3-Hydroxypicolinaldehyde		40–66%	m.p. 78–79°; 83° b.p. 64°/5 mm. diethylacetal, b.p. 120°/3 mm.	165

(*continued*)

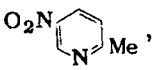
TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			oxime, m.p. 171°; 175–6°	
			thiosemicarbazone-HCl, m.p. 225–35° (dec.)	
			2,4-dinitrophenylhydrazone-HCl salt, m.p. 253–254.5° (dec.); m.p. 305–10° (dec.)	
	 (1) Ac_2O (2) H_2O		diethylacetal, m.p. 82–3° (sublimes)	105,262
			dimethylacetal, m.p. 104–5° (sublimes)	
			2,2,3-triacetyl derivative, m.p. 79–81°	
			oxime hydrochloride, m.p. 218–21°	
	 (1) Ac_2O (2) HCl		b.p. 72–74°/12–14 mm.	140
			oxime, m.p. 173–5°	
3-Methoxypicolinaldehyde	 (1) EtMgBr (2) $HC(OEt)_3$ (3) acid		m.p. 55–56°	140,165
			diethylacetal, b.p. 120°/3 mm.	

			oxime, m.p. 196–7°; 198–9°	
			thiosemicarbazone-HCl salt, m.p. 220–30° (dec.)	
			2,4-dinitrophenylhydrazone-HCl salt, m.p. 269–70° (dec.)	
6-Acetylpicolinaldehyde			m.p. 78°	261
6-Hydroxymethylpicolinaldehyde			m.p. 52°	258,261
			pyridoin, m.p. 187°	
			oxime, m.p. 148°	
6-Carboxypicolinaldehyde			m.p. 165°	260,261,
			pyridoin, m.p. 239°(dec.)	267
			oxime, m.p. 220° (dec.)	
			methyl ester, m.p. 102°	
5-Carbethoxypicolinaldehyde			phenylhydrazone, m.p. 161°	314
4,6-Dichloropicolinaldehyde		48–60%	m.p. 74°	151
			phenylhydrazone, m.p. 195–7°	
4,5,6-Trichloropicolinaldehyde		81.6%	dihydrate, m.p. 65–67°	149
			phenylhydrazone, m.p. 203–4°	

(*continued*)

TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
5-Nitropicolinaldehyde	 , SeO_2, EtOH	19%	m.p. 54–57° oxime, m.p. 190–1° thiosemicarbazone, m.p. 177–9° 2,4-dinitrophenylhydrazone, m.p. 250–2°	97
2-PyCHPhCH$_2$CHO	2-PyCH$_2$Ph, $NaNH_2$, BrCH$_2$CH(OEt)$_2$		diethylacetal, b.p. 169–71°/2.5 mm.	440
2-PyCH$_2$CH$_2$CHO			b.p. 70°/0.5 mm. (very unstable); b.p. 106–8°/9 mm. picrolonate, m.p. 177–8° (dec.) diethylacetal, b.p. 128°/8 mm.; hydrochloride, m.p. 136–8°	25,275 363
2-PyCH(C_3H_7)CH$_2$CHO	2-PyMe, PrLi, XCH$_2$CH(OEt)$_2$	6.8% as acetal	diethylacetal, b.p. 145–8°/8 mm.	363
2-PyCH(C_4H_9)CH$_2$CHO	2-PyMe, BuLi, XCH$_2$CH(OEt)$_2$	5.7% as acetal	diethylacetal, b.p. 156–9°/8 mm.	363
2-PyCH(CO$_2$Et)CH$_2$CH$_2$CHO	[2-PyCHCO$_2$Et]$^-$ Na^+, acrolein	24%	b.p. 115–6°/0.3 mm. n_D^{25} = 1.5073	387

4,6-Dimethyl-3-nitro-picolinaldehyde			m.p. 101°	261
Nicotinaldehyde	3-PyCONHNHSO$_2$Ph, Na_2CO_3, glycerine, 160°	22.5%	b.p. 97–99°/26 mm. phenylhydrazone, m.p. 157.5–158° condensation product with 2,5-diketopiperazine, m.p. 300° reduced product with 2-thiohydantoin, m.p. 249–52°	290
	3-PyCONHNH$_2$, NH_4OH, Na metaperiodate or K ferricyanide	60–70%	b.p. 97–99°/26 mm. phenylhydrazone, m.p. 157°	408
	3-PyCONHNH$_2$, Na_2CO_3, ethylene glycol, 160°	36%	b.p. 85–90°/13 mm. $NaHSO_3$ addition compound, m.p. 157° semicarbazone, m.p. 213–14° methiodide, m.p. 160–3°; 174° methochloride, m.p. 105° *t*-butiodide, m.p. 192° diethylacetal, b.p. 118–20°/15 mm. derivative with aminoacetaldehyde dimeth-	4,307 271

(*continued*)

TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			ylacetal, b.p. 117°/1–2 mm.	
			b.p. 85–90°/13 mm.	7,259,
			m.p. 8°	261,
			D_4^{20} = 1.143	265
			semicarbazone, m.p. 214°	
			thiosemicarbazone, m.p. 203°	
			oxime, m.p. 146°	
			phenylhydrazone, m.p. 158°	
			1,3-diphenyltetrahydroimidazole, m.p. 147°	
			cyanhydrin, m.p. 73°	
			azine, m.p. 148–9°	
			thiosemicarbazone, m.p. 213° (dec.)	10,430
3-PyCN	(1) $SnCl_2$, HCl, $EtO(CH_2)_2O(CH_2)_2OEt$ (2) $H_2NNHCSNH_2$ (3) H_2S		thiosemicarbazone, m.p. 222–23°	132,427
			thiosemicarbazone-$SnCl_2$ complex, m.p. 218–19°	
			methiodide, m.p. 173–5° (dec.)	369

3-$PyCH_2NH_2$, $(CH_2)_6N_4$, HCl		b.p. 95–97°/15 mm. oxime, m.p. 150° 2,4-dinitrophenylhydrazone, m.p. 259°	11
3-PyCONHEt, Sonn-Müller reaction		phenylhydrazone, m.p. 157°	419
3-PyCOCl, catalyst, H_2	17%	phenylhydrazone, m.p. 156–7° oxime, m.p. 148°	85,149
3-PyMgBr, $HC(OEt)_3$, HCl	42–49%	aldehyde-ammonia, m.p. ca 115° thiosemicarbazone, m.p. 222–3° (dec.) 4-methylthiosemicarbazone, m.p. 220–22° 4-ethylthiosemicarbazone, m.p. 224–26° 4-allylthiosemicarbazone, m.p. 181–82° 4-phenylthiosemicarbazone, m.p. 219–20°	152,373, 403
		syn oxime, m.p. 150–51°; acetyl deriv., liquid rhodanine deriv., m.p. 243–5°; m.p. 253–8°	7,140,

(*continued*)

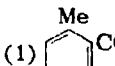
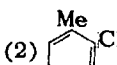
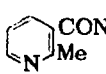
TABLE XIV-1. (*Continued*)

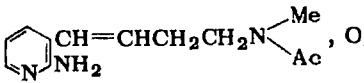
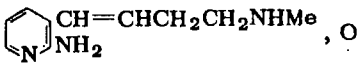
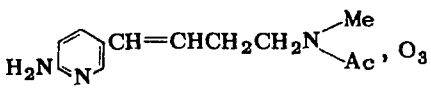
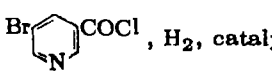
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			diethylacetal, b.p. 105°/ 11 mm.	442
			dibenzylacetal, b.p. 108–12°/2 mm.	
			diallylacetal, b.p. 135–40°/13 mm.	
			diisopropylacetal, b.p. 120–5°/11 mm.	
			dibutylacetal, b.p. 158–60°/11 mm.	
			diisobutylacetal, b.p. 146–8°/11 mm.	
			ethyleneacetal, b.p. 150°/10 mm.	
			glycerylacetal, b.p. 210°/10 mm.	
		40%		12
	$MeCHCH{=}CHNMe_2$ (NMe$_2$ on CH)			
	(1) $H \cdot CONMe_2$, $COCl_2$			
	(2) aq. NH_4Cl, heat			
			dimethylacetal methiodide, m.p. 105°	428

			dimethylacetal ethobromide, m.p. 169° dimethylacetal ethiodide, m.p. 130° dimethylacetal propiodide, m.p. 128° dimethylacetal-2,4-dinitrophenyliodide, m.p. 150° diisopropylacetal methiodide, m.p. 95° di-*i*-butylacetal methiodide, m.p. 84 dimenthylacetal methiodide, m.p. 165°	
6-Methylnicotinaldehyde			phenylhydrazone monohydrate, m.p. 143–4° thiosemicarbazone, m.p. 233–4°	150,152
		75%	b.p. 78°/6 mm. n_D^{25} = 1.5411 sp. gr. = 1.095 oxime, m.p. 160–2°	63
5-Methylnicotinaldehyde	catalyzed gas phase oxidation of 3,5-lutidine		b.p. 68°/0.5 mm. m.p. 37° semicarbazone, m.p. 210°	266

(*continued*)

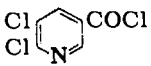
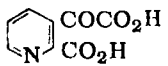
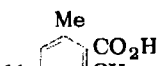
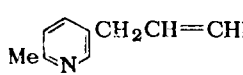
TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			thiosemicarbazone, m.p. 244°	
			phenylhydrazone, m.p. 145°	
			oxime, m.p. 99.5°	
			1-oxide, m.p. 172–3°	
			cyanhydrin, m.p. 99.5°	
4-Methylnicotinaldehyde	 (1) Na metaperiodate		diphenyltetrahydroimidazole der., m.p. 142.5°	
			b.p. 62–64°/3 mm; 109–10°/11 mm.	37
			oxime, m.p. 177.5–180.5°	
	 (2) $Pb(OAc)_4$		semicarbazone, m.p. 195.5–198.5°	
			dimethylhydrazone, b.p. 90–99°/0.5 mm.	
			ethyleneacetal, b.p. 111–13°/2 mm.; n_D^{20} = 1.5280; D_{25}^{25} = 1.154	
			very readily oxidized by air.	
2-Methylnicotinaldehyde	 glycerine	31%	b.p. 94°/12 mm.	95,261
			semicarbazone, m.p. 209°	

2-Aminonicotinaldehyde	 , O_3		m.p. 99° hydrochloride, m.p. 169–70.5° oxime, m.p. 163.5° semicarbazone, m.p. 216° (dec.) phenylhydrazone, m.p. 202–3° thiosemicarbazone, m.p. 224–5°	144,152, 261
	 , O_3 (HCl)			
5-Aminonicotinaldehyde			thiosemicarbazone, m.p. 222–4°	152
6-Aminonicotinaldehyde	 , O_3		m.p. 161° oxime, m.p. 215–6° semicarbazone, m.p. 230° (dec.) phenylhydrazone, m.p. 232° thiosemicarbazone, m.p. 219–21°	144,152, 261
5-Bromonicotinaldehyde	 , H_2, catalyst	17%	phenylhydrazone, m.p. 156–7° thiosemicarbazone, m.p. 261–3°	149,152
5-Chloronicotinaldehyde			m.p. 69–70° phenylhydrazone, m.p. 159–61°	149

(continued)

TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
5,6-Dichloronicotinaldehyde	 , H_2 catalyst	73%	m.p. 69–70° phenylhydrazone, m.p. 158°	151
2-Carboxynicotinaldehyde	 , (1) $NaHSO_3$ (2) HCl (3) NaOH		m.p. 156–8° phenylhydrazone, m.p. 205–6° diphenylhydrazone, m.p. 160–61° Na salt, m.p. 274–5° gives nicotinaldehyde with heat.	45
4,6-Dimethyl-2-hydroxynicotinaldehyde	 , MacFadyen-Stevens reaction	56%	m.p. 210°	134
4,6-Dimethyl-5-hydroxynicotinaldehyde			thiosemicarbazone, m.p. 212–13° (dec.)	132
4-Ethoxymethyl-2-hydroxy-6-methylnicotinaldehyde			thiosemicarbazone, m.p. over 250°	132
6-Methyl-3-pyridylglyoxal	 , O_3		bis-phenylhydrazone, m.p. 191–3°	148
3-PyCOCHCH$_2$CHO CO$_2$Et	3-PyCOCH$_2$OAc, ClCH$_2$CHOEt, NH$_3$ Cl		m.p. 116°	78

3-PyCH=CHCHO	3-PyCH=CHCOCO$_2$H, Cu powder, heat 4.5%	m.p. 69–69.5% sublimes	368
Isonicotinaldehyde	4-PyCH=CHPh, O_3	b.p. 77.3–78.1°/12 mm.; 82–83°/16 mm. solidifies at 12° picrate, m.p. 168–9° phenylhydrazone, m.p. 178–9°; HCl salt, m.p. 270° dec. *p*-nitrophenylhydrazone, m.p. 270° (dec.); HCl salt, m.p. 303–4° (dec.) methiodide, m.p. 105–6°; hydrate, m.p. 114–6° methylhemiacetal-MeI, m.p. 93–7°	401 369
		b.p. 67.5°/7 mm. hydrate, m.p. 78° $D_4^{20} = 1.137$ picrate, m.p. 169° hydrochloride, m.p. 132° semicarbazone, m.p. 216° thiosemicarbazone, m.p. 221°; m.p. 240° oxime, m.p. 129°	7,259, 261, 265, 288, 436

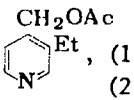
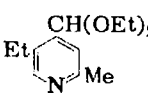
TABLE XIV-1. (*Continued*)

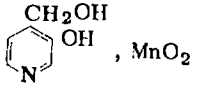
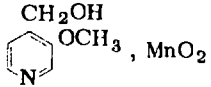
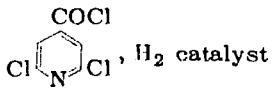
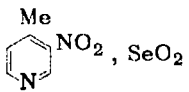
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			phenylhydrazone, m.p. 178°	
			1,3-diphenyltetrahydroimidazole, m.p. 152°	
			cyanhydrin, m.p. 103°	
			azine, m.p. 192–3°	
			rhodanine deriv., m.p. 320–2°	
			thiosemicarbazone, m.p. 215–7°; HCl salt, m.p. 238.5–239.5°	339,432
			dibenzylacetal, b.p. 110–14/2 mm.	
	4-PyCH=CH_2, O_3, MeOH (−40°)	50%	b.p. 84°/12 mm.	63
			n_D^{25} = 1.5352	
			sp. gr. = 1.137	
			oxime, m.p. 285–6°	
			thiosemicarbazone, m.p. 212°	342
			2-phenylthiosemicarbazone, m.p. 207°	
	4-PyCCl_3, $H_2NNHCSNH_2$, aq. HCl.		isolated as thiosemicarbazone, dec. 140°	437
	4-PyCHOHCHOHPy-4, $Pb(OAc)_4$, AcOH		b.p. 102–3°/35 mm.	263
	(a) form, m.p. 214°	70%	monohydrate, m.p. 78°	
	(b) form, m.p. 178–80°	79%		

		bisulfite addition compound (free acid), m.p. 243° (sealed tube)	257,258
		cyanhydrin, m.p. 144–6°	
		derivative with aminoacetaldehyde dimethylacetal, b.p. 116°/1-2 mm.	271
4-$PyCH_3$, SeO_2		thiosemicarbazone, m.p. 234° isonicotinoylhydrazone, m.p. 231°	193,338
		thiosemicarbazone, m.p. 232–4°	152
4-$PyCH_2OH$, SeO_2	61–81%	b.p. 76–78°/12 mm.	129,375
		hydrate, m.p. 78°	
		phenylhydrazone, m.p. 178–80°	
		thiosemicarbazone, m.p. 234–6°	
		acethydrazone, m.p. 139.5°	
(a) 4-$PyCCl_3$, $H_2NNHCSNH_2$, pyridine (b) 4-PyCSSK, $H_2NNHCSNH_2$ (c) 4-PyCSNHPh(K salt), Al alloy, then $H_2NNHCSNH_2$	60% as thiosemicarbazone	thiosemicarbazone, m.p. 240° (dec.)	216
		phenylhydrazone, m.p. 168–73°	
		syn oxime, m.p. 132°; acetyl deriv., m.p. 101–2°	140

(*continued*)

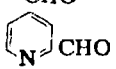
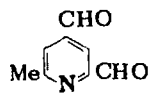
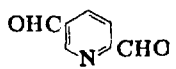
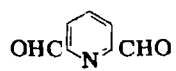
TABLE XIV-1. (*Continued*)

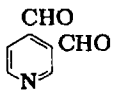
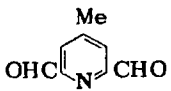
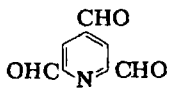
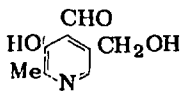
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			thiosemicarbazone, m.p. 221° (dec.)	373
			dimethylacetal-MeI, m.p. 95°	428
			diisopropylacetal-MeI, m.p. 90°	
2-Methylisonicotinaldehyde	catalyzed gas phase oxidation of 2,4-lutidine		b.p. 53–54°/0.5 mm hydrate, m.p. 83°	261,265
3-Ethylisonicotinaldehyde	 (1) H_2O_2, AcOH (2) Ac_2O (3) HCl	30%	b.p. 71–75°/2.5 mm. oxime, m.p. 146.5–148.5° diethylacetal, b.p. 100–2°/1.9 mm.	315
2,6-Dimethylisonicotinaldehyde	catalyzed gas phase oxidation of *s*-collidine		b.p. 59–60°/0.5 mm. phenylhydrazone, m.p. 186°	261,265
5-Ethyl-2-methylisonicotinaldehyde	 (1) $HC(OEt)_3$ (2) HCl	32%	b.p. 64–68°/1 mm. oxime, m.p. 143–4° diethylacetal, b.p. 109–14°/3 mm.	315
5-Ethyl-2-styrylisonicotinaldehyde	 (1) PhCHO, Ac_2O (2) HCl		2,4-dinitrophenylhydrazone, m.p. 248–9° diethylacetal, m.p. 179–225°	326

3-Hydroxyisonicotinaldehyde		30–50%	m.p. 126–8°; 133–4° *oxime*, m.p. 205–6° thiosemicarbazone-HCl salt, m.p. 245–7° (dec.) 2,4-dinitrophenylhydrazone-HCl salt, m.p. 323–5° (dec.)	165
3-Methoxyisonicotinalde		60%	m.p. 36–37° oxime, m.p. 160–1° thiosemicarbazone-HCl salt, m.p. 235–45° (dec.) 2,4-dinitrophenylhydrazone-HCl salt, m.p. 256–8° (dec.)	165
2,6-Dichloroisonicotinaldehyde			m.p. 46–47° phenylhydrazone, m.p. 157–8°	151
3-Nitroisonicotinaldehyde		74% (crude)	m.p. 53–54° dihydrate, m.p. 91–93° 2,4-dinitrophenylhydrazone, m.p. 258° anil with *p*-toluidine, m.p. 92–93°	21

(*continued*)

TABLE XIV-1. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	catalyzed gas phase oxidation of 2,3-lutidine		thiosemicarbazone, dec. over 350°	261,373
	catalyzed gas phase oxidation of 2,4-lutidine		m.p. 73.5° b.p. 51–52°/0.5 mm. hydrate, m.p. 88.5° bis-thiosemicarbazone, m.p. 240.5°	261,265, 373
	catalyzed gas phase oxidation of *s*-collidine		m.p. 115° diphenyltetrahydroimidazole, m.p. 190°	261,265
			isolated as the bis-thiosemicarbazone, m.p. 239°	373
	catalyzed gas phase oxidation of 2,6-lutidine		m.p. 124° b.p. 152–4°/103 mm. diphenyltetrahydroimidazole, m.p. 254° hydrochloride, m.p. 90° oxime, m.p. 211.5°; HCl salt, m.p. 227° (dec.) thiosemicarbazone, m.p. 242°; m.p. 253° phenylhydrazone, m.p. 199.5°	261,265, 267, 341, 373

		(dec.); HCl salt, m.p. 231° (dec.) dicyanhydrin, m.p. 105° (dec.)	
	catalyzed gas phase oxidation of 3,4-lutidine		261
	catalyzed gas phase oxidation of *s*-collidine	m.p. 158.5° diphenyltetrahydroimidazole, m.p. 243°	261,265
		isolated as tris-thiosemicarbazone, m.p. 166°	373
 (pyridoxal)		m.p. 173–4° (dec.) methochloride, m.p. 160° (dec.) oxime, m.p. 225–6° (dec.) monomethylacetal, m.p. 169–70°; methiodide, m.p. 178–9° (dec.) semicarbazone, m.p. 235° (dec.)	161,173, 174

(*continued*)

TABLE XIV-1. (*Continued*)

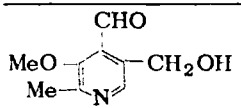
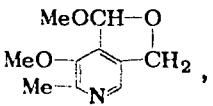
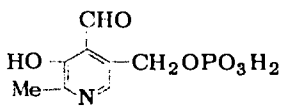
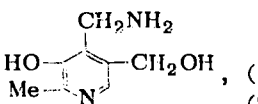
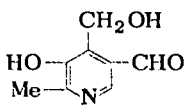
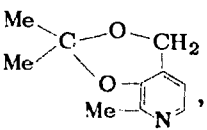
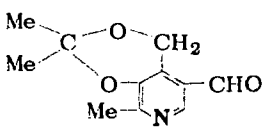
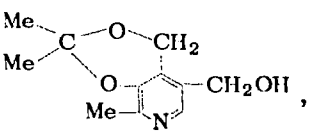
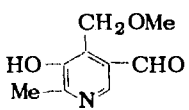
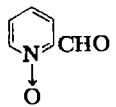
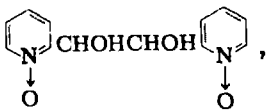
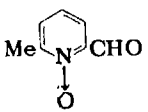
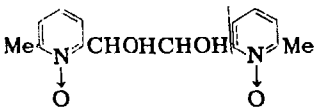
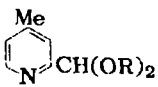
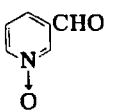
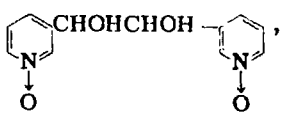
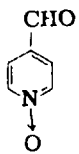
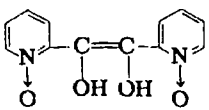
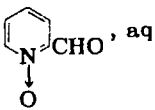
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			m.p. 152–3°  , m.p. 54–5°	
 (codecarboxylase)	 , (1) anhyd. H_3PO_4 (2) oxidation		oxime, m.p. 218°; m.p. 229–30° (dec.)	174,406
 (isopyridoxal)	 , 0·1 N-HCl		m.p. 185–6° (dec.)	217
	 , CrO_3-pyridine		m.p. 61–62°	217
			oxime, m.p. 198–9° (dec.)	161

TABLE XIV-1A. 1-Oxides of Pyridine Aldehydes and Pyridoins

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	2-PyCH(OAc)$_2$ or 2-PyCH(OAlk)$_2$, perphthalic acid, 0°		m.p. 74–6° oxime, m.p. 220–1°	128
	$Pb(OAc)_4$, $CHCl_3$	91%	m.p. 92°; hydrate, m.p. 82° oxime, m.p. 216° semicarbazone, m.p. 243° thiosemicarbazone, m.p. 240° phenylhydrazone, m.p. 238°	256
	 $Pb(OAc)_4$, $CHCl_3$	81%	m.p. 84°; hydrate, m.p. 69° oxime, m.p. 201° semicarbazone, m.p. 243° thiosemicarbazone, m.p. 228° phenylhydrazone, m.p. 227°	256

(continued)

TABLE XIV-1A. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	 perphthalic acid, 0°		m.p. 82–3°	128
	 , perphthalic acid, 0°		m.p. 127–9° semicarbazone, m.p. 212–14°	128
	 , $Pb(OAc)_4$	62%	m.p. 138°; hydrate, m.p. 100° oxime, m.p. 216° semicarbazone, m.p. 207° thiosemicarbazone, m.p. 227° phenylhydrazone, m.p. 186°	256
	4-$PyCH(OAc)_2$ or 4-$PyCH(OAlk)_2$, perphthalic acid, 0°		m.p. 152° semicarbazone, m.p. 236° oxime, m.p. 217° thiosemicarbazone, m.p. 222° phenylhydrazone, m.p. 213°	128,256
	 , aq. KCN			

m.p. 167° 256

m.p. 191° 256

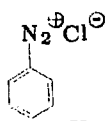
TABLE XIV-2. 2-Pyridine Ketones

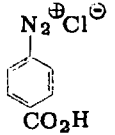
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
2-PyCOMe	Calcium acetate, calcium picolinate, dry dist.		b.p. 192° picrate, m.p. 131° mercuric chloride deriv., m.p. 150° methiodide, m.p. 161° ethiodide, m.p. 205° deriv. with ICl, m.p. 116° oxime, m.p. 120° phenylhydrazone, m.p. 155°	113
	2-PyCN, MeMgX	49%	b.p. 78°/12 mm.; 65-66°/8 mm. oxime, m.p. 121° picrate, m.p. 130-1° phenylhydrazone, m.p. 155.5-56°	289,379
	(1) 2-$PyCO_2Et$, CH_3CO_2R, base (2) acid hydrolysis		b.p. 188-9°; 78°/11 mm. oxime, m.p. 120°; *p*-toluenesulfonyl ester, m.p. 81-2° thiosemicarbazone, m.p. 158-60° oxime methiodide, m.p. 163-4°	10,79,215 254,269, 309,427

			hydrochloride, m.p. 183–5 ° chloroplatinate, m.p. 220 ° nitrate, m.p. 125 ° (dec.)	
	2-PyCHOHMe, NBS, EtOH	65%	b.p. 82–83.5 °/13–15 mm. n_D^{25} = 1.5153 phenylhydrazone, m.p. 156–8 ° oxime methiodide: "A" configuration, m.p. 101–3 ° "B" configuration, m.p. 185–6 ° thiosemicarbazone, m.p. 158–60 ° 1-oxide, picrate, m.p. 122–23.5 ° cyanhydrin hydrate, m.p. 150–1 ° isonicotinoylhydrazone, m.p. 180 ° nicotinoylhydrazone, m.p. 185 °	391 61,140, 341,430
2-PyCOEt	Calcium propionate calcium picolinate, heat	17%	b.p. 205 ° base darkens in air ethiodide, m.p. 160 °	109

(*continued*)

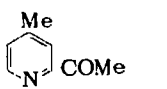
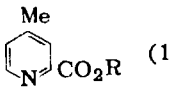
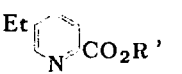
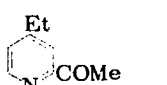
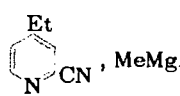
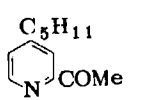
TABLE XIV-2. (*Continued*)

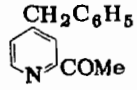
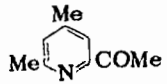
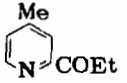
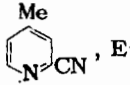
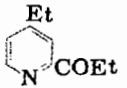
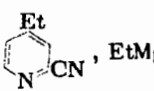
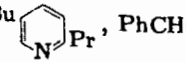
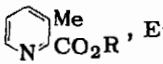
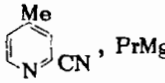
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			deriv. with ICl, m.p. 124°	
			oxime, m.p. 106°; benzoate, m.p. 69°; acetate, m.p. 46°	
			phenylhydrazone, m.p. 142°	
	2-PyCN, EtMgX	75%	b.p. 71.8–72.8°/5 mm.; 80–4°/5 mm.	289,379
			$n_D^{25} = 1.5119$	
			picrate, m.p. 126.5–127.5°	
			phenylhydrazone, m.p. 139–41°	
			oxime, m.p. 106°	
	(1) 2-$PyCO_2Et$, $C_2H_5CO_2Et$, NaOEt		b.p. 205°	309
	(2) hydrolysis		phenylhydrazone, m.p. 140–3°	
			hydrochloride, m.p. 148–50°	
			chloroplatinate, m.p. 188°	
2-PyCOPr	(1) 2-$PyCHC_3H_7$, CO_2H +  CO_2H	94% as hydrazone	b.p. 215–7°	119
			picrate, m.p. 75°	
			p-carboxyphenylhydrazone, m.p. 243° (dec.)	

	(2) pyruvic acid	81% as ketone	$n_D^{20} = 1.5078$ $D_{20}^{20} = 1.040$	
	2-PyC( $CO_2Na)_2$, C_3H_7	74% as hydrazone		119
	(1) 2-$PyCO_2R$, $PrCO_2R$, base (2) hydrolysis		b.p. 217–8° picrate, m.p. 75°	309
	Calcium butyrate, calcium picolinate, distillation		b.p. 216–20° deriv. with mercuric chloride, m.p. 78° methiodide, m.p. 79° deriv. with ICl, m.p. 85° oxime, m.p. 48°; benzoate, m.p. 56–7° phenylhydrazone, m.p. 82°	112
2-$PyCOCHMe_2$	2-PyCOMe, MeI, K t-butoxide	48%	b.p. 87.5–88.5°/7 mm. $n_D^{25} = 1.5000$ 2,4-dinitrophenylhydrazone, m.p. 181.0–181.4°	391
2-$PyCOC_6H_{13}$	2-PyCN, $C_6H_{13}MgX$	53%	b.p. 125.8–126.4°/5 mm. $n_D^{25} = 1.4955$	379

(*continued*)

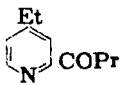
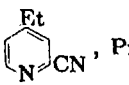
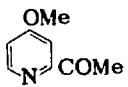
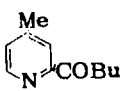
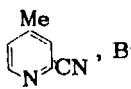
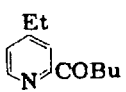
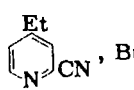
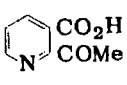
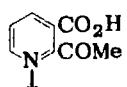
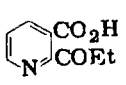
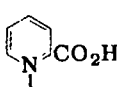
TABLE XIV-2. (*Continued*)

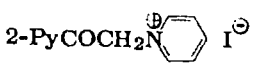
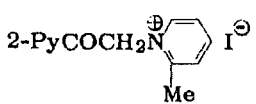
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			phenylhydrazone, m.p. 82–82.5°	
			picrate, m.p. 85.5–86°	
	(1)  CH_3CO_2R, base (2) hydrolysis		b.p. 198–200° chloroplatinate, m.p. 162° nicotinoylhydrazone, m.p. 165° isonicotinoylhydrazone, m.p. 156°	61,309
	 (1) CH_3CO_2R, base (2) hydrolysis	42%	b.p. 75°/7 mm. oxime, m.p. 125–8° semicarbazone, m.p. 195–8°	291,443
	(1)  CH_3CO_2R, base (2) hydrolysis		b.p. 113°/16 mm.	321
	 , MeMgX	30%	b.p. 100–5°/7 mm. semicarbazone, m.p. 202–4°	291
			b.p. 112–14/3 mm. semicarbazone, m.p. 152–3	443

			b.p. 149–51°/3 mm. semicarbazone, m.p. 198–9°	443
			b.p. 78–9/1 mm. semicarbazone, m.p. 200–200.5	443
	 , EtMgX		b.p. 93°/9 mm. semicarbazone, m.p. 184–9° oxime, m.p. 93–95°°	291
	 , EtMgX	24%	b.p. 113–5°/8 mm. semicarbazone, m.p. 193–6°	291
	(1)  , PhCHO, Ac_2O (2) $KMnO_4$		m.p. 95–98° semicarbazone, m.p. 139–40°	159
	(1)  , $EtCO_2R$, base (2) hydrolysis		m.p. 45–46°	360
	 , PrMgX		b.p. 85–90°/9 mm. semicarbazone, m.p. 172–4° oxime, m.p. 113–15°	291

(*continued*)

TABLE XIV-2. (*Continued*)

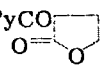
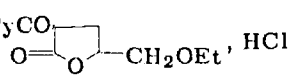
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	 , PrMgX	15%	b.p. 118–23 °/10 mm. semicarbazone, m.p. 152–4 ° m.p. 58.5–9°	291
			semicarbazone, m.p. 215–16°	443
	 , BuMgX		b.p. 103 °/7 mm. semicarbazone, m.p. 163–5 ° oxime, m.p. 88–90 °	291
	 , BuMgX	12%	b.p. 123–8 °/5 mm. semicarbazone, m.p. 148–50 °	291
	 , H_2—Pd		Sublimes m.p. 127–8 ° *p*-nitrophenylhydrazone anhydride, m.p. 268 ° 1-oxide, m.p. 247–8 °	17,296
	 $(EtCO)_2O$	5%	m.p. 195–6 °	17

2-PyCOCH$_2$Br	(1) 2-PyCOMe, Br_2, CCl_4 (2) Na_2CO_3	46%	b.p. 88°/1 *mm.*	269
	2-PyCOCH$_2$CO$_2$Et, aq. HBr	89%	hydrobromide, m.p. 204–8° (dec.)	417
2-PyCOCH$_2$CN			m.p. 93–4°	443
2-PyCOCH$_2$OAc	2-PyCOCH$_2$Br, KOAc		b.p. 70–79°/0.005 mm. needles, m.p. 43–43.7°	417
2-PyCOCH$_2$OH	2-PyCOCHN$_2$, 50% AcOH		m.p. 160° (dec.) chloraurate, m.p. 161° chloroplatinate, m.p. 214–15° (dec.) reineckate, m.p. 180–5° (dec.) *p*-nitrophenylhydrazone, m.p. 208–10°	416
2-PyCOCHN$_2$	(1) 2-PyCO$_2$H, $CSCl_2$ (2) CH_2N_2		unstable oil chloraurate, m.p. 118–20° phenylhydrazone, m.p. 220°	416
	2-PyCOMe, I_2, pyridine	86%	m.p. 198–199° (dec.) perchlorate, m.p. 188–9°	222
	2-PyCOMe, 2-PyMe, I_2	42%	m.p. 188–9° perchlorate, m.p. 140–2°	222

(*continued*)

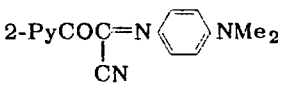
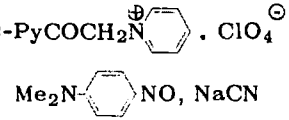
TABLE XIV-2. (*Continued*)

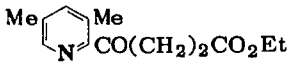
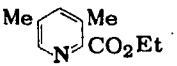
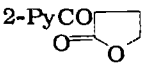
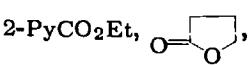
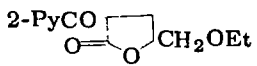
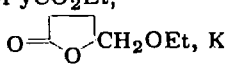
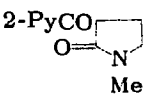
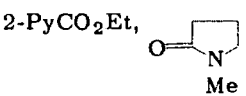
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
2-$PyCOCH_2NH_2$	2-PyCOC(CO_2Et)=NOH, reduction, hydrolysis	60%	hydrochloride, m.p. 178–80° (dec.)	59
	2-PyCMe=NOtosyl, KOEt		hydrochloride, m.p. 171–2°	79
C_6H_5-(2-pyridyl)-COMe			m.p. 75–6°	443
C_6H_5 (2-pyridyl)-$COCH_3$			m.p. 75–6°	443
2-$PyCO(CH_2)_3NH_2$	2-PyCO-(2-oxopyrrolidine), hydrolysis		dihydrochloride, m.p. 174–5° deriv. with mercuric chloride, m.p. 194° (dec.) phenylhydrazone dihydrochloride, m.p. 168–9° sulfonamide deriv. (2-HCl salt), m.p. 227° (dec.) *N*-benzoyl deriv., m.p. 89–90°	413
2-$PyCO(CH_2)_3NHMe$	2-PyCO-(1-Me-2-oxopyrrolidine), hydrolysis		dihydrochloride, m.p. 183–4° phenylhydrazone-HCl salt, m.p. 221–2° (dec.)	409

2-PyCO(CH$_2$)$_3$NEt$_2$	(a) 2-PyCO$_2$Et, Et$_2$N(CH$_2$)$_3$-CO$_2$Et, NaOEt (b) [2-PyCOCHCO$_2$Et]$^{\ominus}$ Na$^{\oplus}$, Et$_2$NCH$_2$CH$_2$Cl		b.p. 110.5 °/1 mm. picrate, m.p. 110–11 °	36
2-PyCO(CH$_2$)$_3$OH	 , hydrolysis		hydrochloride, m.p. 167.5–8 ° phenylhydrazone, α-form, m.p. 96–97 °; hydrochloride, m.p. 187–8 °. does not undergo Fischer indole reaction. phenylhydrazone, β-form, m.p. 52–56 °; hydrochloride, m.p. 257–257.5 °; undergoes Fischer indole reaction.	114,421
2-PyCO(CH$_2$)$_3$OEt	2-PyCN, EtO(CH$_2$)$_3$MgBr	62%	b.p. 125 °/5 mm.	84
2-PyCOCH=CHCH$_2$OEt	2-PyCOCH$_2$CH$_2$CHOHCH$_2$OEt, distillation		b.p. 85–87 °/0.001 mm. 2,4-dinitrophenylhydrazone, m.p. 167–8 °	414
2-PyCO(CH$_2$)$_2$CHOHCH$_2$OEt	 , HCl		2,4-dinitrophenylhydrazone, m.p. 167–8 ° semicarbazone, m.p. 251–2 ° (dec.) reineckate, m.p. 117–8 °	414

(*continued*)

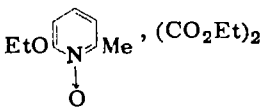
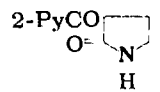
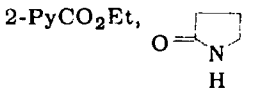
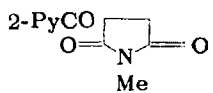
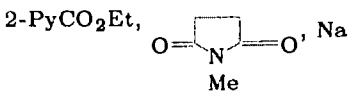
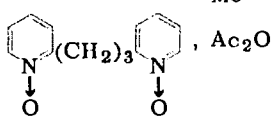
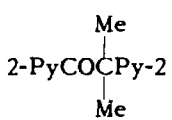
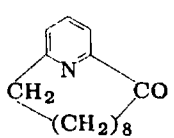
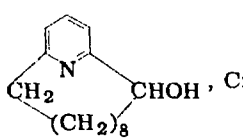
TABLE XIV-2. (*Continued*)

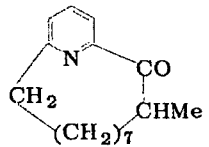
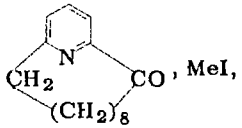
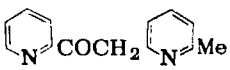
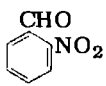
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
		97% (crude)	m.p. 160–1°	222
2-PyCOCH$_2$CO$_2$Et	(1) 2-PyCO$_2$R, CH$_3$CO$_2$R, base (2) hydrolysis		Na salt, m.p. 234° chloroplatinate, m.p. 175° phenylpyrazolone, m.p. 179° phenylhydrazone, m.p. 122° b.p. 150°/2 mm. (dec.)	79,309
	(1) 2-PyCO$_2$R, CH$_3$CO$_2$R, base (2) hydrolysis	62–70% 92% as Na salt	b.p. 115–24°/0.4–0.5 mm.; 120–30°/2 mm. hydrochloride, m.p. 117–8° (dec.) isonitroso deriv., m.p. 141–141.5° 1-phenyl-3-(α-pyridyl)-5-pyrazolone, m.p. 177–8° n_D^{20} = 1.5181–1.5184 D_4^{20} = 1.1639 Na salt, yellow crystals	59,137, 232, 269
2-PyCO(CH$_2$)$_2$CO$_2$Et	(1) 2-PyCO$_2$Et, diEt succinate, NaOEt (2) hydrolysis		b.p. 135–40°/0.2 mm. picrolonate, m.p. 104°	81

	 (1) diEt succinate (2) dil. HCl (3) esterification	m.p. 68–69°	360
	 K or NaOEt	b.p. 144–9°/0.3 mm. m.p. 46.5–47.5°; 50–51° reineckate, m.p. 156–9°	114,413
		b.p. 163–6°/0.003 mm.; thiosemicarbazone, m.p. 124–5° deriv. with mercuric chloride, m.p. 75° reineckate, m.p. 117° 2,4-dinitrophenylhydrazone, m.p. 164–5° deriv. with p-hydrazinobenzenesulfonic acid, m.p. 235°	412,414
		m.p. 82–84° picrate, m.p. 137–8° deriv. with mercuric chloride, m.p. 212–3° (dec.)	409

(*continued*)

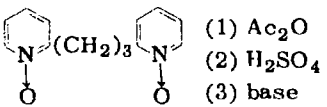
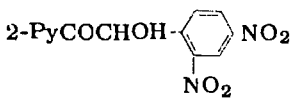
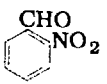
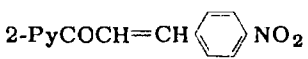
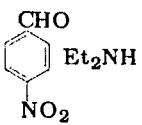
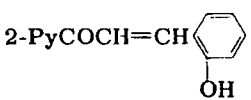
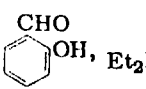
TABLE XIV-2. (*Continued*)

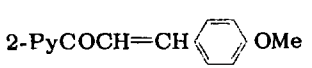
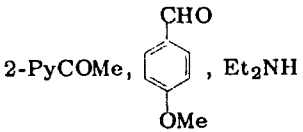
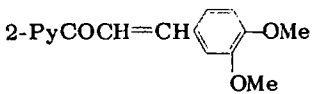
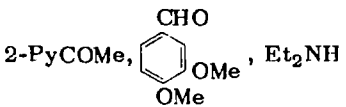
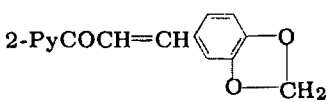
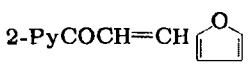
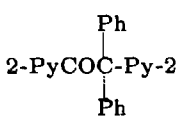
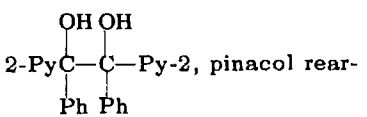
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	 KOEt	75.6%	obtained as 1-oxide, m.p. 116° m.p. 99.5°	2a
	 , NaOR		m.p. 126–8° deriv. with mercuric chloride, m.p. 223° (dec.)	413
			m.p. 90–91° picrate, m.p. 94–95°	413
2-PyCO(CH$_2$)$_2$Py-2	 , Ac_2O	18%	b.p. 102–4°/0.1 mm. picrate, m.p. 156.5–157.5° picrolonate, m.p. 203° methiodide, m.p. 180° n_D^{22} = 1.5972	270
			m.p. 88–90°	29
	 , CrO_3-	93%	m.p. 47–48° 2,4-dinitrophenylhydrazone, m.p. 191–2°	35

	 , MeI, K t-butoxide		picrolonate, m.p. 113–5° (dec.)	35
2-PyCOCH$_2$Ph	(1) 2-PyCN, PhCH$_2$MgX (2) hydrolysis		b.p. 138–42°/2 oxime, m.p. 157° semicarbazone, m.p. 151–2°	289,443
2-PyCOCH$_2$Py-2	2-PyCH$_2$Li, 2-PyCN	18%	m.p. 89–90° ketimine, m.p. 100–1°	398,142
2-PyCOCHOHPy-2			1,1′-dioxide, m.p. 152–3° (dec.)	301
	 CH$_2$Li, 2-PyCO$_2$Me	66.4%	b.p. 156–7°/1.2 mm. m.p. 48–9° picrate, m.p. 218.5–219.5°	142
2-PyCOCH=CHPh	2-PyCOMe, PhCHO, NaOH or or Et$_2$NH		m.p. 75°; m.p. 71° hydrochloride, m.p. 150–3° deriv. with mercuric chloride, m.p. 173° picrate, m.p. 121–2°	110,219, 251
2-PyCOCH=CH 	2-PyCOMe,  , NaOH		*trans*-isomer: m.p. 141° chloroplatinate, m.p. 174° phenylhydrazone, m.p. 137°	110

(*continued*)

TABLE XIV-2. (*Continued*)

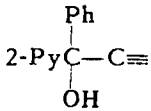
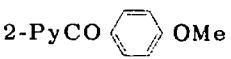
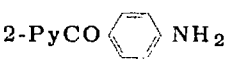
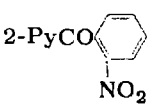
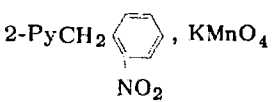
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			picrate, m.p. 152° (dec.) tetrabromide m.p. 120° *cis*-isomer: m.p. 153° chloroplatinate, m.p. 180°	
2-PyCOCH$_2$CH$_2$Py-2	 (1) Ac_2O (2) H_2SO_4 (3) base	18%	b.p. 102–4°/0.1 mm.; $n_D^{22.5} = 1.5972$ picrate, m.p. 156.5–157.5° methiodide, m.p. 180° picrolonate, m.p. 203°	270
	2-PyCOMe, 		m.p. 106° deriv. with mercuric chloride, m.p. 164° chloroplatinate, m.p. 141° (dec.)	110
	2-PyCOMe,  Et_2NH		m.p. 154°	219
	2-PyCOMe,  Et_2NH		m.p. 147–8°	219

			m.p. 84°	219
			m.p. 116-7°	219
	2-PyCOMe, piperonal, Et_2NH		m.p. 153°	219
	2-PyCOMe, furfural, Et_2NH		m.p. 53-4°	219
	 rangement			200
2-PyCOPy-2	2-PyCOCOPy-2, PbO, 140°		m.p. 54° picrate, m.p. 180-1° hydrochloride, m.p. 154° (dec.)	264
	2-PyMgI, 2-PyCO_2Et	10%	m.p. 52-53°	187

(*continued*)

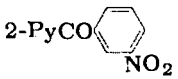
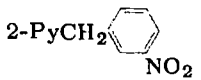
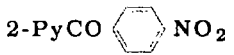
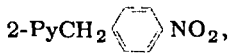
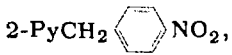
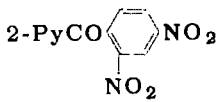
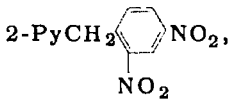
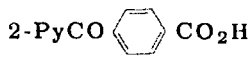
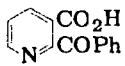
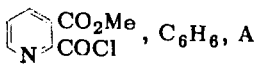
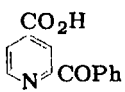
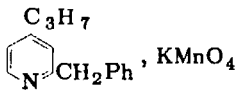
TABLE XIV-2. (*Continued*)

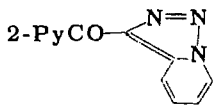
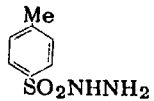
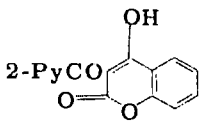
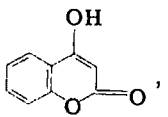
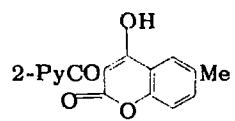
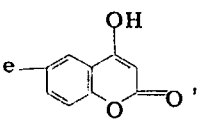
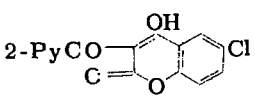
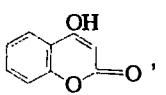
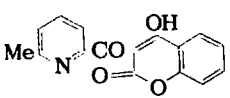
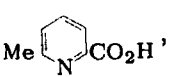
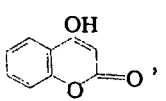
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			b.p. 115–25 °/0.1 mm. picrate, m.p. 180–1 ° semicarbazone, m.p. 217–8 °	
H 2-PyCOCPy-2 OAc			*p*-nitrophenylhydrazone, m.p. 161 °	104
2-PyCOPh	2-PyCOCl, $AlCl_3$, CS_2, C_6H_6		b.p. 182 °/14 mm. colorless oil chloroplatinate, m.p. 193 ° (dec.)	418
	2-$PyCH_2Ph$, $KMnO_4$, H_2SO_4		b.p. 315–19 °/750 mm. picrate, m.p. 128–9 °	378
	2-$PyCH_2Ph$, $KMnO_4$ or CrO_3	90%	b.p. 317 °/763 mm. picrate, m.p. 130 ° phenylhydrazone, m.p. 135–7 ° oxime, "a" form, m.p. 150–2 ° oxime, "b" form, m.p. 165–7 ° $D_{20}^{20} = 1.1558$ $D_0^0 = 1.1710$	68
	2-$PyCH_2Ph$, $KMnO_4$ or CrO_3	89–93%	b.p. 170–2 °/10 mm. hydrochloride, m.p. 126–8 °	87

			picrate, m.p. 122–3°	
				131
			oxime methiodide, "B" configuration, m.p. 195°	61,140
			b.p. 165°/7 mm. oxime, m.p. 152° isonicotinoylhydrazone, m.p. 204°	289
	2-PyCOCl, anisole, $AlCl_3$		m.p. 93° chloroplatinate, m.p. 210° (dec.) picrate, m.p. 176° phenylhydrazone, m.p. 103°	418
	reduction of nitro compound with $SnCl_2$ or $(NH_4)_2S$	good	m.p. 138° picrate, m.p. 190° hydrochloride, m.p. > 190°	212
			m.p. 118°	294,404

(*continued*)

TABLE XIV-2. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	 , $KMnO_4$		m.p. 122°	52,74,
	 , $KMnO_4$		m.p. 110°; m.p. 105° hydrochloride, m.p. 187°	52,74
	 , $KMnO_4$	85%	m.p. 99-100° hydrochloride, m.p. 173° phenylhydrazone, m.p. 171°	212
	 , $KMnO_4$		m.p. 148°	74
			m.p. 229.3-230.3°	388
	 , C_6H_6, $AlCl_3$		m.p. 176°	203
	 , $KMnO_4$		m.p. 225-30°	359

	2-PyCOCOPy-2, 	66%	m.p. 151° der. with 3,4-dinitrobenzoic acid, m.p. 158-9° (dec.)	50
	2-$PyCO_2H$,  , $POCl_3$		m.p. 97-99°	438
	2-$PyCO_2H$, Me  , $POCl_3$		m.p. 116-8°	438
	2-$PyCO_2H$, Cl  , $POCl_3$		m.p. 156-8°	438
	  , $POCl_3$		m.p. 87-9°	438

(continued)

TABLE XIV-2. (*Continued*)

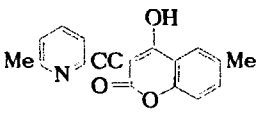
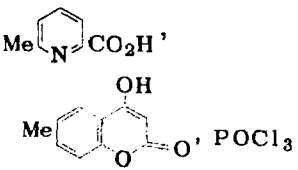
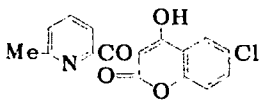
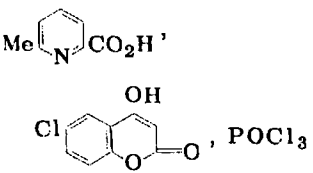
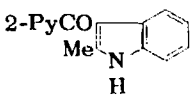
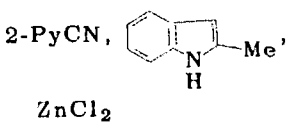
Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
			m.p. 115-7°	438
			m.p. 161-3°	438
		92%	ketimine base, m.p. 234-5° (dec.) *ketimine hydrochloride* m.p. 265-6° (dec.)	367

TABLE XIV-3. Preparation and Properties of 3-Pyridyl Ketones

Compound	Method of preparation	Yield	Physical Properties, derivatives	Ref.
3-PyCOMe	(1) 3-$PyCO_2R$, CH_3CO_2R, base		b.p. 80°/5 mm.; b.p. 218–8°	59,215
	(2) acid		isonitroso derivative, m.p. 166.5–67°	
			phenylhydrazone, 201.5–202° (dec.)	
			picrate, m.p. 172–73°	
	3-PyCN, MeMgI	35%	b.p. 222–23°	327
			hydrochloride, m.p. 80° (dec.)	
	3-PyCN, MeMgI	48–52%	b.p. 217–20°	10,227
			oxime, m.p. 113°	
			thiosemicarbazone, m.p. 217° (dec.)	
	3-PyCN, MeMgX	43%	b.p. 219–21°/760 mm.	379
			mercurichloride, m.p. 158–59.5°	
			hydantoin (5,5-substituted), m.p. 165–70°	
			$n_D^{20} = 1.5311$	
			1-oxide, m.p. 145–7°	198
			1-oxide, 2,4-dinitrophenylhydrazone, m.p. 252–6°	
			1-oxide, metho-*p*-toluenesulfonate, m.p. 115–17°	

(*continued*)

TABLE XIV-3. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	3-PyCN, MeMgX		m.p. 13–14° b.p. 90–92°/5 mm. hydrochloride, m.p. 176–77.5°	370
	calcium nicotinate, calcium acetate, dry distillation		b.p. 220° phenylhydrazone, m.p. 137° oxime, m.p. 112° oxime hydrochloride, m.p. 204° mercurichloride, m.p. 158°	111
	from tobacco fermentation		mercurichloride, m.p. 161° picrate, m.p. 130°	121
	calcium nicotinate, acetic acid, thoria, 520–44°		b.p. 105–108°/22–33 mm. picrate, m.p. 133.8–34.8°	393
	(1) 3-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 217–21° phenylhydrazone, m.p. 134–37°	180
	(1) 3-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 106°/12 mm. oxime, m.p. 130.5°	78

	(1) 3-$PyCO_2R$, CH_3CO_2R, base (2) acid	75%	b.p. 85–88°/5 mm. phenylhydrazone, m.p. 138° oxime methiodide: "A" config., m.p. 103–6° "B" config., m.p. 213–4° thiosemicarbazone, m.p. 217° (dec.) nicotinoylhydrazone, m.p. 171° isonicotinoylhydrazone, m.p. 176° methiodide, m.p. 160–3°	61,140, 353,430 4
3-PyCOEt	(1) 3-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 96–99°/5 mm.	353
	(1) 3-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 230–232° phenylhydrazone, m.p. 145° oxime, m.p. 115° mercurichloride, m.p. 130°	108
	3-PyCN, EtMgX	24%	b.p. 205–20° mercurichloride, m.p. 129–29.5°	379

(*continued*)

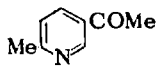
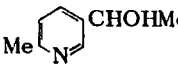
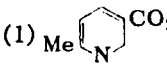
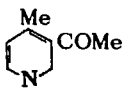
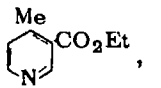
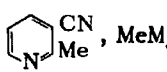
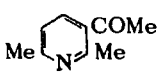
TABLE XIV-3. (*Continued*)

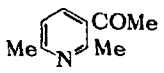
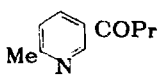
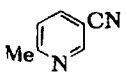
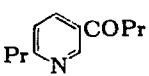
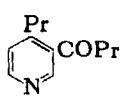
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			hydantoin (5,5-substituted), m.p. 160–61°	
			thiosemicarbazone, m.p. 198° dec.	430
3-PyCOPr	3-PyCN, PrMgBr	40%	b.p. 94–98/3 mm. $n_D^{20} = 1.5136$	120
	3-PyCOCl + PrCdCl	30%	$D_{20}^{20} = 1.043$	120
			phenylhydrazone, m.p. 129–30°	
			2,4-dinitrophenylhydrazone, m.p. 153–54°	
			picrate, m.p. 103–104°	
			semicarbazone, m.p. 167–67.5°	
			thiosemicarbazone, m.p. 182–3°	430
	3-PyCN, PrMgBr		b.p. 240–48°	227
			semicarbazone, m.p. 169–70°	
			phenylhydrazone, m.p. 129–30°	
	calcium nicotinate, calcium butyrate, distillation		b.p. 246–52° phenylhydrazone, m.p. 182°	108

			phenylhydrazone, sulfate salt, m.p. 283° mercuric chloride, m.p. 173° ethiodide, m.p. 192°	
	Ethyl *nicotinate*, Ethyl butyrate, ThO_2, heat		b.p. 124–29°/22–23 mm. $n_D^{20} = 1.5212$ phenylhydrazone, m.p. 129–30° mercurichloride, m.p. 114.5–15.5° thiosemicarbazone, m.p. 183–84°	393 10
	(1) 3-$PyCO_2R$, $C_3H_7CO_2R$, base (2) acid		b.p. 107–11°/16 mm.	353
3-$PyCOC_6H_{13}$	3-PyCN + $C_6H_{13}MgX$	38%	b.p. 148–51°/7 mm. $n_D^{25} = 1.5029$ picrate, m.p. 97.2–97.7° phenylhydrazone, m.p. 117–20° 2,4-dinitrophenylhydrazone, m.p. 118.5–119° oxime, m.p. 62–3° hydantoin (5,5-substituted), m.p. 156–63° oxime, m.p. 62–63°	379

(*continued*)

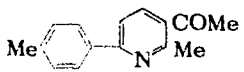
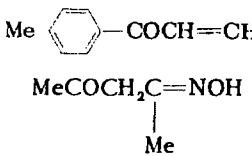
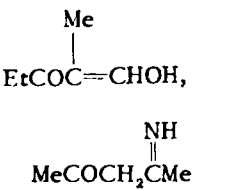
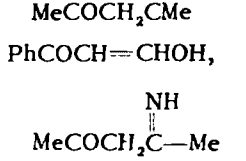
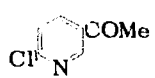
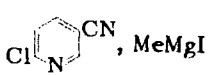
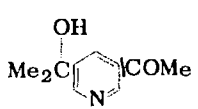
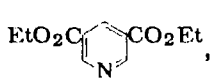
TABLE XIV-3. (*Continued*)

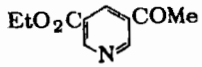
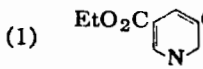
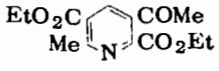
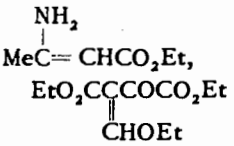
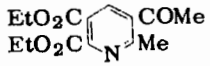
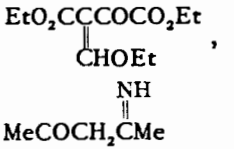
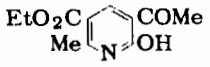
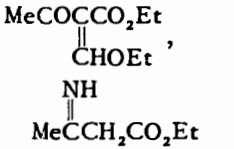
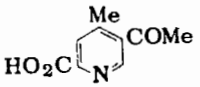
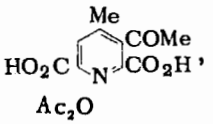
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 , CrO_3, AcOH	80–90%	b.p. 232–3° chloroplatinate, m.p. 195° (dec.) cyanhydrin, m.p. 103–4°	210
	(1)  , CH_3CO_2R, base (2) hydrolysis		b.p. 230–231° picrate, m.p. 192° mercurichloride, m.p. 128° methiodide, m.p. 156.5°	302 28
	(1)  , CH_3CO_2Et, NaOEt (2) hydrolysis		b.p. 105°/12 mm.; 57–8°/1–2 mm. picrate, m.p. 147° chloroplatinate, m.p. 206–7°	325, 392, 319
	 , MeMgI		b.p. 75–78°/2 mm; 98–100/12 mm.	344 98
	oxidation of corresponding carbinol (CrO_3=AcOH)	29.5%	b.p. 230° oxime, m.p. 182°	210
	(1)  , CH_3CO_2R, base		b.p. 120°/19 mm. picrate, m.p. 130°	96

	(2) hydrolysis $EtOCH{=}CHCH(OEt)_2$, $MeCOCH_2C(Me){=}NOH$		b.p. 108 °/12 mm. dihydrate, m.p. 41–2 ° picrate, m.p. 129–30 °	92
	(1) $MeCOCH_2COMe$, NH_3 or NH_4^+, heat (2) $MeCOCH_2COMe$, $MeCOCH_2C(Me){=}NOH$,			435
	 , PrMgI	27%	b.p. 126°/12 mm.	147
	$MeCOCH{=}CHCl$, $PrCOCH{=}CHNH_2$, 25°		b.p. 126–36°/11 mm. picrate, m.p. 140–1°	158
	$PrCOCH{=}CHCl$, $PrCOCH{=}CHNH_2$, 25°	85%	picrate, m.p. 132° (dec.) methiodide, m.p. 98° (dec.)	158
	$PrCOCH{=}CHONa$, $AcONH_4$		b.p. 152°/13 mm. oxime, m.p. 85–6°	26
	3-PyCN, PrMgBr	22%	b.p. 108–11°/3 mm. picrate, m.p. 126° $n_D^{20} = 1.5058$ $D_{20}^{20} = 0.982$	120

(*continued*)

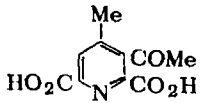
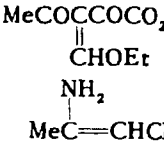
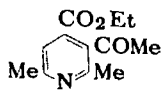
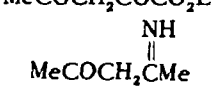
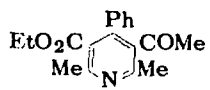
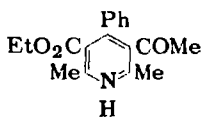
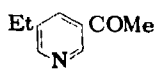
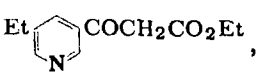
TABLE XIV-3. (*Continued*)

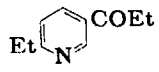
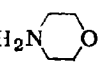
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			m.p. 78° picrate, m.p. 163–4° semicarbazone, m.p. 207° oxime, m.p. 127° hydrochloride, m.p. 150–1°	19
		45%	m.p. 60° picrate, m.p. 118° semicarbazone, m.p. 201° oxime, m.p. 128°	19
		50%	m.p. 90° hydrochloride, m.p. 143–4° picrate, m.p. 166° semicarbazone, m.p. 212° oxime, m.p. 106°	19
		30%	m.p. 104° phenylhydrazone, m.p. 164°	329
			m.p. 128°	303

	(1)  , CH_3CO_2Et, KOEt (2) dil. H_2SO_4		m.p. 69.5–70.5° picrate, m.p. 124–5° oxime, m.p. 149.5–50.5° semicarbazone, m.p. 238–238.5°	243
		82.5%	b.p. 180–5°/2.5 mm. m.p. 67–68° free acid, m.p. 210–13° (dec.)	47
		65–70%	b.p. 165–7°/0.5 mm. m.p. 62–63° free acid, m.p. 165–6° (dec.)	47
			m.p. 210–13°	47
	 Ac_2O			285

(*continued*)

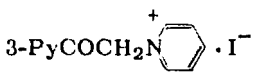
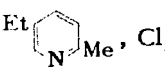
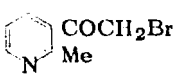
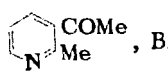
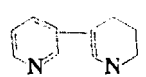
TABLE XIV-3. (*Continued*)

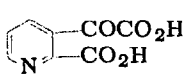
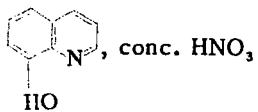
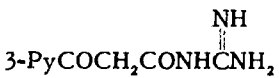
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	$MeCOCH_2COCO_2H$, NH_3		m.p. 175°	285
		47%	b.p. 132–7°/0.8 mm. m.p. 94–95° free acid, m.p. 154–6° (dec.)	47
		65%	m.p. 30–31° picrate, m.p. 160° free acid, m.p. 206–7°	286
	 dil. HNO_3		m.p. 140°	208
	 hydrolysis		b.p. 63–4°/0.3 mm. $n_D^{20} = 1.5211$ $d_{20} = 0.9879$ oxime, m.p. 147.5–8° semicarbazone, m.p. 218–9	243

	EtCOCH=CHONa, $AcONH_4$		b.p. 247–8° picrate, m.p. 217° deriv. with mercuric chloride, m.p. 178° (dec.) oxime, m.p. 104°	27
3-$PyCOCH_2OAc$	3-$PyCOCHN_2$, AcOH	64%	m.p. 84–85° picrate, m.p. 158°	93
	3-$PyCOCH_2Br$, KOAc	65%	m.p. 83–83.5°	417
3-$PyCOCH_2Br$	3-$PyCOCH_2CO_2Et$, HBr	90.1%	hydrobromide, m.p. 181–4° (dec.)	417
	(1) 3-PyCOCl, CH_2N_2 (2) 48% HBr	82%		55
3-$PyCOCH_2Cl$	3-$PyCOCHN_2$, HCl		m.p. 51–52° hydrochloride, m.p. 245–50° (dec.) picrate, m.p. 132° quat. salt with pyridine, m.p. 129–30°	94
3-$PyCOCHN_2$	3-PyCOCl, CH_2N_2	22%	m.p. 74° picrate, m.p. 155–6° (dec.)	93
3-$PyCOCH_2NH_2$	(1) 3-PyCOC(=NOH)CO_2Et, reduction (2) hydrolysis	70% as di HCl salt	*p*-chlorobenzoyl derivative, m.p. 152–152.5° hydrochloride, m.p. 172° (dec.)	59,79
3-$PyCOCH_2N$ 	3-$PyCOCH_2Br$, morpholine	83%	m.p. 64–68°	55

(*continued*)

TABLE XIV-3. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			dihydrochloride, m.p. 197–205°	
			dipicrate, m.p. 158–62°	
	3-$PyCOCH_3$, I_2, pyridine		m.p. 202-3° (dec.)	222
			perchlorate, m.p. 191–2°	
chloride			m.p. 125-30° dec.	94
3-$PyCOCH_2OH$	(1) 3-PyCOCl, CH_2N_2 (2) HCl (3) Na_2CO_3		m.p. 41–42° picrate, m.p. 142–3°	94
3-$PyCOCCl_3$	3-PyEt, Cl_2, HCl, u.v. light		hydrochloride, m.p. 171–2°	425
	 , Cl_2, HCl, u.v. light		hydrochloride, m.p. 166–7°	425
	 , Br_2, HBr	61–64%	hydrobromide, m.p. 210–11°	98
	 ·HBr, NaOAc, AcOH	60–62%	m.p. 66–7°	98
3-$PyCO(CH_2)_3NH_2$	 , carbonyl reagents		derivatives obtained	156

3-PyCO$(CH_2)_3$NHMe	 , HCl, heat	12%	picrate, m.p. 158–60° deriv. with mercuric chloride, m.p. 211–3° b.p. 140–50°/0.005 mm.	155,364
3-PyCO$(CH_2)_3NEt_2$	(a) 3-PyCO_2Et $Et_2N(CH_2)_3CO_2Et$, NaOEt (b) (3-PyCOCH$CO_2Et)^-Na^+$, $ClCH_2CH_2NEt_2$		b.p. 131.5–34°/0.005 mm. oxime, b.p. 185°/1 mm. dipicrolonate, m.p. 201°	36
3-PyCO$(CH_2)_3$OEt	3-PyCN, EtO$(CH_2)_3$MgBr	47%	b.p. 141–3°/5 mm.	83
	 , conc. HNO_3		m.p. 174–6° (dec.)	45
	3-PyCOCH$_2CO_2$Et, guanidine carbonate		m.p. 283–8°	249
3-PyCOCH$_2CO_2$Et	3-PyCO_2R, CH_3CO_2Et, NaOR	50–70%	hydrochloride, m.p. 156–57.5°	370
	3-PyCO_2R, CH_3CO_2Et, NaOR		b.p. 125–35°/1 mm.	78
	3-PyCO_2R, CH_3CO_2Et NaOR	37%	hydrochloride, m.p. 154–55° isonitroso derivative, m.p. 151–52°	59
	3-PyCO_2R, CH_3CO_2Et, NaOR	67%	b.p. 121–23°/0.4 mm.	137

(*continued*)

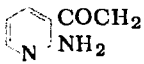
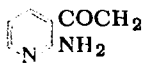
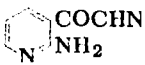
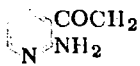
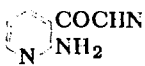
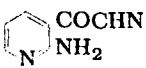
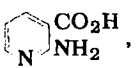
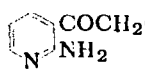
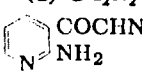
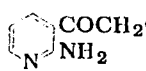
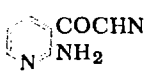
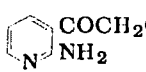
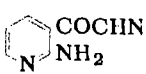
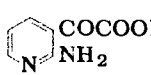
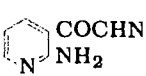
TABLE XIV-3. (*Continued*)

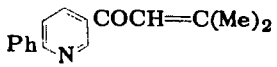
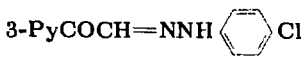
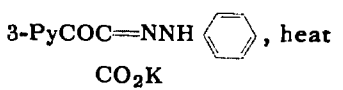
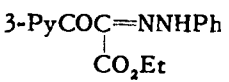
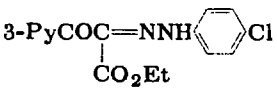
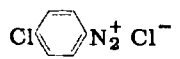
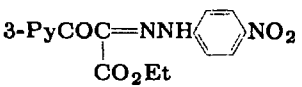
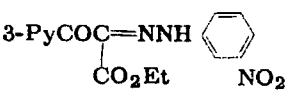
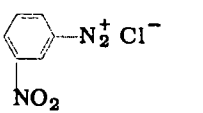
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	3-$PyCO_2R$, CH_3CO_2Et, NaOR	50%	b.p. 132–33°/1–2 mm.	232
3-PyCOCHCO$_2$Et (Bu)	3-$PyCOCH_2CO_2Et$, NaOEt, C_4H_9Br		b.p. 110°/2 mm.	232
3-$PyCOCH_2CO_2$(*i*-Pr)	3-$PyCO_2R$, CH_3CO_2(*i*-Pr) NaOR	64%	b.p. 130–33°/1 mm.	353
3-PyCOCHCO$_2$(*i*-Pr) (Me)	3-$PyCO_2R$, $CH_3CH_2CO_2$(*i*-Pr), NaOR	36%	b.p. 134–36°/3 mm.	353
3-PyCOCHCO$_2C_4H_9$(t) (Et)	3-$PyCO_2R$, $C_3H_7CO_2Bu$, NaOR	58%	b.p. 132°/15 mm.	353
3-$PyCOCH(CO_2Et)CH_2CO_2Et$	3-$PyCO_2Et$, CH_2CO_2Et | CH_2CO_2Et $NaNH_2$	50–56%	b.p. 160–62°/1 mm.	64
3-$PyCOCH_2CONHC(=NH)NH_2$	3-$PyCOCH_2CO_2Et$, guanidine carbonate		m.p. 283–8° (dec.)	249
3-PyCOCH(CH$_2$)$_2$CO$_2$Et (CO$_2$Et)	3-$PyCO_2R$, diethyl succinate, base	8%	b.p. 202–204°/5 mm.	353
3-PyCOCHCO$_2$(tert. Bu) (Me)	3-$PyCO_2R$, $CH_3CH_2CO_2$ (tert. Bu)	54%	b.p. 120–24°/1.5 mm.	353
3-$PyCOCH_2CH_2CO_2H$	Degradation of nicotine by soil bacteria		m.p. 161–62° semicarbazone, m.p. 228–29°	390

	3-PyCOCH(CO_2Et)CH_2-CO_2Et, hydrolysis	76%	m.p. 161.5–63° oxime, m.p. 165–66° acetylhydrazone, m.p. 195–98°	64
3-PyCOCHCOOEt CH_3	3-PyCOCH(CO_2Et)CH_2-CO_2Et, hydrolysis		b.p. 131–34°/1 mm. oxime, m.p. 96.5–97.5°	57
	(1) 3-PyCO_2R, $C_2H_5CO_2Et$, base (2) acid	13%	b.p. 122–23°/2 mm. hydrochloride, m.p. 126–27° (dec.)	59,232
3-PyCOCH(Et)CO_2Et	3-PyCOCH$_2$CH(CO_2R), EtBr		b.p. 120–30°/2 mm.	232
Et-Py-$COCH_2CO_2Et$			picrate, m.p. 135–6°	243
Me-Py-$COCHN_2$	Me-Py-CO_2H (1) $SOCl_2$, 0°C. (2) CH_2N_2		m.p. 71–73° picrate, m.p. 111–18°	319
Py-$COCHN_2$-CO_2Me	Py-COCl-CO_2Me CH_2N_2		m.p. 68–70°	274
Py-$COCH_2OAc$-NH_2	Py-$COCHN_2$-NH_2		m.p. 138–39°	274
Py-$COCH_2OAc$-Me	Py-$COCH_3$-Me (1) Br_2 (2) KOAc-EtOH			344

(*continued*)

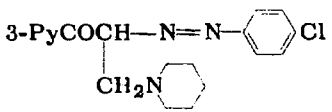
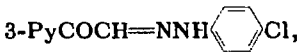
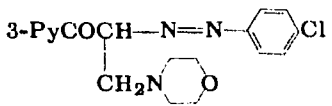
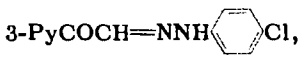
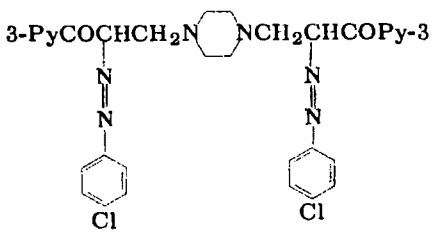
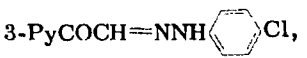
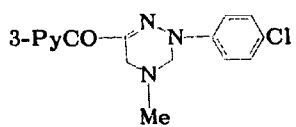
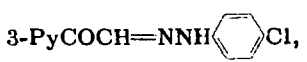
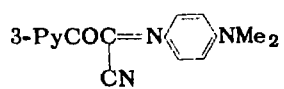
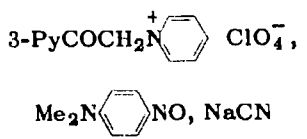
TABLE XIV-3. (*Continued*)

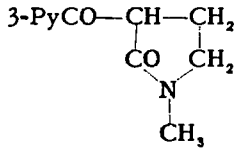
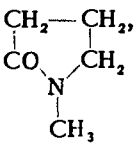
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 , $(CH_2)_6N_4$	62%	free amine unstable dihydrobromide, m.p. 254° (dec.)	274
	 , conc. HBr	83%	m.p. 113° hydrobromide, m.p. 217° (dec.)	274
	 , 5N HCl		m.p. 146°	274
	 , (1) PCl_5-CH_3COCl (2) CH_2N_2	77%	photosensitive, m.p. 163° (dec.)	274
	 , N, H_2SO_4		m.p. 139.5°	274
	 , HCO_2H, 100°		m.p. 143° (dec.)	274
	 , N-H_2SO_4		m.p. over 350°	274
			m.p. 197–9° (dec.)	189

	(1) $C_6H_5NMe_2$, 180° (2) nitrosation, $FeCl_3$ (3) $FeCl_3$, oxidation (4) dil. alkali			
	$(CH_3)_2C:CHCOCH:CHONa$, $AcONH_4$, (AcOH-EtOH)		m.p. 73–74° picrate, m.p. 175–76° mercurichloride, m.p. 135°	26
		26%	m.p. 150–1°	154
	$(3\text{-PyCOCHCO}_2\text{Et})^-Na^+$, $PhN_2^+Cl^-$	20%	m.p. 77–78°	154
	$(3\text{-PyCOCHCO}_2\text{Et})^-Na^+$, 	77%	m.p. 91–93° free acid, m.p. 175–6° potassium salt, m.p. 215°	154
	$(3\text{-PyCOCHCO}_2\text{Et})^-Na^+$, 	73%	m.p. 132–3° free acid, m.p. 178–80° potassium salt, m.p. 230°	154
	$(3\text{-PyCOCHCO}_2\text{Et})^-Na^+$, 	75%	m.p. 105–7° free acid, m.p. 190–2° potassium salt, m.p. 300°	154

(*continued*)

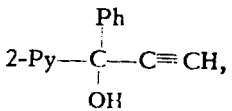
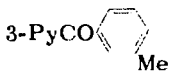
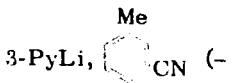
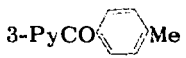
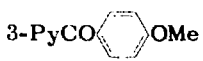
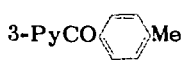
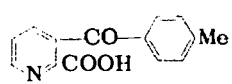
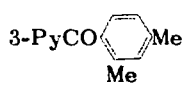
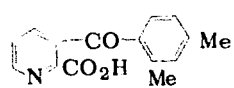
TABLE XIV-3. (*Continued*)

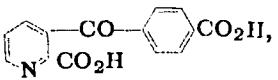
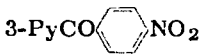
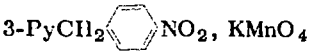
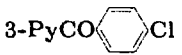
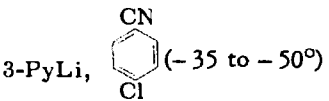
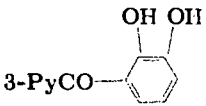
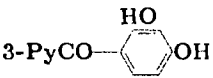
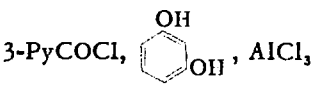
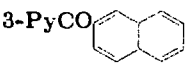
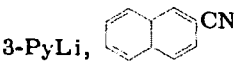
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 H_2CO, piperidine	25%	m.p. 117–9°	154
	 H_2CO, morpholine	28%	m.p. 119–21°	154
	 H_2CO, piperazine	45%	m.p. 200–2°	154
	 H_2CO, $MeNH_2$	19%	m.p. 146–8°	154
		93% (crude)	m.p. 156–7°	222

	3-$PyCO_2Et$,  NaOEt		b.p. 152-154°/0.02-0.03 mm. picrate, m.p. 154–55°	155,364
3-PyCOPh	3-PyCOCl, C_6H_6, $AlCl_3$; (CS_2)		b.p. 180°/12 mm. (yellow oil) m.p. 39° chloroplatinate, m.p. 245° thiosemicarbazone, m.p. 175–76°	10,418
	3-PyCOCl, C_6H_6, $AlCl_3(CS_2)$	90–96%	b.p. 107–10°/0.3 mm.; 141–45°/4 mm. $n_D^{26} = 1.6088$	386
	3-PyLi, PhCN(– 35° to – 50°)	60.9%	m.p. 32–34° b.p. 139–42°/2 mm.	122
	3-PyCN, PhMgBr, hydrolysis	96.0%	b.p. 318–19° oxime, m.p. 161°	228
	 decarboxylation		b.p. ca. 307°	202
	 decarboxylation		b.p. 307° phenylhydrazone, m.p. 143.5°	31

(*continued*)

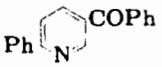
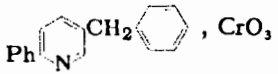
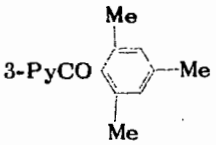
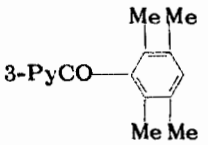
TABLE XIV-3. (*Continued*)

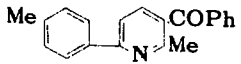
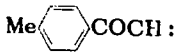
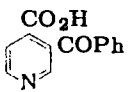
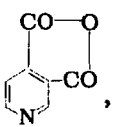
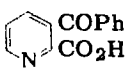
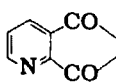
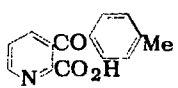
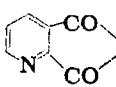
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
		70–80%		131
	 (– 35 to – 50°)	41.9%	m.p. 37–38° b.p. 148–50°/2 mm.	122
	 (– 35 to 50°)	52.4%	m.p. 78–78.5° b.p. 175–76°/6 mm.	122
	3-PyCOCl, C_6H_5OMe, $AlCl_3$		m.p. 99° chloroplatinate, m.p. 267° (dec.) picrate, m.p. 185° phenylhydrazone, m.p. 157°	418
	 decarboxylation		m.p. 78° oxime, m.p. 167°	157,188
	 decarboxylation		b.p. 240° picrate, m.p. 134°	157

	 decarboxylation		m.p. 267° phenylhydrazone, m.p. 246–48°	125
			m.p. 106° picrate, m.p. 185–87°	52
		15.6%	m.p. 88–89° b.p. 150–53°/2 mm.	122
			m.p. 154–6°	429
			m.p. 188–90° sulfate, m.p. 190–2° hydrochloride, m.p. 246–8°	439
	 (–35 to –60°)	32.5%	m.p. 77.8° b.p. 197–200°/2 mm.	122
$3\text{-Py})_2CO$	3-PyCO_2H, pyrolysis		dipicrate, m.p. 135°	239
	$EtOCH:CHCH(OEt)$, $C_6H_5COCH_2C(:NH)Me$		b.p. 170–73°/12 mm. perchlorate, m.p. 172–72°	92

(*continued*)

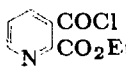
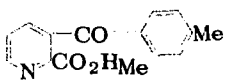
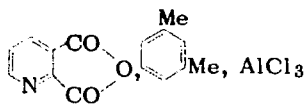
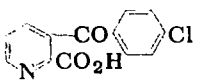
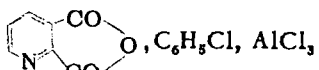
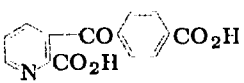
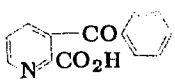
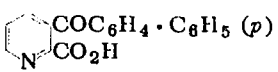
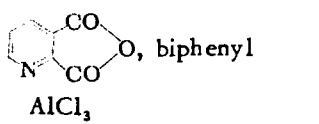
TABLE XIV-3. (*Continued*)

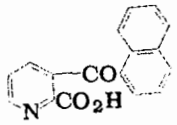
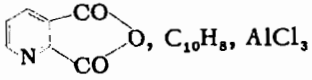
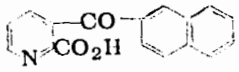
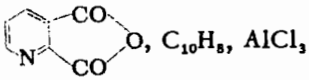
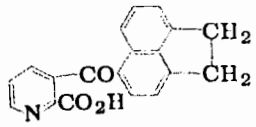
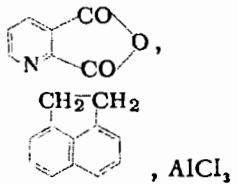
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	(1) $CH{\equiv}CCOC_6H_5$ (2) $CH_2{=}CCH:CHCOPh$, COPh $AcONH_4$, AcOH		m.p. 86–87°	186
	$PhCOC{\equiv}CH$, $(NH_4)_2CO_3$		m.p. 84–85°	49
	(a)  , CrO_3 (b) $PhCOCH{=}CHONa$, NH_4OAc, AcOH	40%	hydrochloride, m.p. 202° (dec.) picrate, m.p. 175° nitrate, m.p. 135–36° sulfate, m.p. 137–38° oxime, m.p. 183–84°	28
	 , C_6H_6, $AlCl_3$		b.p. 167°/0.45 mm.	2
	3-PyCOCl, mesitylene, $AlCl_3$	50.5%	b.p. 96–98°/0.1 mm. picrate, m.p. 167–8°	130
	3-PyCOCl, durene, $AlCl_3$	32%	m.p. 80.5–81.5° picrate, m.p. 183–5°	130

	 PhCOCH$_2$C(Me) : NH,		m.p. 84° picrate, m.p. 191°	18,19
	PhCOCH : CHOH, PhCOCH$_2$C(Me)=NH		m.p. 77°	19
	MeCOCH$_2$COCO$_2$Et PhCOCH$_2$C(Me) : NH	60%	m.p. 66° b.p. 220°/13 mm. hydrochloride, m.p. 188–89° free acid, m.p. 255–58° (dec.)	286
	 , C$_6$H$_6$, AlCl$_3$		m.p. 270°	202
	 , C$_6$H$_6$, AlCl$_3$		m.p. 147°	31,203
	 CH$_6$C H$_5$, AlCl$_3$		m.p. 169° oxime, m.p. 217°	125,157, 188

(*continued*)

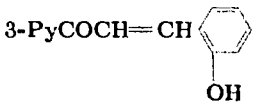
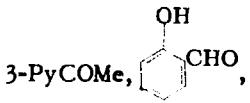
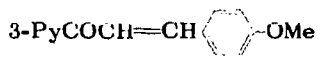
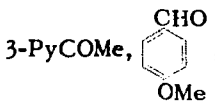
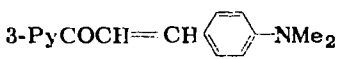
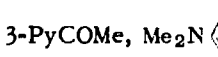
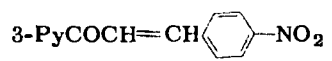
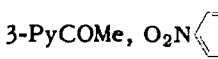
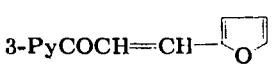
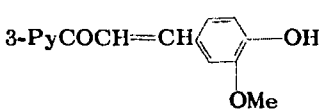
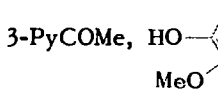
TABLE XIV-3. (*Continued*)

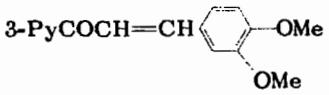
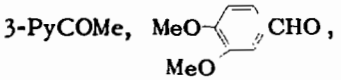
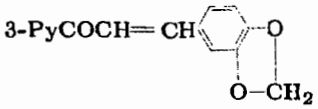
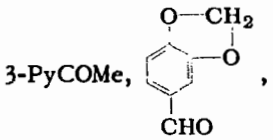
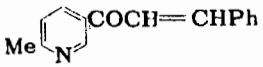
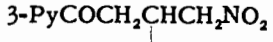
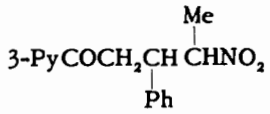
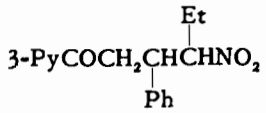
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 $AlCl_3$	almost 100%	m.p. 169°	157
			m.p. 142°	157
			m.p. 147° hydrochloride, m.p. 164° sulfate, m.p. 165° copper complex, m.p. 281° amide, m.p. 176°	214
	 oxidation		dimethyl ester, m.p. 110–11°	125
	 $AlCl_3$		m.p. 170–71°	183

			m.p. 155° hydrochloride, m.p. 179–80° methyl ester, m.p. 100–101°	183,184
			m.p. 145° hydrochloride, m.p. 172–73° methyl ester, m.p. 80–82° hydrate, m.p. 109°	183,184
			m.p. 168–69° hydrochloride, m.p. 175° methyl ester, m.p. 113–14° hydrate, m.p. 121°	183
3-PyCOCH$_2$Ph	3-PyCOCHPh, 48% HBr CN		m.p. 58–59° hydrobromide, m.p. 225–8° (dec.) oxime, m.p. 124.5–125.5°	57
3-PyCOCHPh CN	3-PyCO$_2$Et, PhCH$_2$CN, NaOEt	71%	m.p. 142–3°	57
3-PyCOCHCO$_2$Et Ph	3-PyCO$_2$Et, PhCH$_2$CO$_2$Et, NaOEt	17%	b.p. 168–70°/2 mm. m.p. ca. 65°	232
3-PyCOCH=CHPh	3-PyCOMe, PhCHO, Et$_2$NH	92%	m.p. 84–85°	205,219

(*continued*)

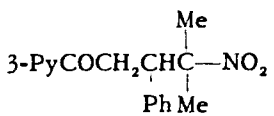
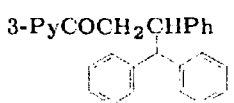
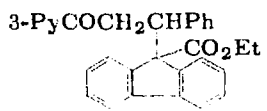
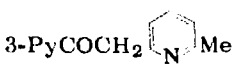
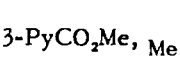
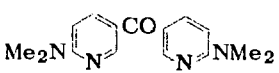
TABLE XIV-3. (*Continued*)

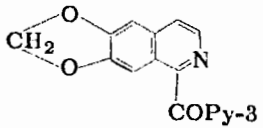
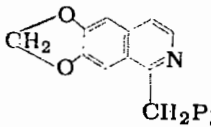
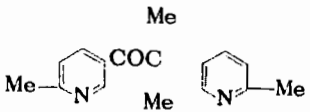
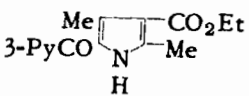
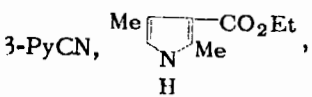
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 Et$_2$NH		m.p. 174°	219
			m.p. 93°	219
	3-PyCOMe,  Et$_2$NH		m.p. 74–5°	219
	3-PyCOMe,  Et$_2$NH		m.p. 186–7°	219
	3-PyCOMe, furfural, Et$_2$NH		m.p. 84°	219
	3-PyCOMe,  Et$_2$NH		m.p. 185–6°	219

	 Et_2NH		m.p. 98°	219
	 Et_2NH		m.p. 154°	219
	 Et_2NH		m.p. 74.5° picrate, m.p. 228–9°	251
	3-PyCOCH=CHPh, $MeNO_2$, Et_2NH	75%	m.p. 97–99° oxime, m.p. 113–4°	205
	3-PyCOCH=CHPh, $EtNO_2$, Et_2NH		m.p. 91–2°; isomer, m.p. 82–4° hydrochloride, m.p. 178–9° oxime, m.p. 152–4° picrate, m.p. 134–5°	205
	3-PyCOCH=CHPh, $PrNO_2$, Et_2NH	86%	m.p. 145–6° oxime, m.p. 143–4° isomer, m.p. 84–5° isomer-picrate, m.p. 138–9° isomer-oxime, m.p. 152–3°	205

(continued)

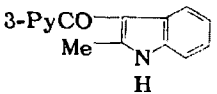
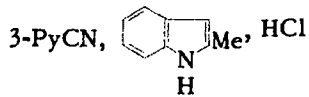
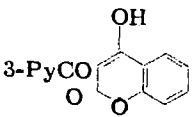
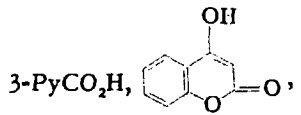
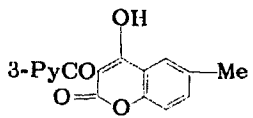
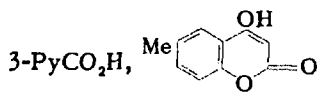
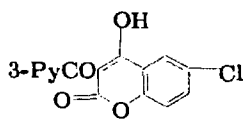
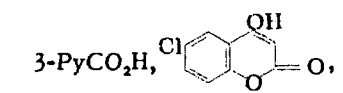
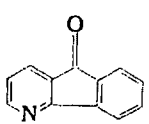
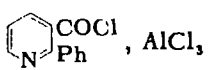
TABLE XIV-3. (*Continued*)

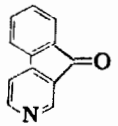
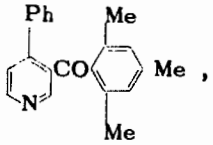
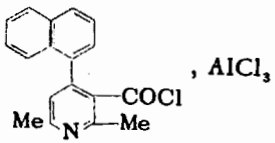
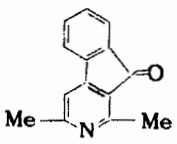
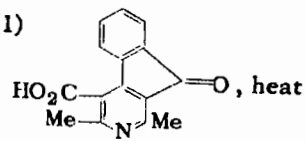
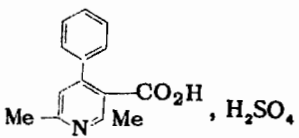
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	3-PyCOCH=CHC$_6$H$_5$, *i*-PrNO$_2$, Et$_2$NH	95%	picrate, m.p. 189–90° phenylhydrazone, "a" isomer, m.p. 173–5°; "b" isomer, m.p. 128–30°	205
	3-PyCOCH=CHPh, fluorene, NaOH	55%	m.p. 258–60°	205
	3-PyCOCH=CHPh, 9-carbethoxyfluorene, NaOH		m.p. 91–2°	205
3-PyCOCH$_2$Py-2	3-PyCN, 2-PyCH$_2$Li		m.p. 71.5–73° oxime, m.p. 135–136.5° picrate, m.p. 187.3–187.8	57,142
	3-PyCO$_2$Me, 	62.3%	b.p. 160–1°/1.2 mm. picrate, m.p. 198.2–198.8°	142
	hydrolysis of corresponding thioketone	100%	m.p. 169–70° oxime, m.p. 207°	73
3-PyCOPy-3			m.p. 105–7°	301

3-PyCOCH$_2$Py-3	3-PyCO$_2$R, 3-PyMe, KNH$_2$	13.2%	b.p. 169–73°/3 mm. m.p. 79.8–80.6° dipicrate, m.p. 199.5–200°	277
	 air, KOH	60%	m.p. 176–7°	292
Me 3-PyCOCPy-3 Me	(1) 3-PyCOMe, u.v. light (2) conc. H_2SO_4		m.p. 51–2° oxime, m.p. 175–7°	29
			m.p. 87–8°	29
Ph 3-PyCOCPy-3 Ph	OH OH 3-PyC—CPy-3, Ph Ph pinacol rearrangement			200
	 HCl	37%	m.p. 155–6° 2,4-dinitrophenylhydrazone, m.p. 222°	367

(*continued*)

TABLE XIV-3. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
		62%	m.p. 202.5°	369
	 $POCl_3$		m.p. 91–93°	438
	 $POCl_3$		m.p. 117–9°	438
	 $POCl_3$		m.p. 140°	438
	 $AlCl_3$		m.p. 139.5–141.5°	2,355

	 polyphosphoric acid	48%	m.p. 155.5–156.5°	130, 444, 445
		59%	m.p. 212–3°	191
	(1) 		m.p. 158–60° oxime, m.p. 280–1° picrate, m.p. (dec.) 234° methiodide, m.p. 225–7°	42,191, 276
	(2) 	quant.		

(*continued*)

TABLE XIV-3. (*Continued*)

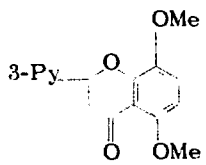
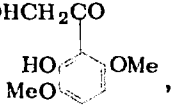
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	3-PyCHOHCH$_2$CO  Amberlite IRA 400 (OH^-) resin		m.p. 173–4°	38

TABLE XIV-4. Preparation and Properties of 4-Pyridyl Ketones

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
4-PyCOMe	(1) 4-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 212–14°; 77°/5 mm. picrate, m.p. 120–30° chloroplatinate, m.p. 205° phenylhydrazone, m.p. 150° oxime, m.p. 142° mercurichloride, m.p. 183–84°	59,215, 309
	(1) 4-$PyCO_2R$, CH_3CO_2R, base (2) acid	82–89%	b.p. 90°/8 mm. phenylhydrazone, m.p. 146.5–47.5° methiodide, m.p. 171–72.5° methobromide, m.p. 183–84° dibromide, m.p. 98–99° (resolidifies, melts at 205° (dec.)) 1-oxide, m.p. 132.5–5° 1-oxide, 2,4-dinitrophenylhydrazone, m.p. 255–9°	197 198

(*continued*)

TABLE XIV-4. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			1-oxide, picrofonate, m.p. 138–9° dec.	
	(1) 4-$PyCO_2R$, CH_3CO_2R, base (2) acid		thiosemicarbazone, m.p. 218°	10
	(1) 4-$PyCO_2R$, CH_3CO_2R, base (2) acid		b.p. 106°/25 mm. picrate, m.p. 128°	77
			oxime methiodide: "A" configuration, m.p. 104–9° "B" configuration, m.p. 191–3°	140
			thiosemicarbazone, m.p. 222° (dec.)	430
			isonicotinoylhydrazone, m.p. 151°	61
4-PyCOEt	(1) 4-$PyCOCH(Na)CO_2R$, CH_3I (2) acid		chloroplatinate, m.p. 205° aurichloride, m.p. 163–64°	309
			imine, b.p. 101°/3 mm.; $n_D^{22} = 1.6060$	48
4-PyCOPr	(1) 4-$PyCO_2R$, $C_3H_7CO_2R$, base (2) acid		b.p. 229–31° picrate, m.p. 96°	309

	(1) 4-$PyCOCH_2CO_2Et$, Na, EtBr (2) dil. HCl	20%	b.p. 107–108.5°/9 mm.	65
4-PyCOBu	(1) 4-$PyCO_2R$, $C_4H_9CO_2R$, base (2) acid		b.p. 239–40° picrate, m.p. 101°	309
			imine, b.p. 127–8°/6 mm.; $n_D^{21} = 1.5257$	48
4-$PyCOCH_2CO_2Et$	4-$PyCO_2R$, CH_3CO_2Et, NaOR	63%	b.p. 132–35°/1–2 mm. m.p. 54°	232
	4-$PyCO_2R$, CH_3CO_2Et, NaOR	54%		192
	4-$PyCO_2R$, CH_3CO_2Et, NaOR	80%	m.p. 57–58° hydrochloride, m.p. 170–74° (dec.) isonitroso der., m.p. 162.5–63°	59
	4-$PyCO_2R$, CH_3CO_2Et, NaOR	69%	m.p. 53–55° b.p. 118–20°/0.4 mm.	137
	4-$PyCO_2R$, CH_3CO_2Et, NaOR		hydrochloride, m.p. 165° chloroplatinate, m.p. 156° copper salt, m.p. 183–84° phenylpyrazolone, m.p. 215°	309
4-PyCOCHMeCO_2Et	4-$PyCO_2R$, $EtCO_2Et$, NaOR	25%	m.p. 55–56° b.p. 118–20°/2 mm.	232

(continued)

TABLE XIV-4. (*Continued*)

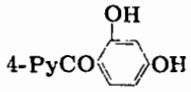
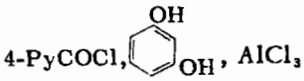
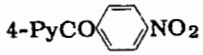
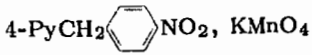
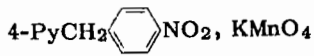
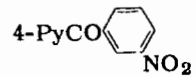
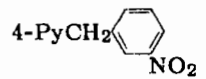
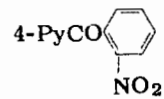
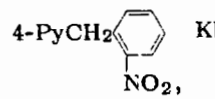
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
4-PyCOCHCO$_2$Et Et	4-PyCOCH$_2$CO$_2$Et, EtBr, NaOR		b.p. 120–5°/2 mm.	232
4-PyCOCHCO$_2$Et Ph	4-PyCO$_2$Et, PhCH$_2$CO$_2$Et, NaOEt	50%	m.p. 105°	232
4-PyCOCH$_2$OAc	4-PyCOCH$_2$Br, KOAc		m.p. 65.5–66.5° (platelets) b.p. 78–84°/0.003–0.004 mm.	417
	4-PyCOCHN$_2$, CH$_3$COOH, reflux		m.p. 68–69° picrate, m.p. 148° (dec.)	94
4-PyCOCH$_2$Cl	4-PyCOCHN$_2$, HCl		(compd. + 1-CH$_3$OH), m.p. 103° (dec.)	94
4-PyCOCH$_2$Br	4-PyCOCH$_2$COOEt, aq. HBr, Br$_2$	62.5%	hydrobromide, m.p. 198–201°	417
4-PyCOCHN$_2$	4-PyCOCl, CH$_2$N$_2$	57% vs. acid	m.p. 35–36° picrate, m.p. 244°	94
4-PyCOCH$_2$NH$_2$	4-PyCOCCOOEt (1) Reduction (2) Hydrolysis NOH	65%	dihydrochloride, m.p. 240–45° (dec.)	59
4-PyCOCH$_2$—N$^+$ · I$^-$	4-PyCOMe, I$_2$, pyridine	57% (crude)	m.p. 168–9° perchlorate, m.p. 154–5°	222

4-PyCOCH$_2$CH$_2$ 	(1) BzCH$_2$CH$_2$CO$_2$Et, 4-PyCO$_2$Et, NaOEt (2) hydrolysis		m.p. 44° dihydrochloride, m.p. 165–6° oxalate, m.p. 190.5–191°	337
4-PyCO(CH$_2$)$_3$NEt$_2$	(a) 4-PyCO$_2$R + (C$_2$H$_5$)$_2$NCH$_2$CH$_2$-CH$_2$CO$_2$C$_2$H$_5$, NaOEt (b) 4-PyCOCH(Na)CO$_2$R, ClCH$_2$ CH$_2$N(C$_2$H$_5$)$_2$	58% 4%	b.p. 122–28°/1 mm.	36
4-PyCO(CH$_2$)$_3$CN	4-PyCOMe, CH$_2$=CHCN, "Triton-B"		m.p. 139–40°	65
4-PyCOPh	4-PyCH$_2$C$_6$H$_5$, KMnO$_4$ oxidation		b.p. 313.5–14°/742 mm. m.p. 71.5–72.5° hydrochloride, m.p. 195–97° picrate, m.p. 159–60°	87
	4-PyCH$_2$C$_6$H$_5$, CrO$_3$ or KMnO$_4$ oxidation		m.p. 72° b.p. 315°/762 mm. picrate, m.p. 160° phenylhydrazone, m.p. 180–82°	68
	4-PyCH$_3$C$_6$H$_5$, KMnO$_4$ oxidation		b.p. 315° m.p. 72° picrate, m.p. 160°	228
	4-PyCH$_2$C$_6$H$_5$, KMnO$_4$ oxidation		m.p. 72° picrate, m.p. 160°	378
	4-PyCHOHC$_6$H$_5$, KMnO$_4$			67

(*continued*)

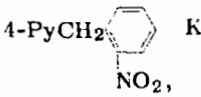
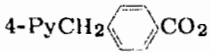
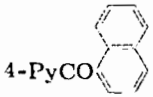
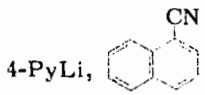
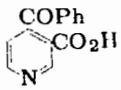
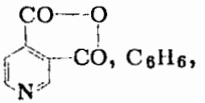
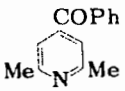
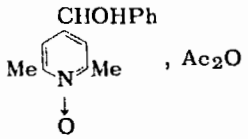
TABLE XIV-4. (*Continued*)

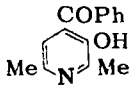
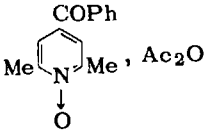
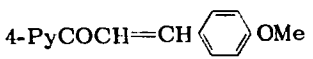
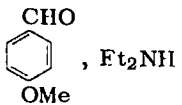
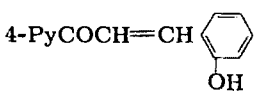
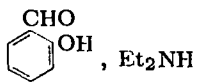
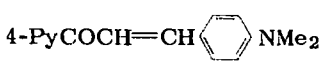
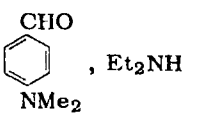
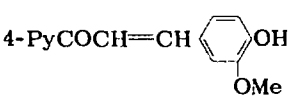
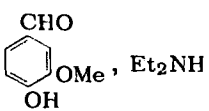
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 decarboxylation		light yellow oil, b.p. 300°	312
	 decarboxylation		m.p. 72° b.p. ca 300°	202
			oxime methiodide, "B" configuration, m.p. 215–7°	139
			imine, b.p. 126°/0.5 mm.; 135°/2 mm.; n_D^{21} = 1.6098	48
	4-$PyCH_2Ph$, SeO_2, AcOH	81%	m.p. 69–75° methiodide, m.p. 174–6° methobromide, m.p. 165–8°	242
	4-PyLi, PhCN	27.6% (from 4-PyBr)	m.p. 71.8–72.4°	396
4-PyCO  NH_2	4-PyCO  NO_2, $SnCl_2$		m.p. 154–5° picrate, m.p. 186° hydrochloride m.p. 226°	212

		m.p. 271.8–272.6°	439
		m.p. 123–24° hydrochloride, m.p. 202° phenylhydrazone, m.p. 226° oxime, m.p. 209°	87
		m.p. 121–22° hydrochloride, m.p. 202° phenylhydrazone, m.p. 226° oxime, m.p. 209°	212
		m.p. 123–24°	74
		m.p. 129° hydrochloride, m.p. 245°	52,87
		m.p. 75°	87

(*continued*)

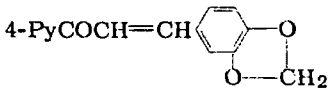
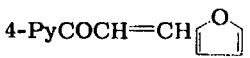
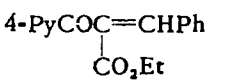
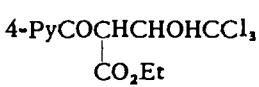
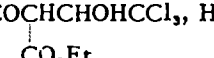
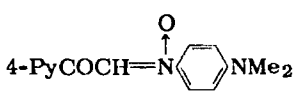
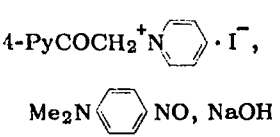
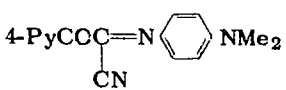
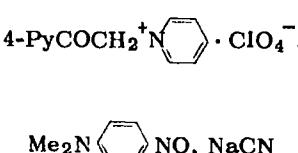
TABLE XIV-4. (*Continued*)

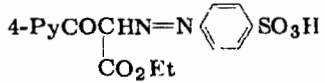
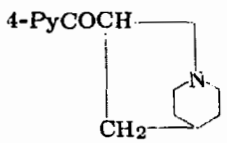
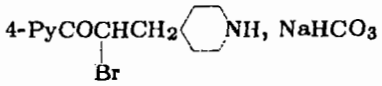
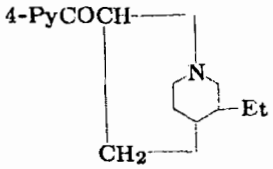
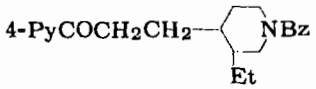
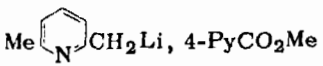
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 $KMnO_4$ oxidation		m.p. 77–78°	294
		26%	m.p. 299–300° oxime, m.p. 245–46°	388
			b.p. 181°/0.04 mm. m.p. 49–50° picrate, m.p. 166.7–167.1° oxime, m.p. 194–5°	396
			m.p. 216°	312
			m.p. 226° hydrochloride, m.p. 240°	202
			b.p. 157°/0.4 mm. picrate, m.p. 175°	446

		b.p. 125–30°/0.4 mm. m.p. 150–2°	446
4-PyCOCH=CHPh	4-PyCOMe, PhCHO, Et_2NH	m.p. 87–88° picrate, m.p. 198–9°	219, 251
		m.p. 115–6°	219
		m.p. 181–2°	219
		m.p. 127–8°	219
		m.p. 222°	219

(*continued*)

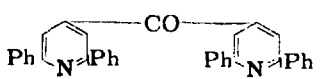
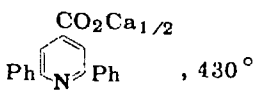
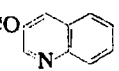
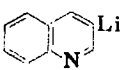
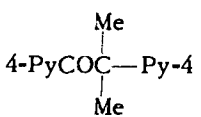
TABLE XIV-4. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	4-PyCOMe, piperonal, Et_2NH		m.p. 140°	219
	4-PyCOMe, furfural, Et_2NH		m.p. 77°	219
	4-$PyCOCH_2CO_2Et$, PhCHO piperidine		m.p. 110–12°	246
	4-$PyCOCH_2CO_2Et$, chloral hydrate		m.p. 139–41°	246
4-$PyCOCH_2CHOHCCl_3$			m.p. 177–8°	246
		44% crude	m.p. 122–123.5°	222
		93% crude	m.p. 188–9°	222

			m.p. 175–6° Na salt, m.p. 213–4° ethyl ester, m.p. 78–80°; hydrochloride, m.p. 132–4° methyl ester, m.p. 138–40°	154
			Na salt, m.p. 232–5°	154
			m.p. 117–18° dihydrochloride, m.p. 221–23°	337
			m.p. 91–92°	336
		90.5%	m.p. 111–111.7° picrate, m.p. 200–200.5°	142
4-PyCOPy-2	4-PyLi, 2-PyCN	27–28%	m.p. 122–122.5°	396
4-PyCOPy-3	4-PyLi, 3-PyCN	4–5%	m.p. 120.9–121.3°	396

(*continued*)

TABLE XIV-4. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
4-PyCOCH$_2$Py-4	4-PyCO$_2$Me, 4-PyMe, NaNH$_2$		m.p. 116–18°	305
4-PyCOCH$_2$Py-3	4-PyCO$_2$R, 3-PyMe, KNH$_2$	27.8%	b.p. 169–70°/3 mm. m.p. 65.8–66.8° picrate, m.p. 174.3–75°	277
4-PyCOCH$_2$Py-2	2-PyCH$_2$Li, 4-PyCO$_2$Me	75.7%	m.p. 114.7–115.2°	142
4-PyCOPy-4	(a) 4-PyLi, 4-PyCN	29%	m.p. 136.2–137.5°	396
	(b) 4-PyLi, 4-PyCO$_2$Et	31%	phenylhydrazone, m.p. 250.3–250.8°	
	 , 430°	75%	m.p. 202–3° oxime, m.p. 236° 2,4-dinitrophenylhydrazone, m.p. 302–3°	351
4-PyCO 	4-PyCN, 		m.p. 146.7–147.0°	396
			m.p. 77.5–78.5°	29

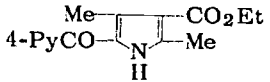
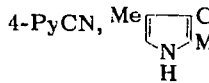
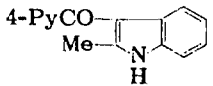
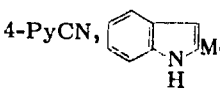
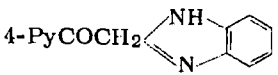
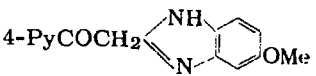
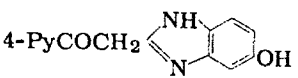
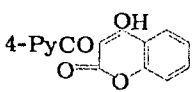
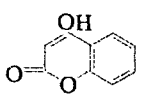
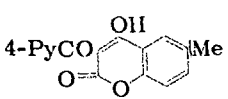
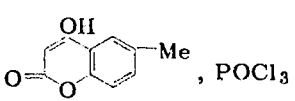
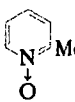
		55%	m.p. 196° 2,4-dinitrophenylhydrazone, m.p. 279°	367
		50%	m.p. 238–9°	367
	4-PyCOCH$_2$CO$_2$Et, *o*-phenylenediamine		m.p. 211–12° hydrochloride, m.p. 230–5°	246
	4-PyCOCH$_2$CO$_2$Et, 		m.p. 317–9° dihydrochloride, m.p. 275–7°	246
	hydrolysis of methyl ether		m.p. over 370°	246
	4-PyCO$_2$H,  , $POCl_3$		m.p. 102–4°	438
	4-PyCO$_2$H,  , $POCl_3$		m.p. 120–2°	438

TABLE XIV-5. Preparation and Properties of 2-Pyridine Side-chain Ketones

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-$PyCH_2COMe$	2-$PyCH_2Li$, CH_3CN	35%	picrate, m.p. 139–40°	58,398
			b.p. 70–95°/5 mm.; m.p. 54°	
			N-benzoylketimine, m.p. 63–64°	
	2-$PyCH_2Li$, Ac_2O	16.4%	b.p. 92°/1.5 mm.	400
			picrate, m.p. 140–40.5°	
			picrolonate, m.p. 179.5–81°	
	2-$PyCH_2Li$, CH_3CO_2Et		picrate, m.p. 140–40.5°	24
	2-$PyCH_2Li$, CH_3CO_2Me	36.3%	b.p. 102–102.5°/10 mm.	141
	2-$PyCH_2Li$, CH_3COCl	23.6%	picrate, m.p. 216–17° (dec.)	206
			picrolonate, m.p. 229–30° (dec.)	
	2-$PyCH_2Li$, CH_3COCl		b.p. 175–80°/2.5 mm.	139
			picrate, m.p. 140°	

	2-$PyCH_2Li$, CH_3CO_2Me	25%	b.p. 50–60°/0.5–1 mm. picrate, m.p. 141–2°	23
	2-PyMe, CH_3CO_2Me, PhNa	59%	b.p. 75–78°/2 mm.	330
	 Me, $CH_2{=}C{=}O$, H_2SO_4	50%		190
2-$PyCH_2COEt$	2-$PyCH_2Li$, $EtCO_2Me$	50%	b.p. 99–103°/5 mm.	141
	2-$PyCH_2Li$, $EtCO_2Me$	35%	b.p. 80–90°/2 mm. picrate, m.p. 146–7°	23
	2-PyMe, $EtCO_2R$: (a) PhNa	55%	b.p. 83–6°/2 mm.;	330
	(b) $(i\text{-}Pr)_2NNa$	48%	b.p. 73–5°/0.77	
	(c) PhLi	62%	mm.	
	(d) $(i\text{-}Pr)_2NLi$	62%		
2-$PyCH_2COCHMe_2$	2-$PyCH_2Li$, Me_2CHCO_2Me	60.5%	b.p. 79–85°/2 mm.	141
2-$PyCH_2COCH_2CHMe_2$	2-$PyCH_2Li$, $Me_2CHCH_2CO_2Me$	67%	b.p. 114–7°/6 mm.	141
2-$Py(CH_2)_2COMe$	2-$Py(CH_2)_2C{\equiv}CH$, $HgSO_4$—H_2SO_4	45%	b.p. 118°/14 mm. semicarbazone, m.p. 132–3°	279
2-$Py(CH_2)_3COMe$	2-$PyCH{:}CH_2$, CH_3COCH_3, "Triton B"	1–2%	picrate, m.p. 111–12°	

(*continued*)

TABLE XIV-5. (*Continued*)

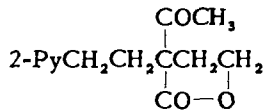
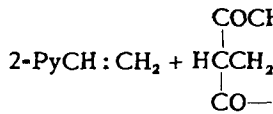
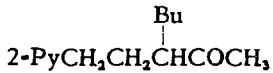
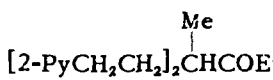
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	2-PyCH : CH_2 + $CH_3COCH_2CO_2Et$ (1) Na (2) HCl		n_D^{22}, 1.5062 picrate, m.p. 111–11.5° 2,4-dinitrophenylhydrazone, m.p. 189–90° oxime-monohydrate, m.p. 55–56°	39,41 91
2-Py$(CH_2)_4COMe$	2-Py$(CH_2)_4C{\equiv}CH$, $HgSO_4$—H_2SO_4	61%	b.p. 106°/0.7 mm. semicarbazone, m.p. 106.5°	279
2-Py$(CH_2)_5COMe$	2-Py$(CH_2)_5C{\equiv}CH$, $HgSO_4$—H_2SO_4	50%	b.p. 120°/0.8 mm. semicarbazone, m.p. 106–7°	279
2-Py$(CH_2)_3COCH_2OH$	(1) 2-Py$(CH_2)_2C(CO_2Et)(OEt)_2$, $LiAlH_4$ (2) HCl	42%	n_D^{20} = 1.5289	311
2-$PyCH_2COCH_2OEt$	2-$PyCH_2Li$, $EtOCH_2COOEt$	75.3%	b.p. 115–17°/1.5 mm. picrate, m.p. 118.5–19°	415

			semicarbazone, m.p. 64–66° 2,4-dinitrophenylhydrazone, m.p. 212–14° (dec.)	
	(a) 2-PyMe, $EtOCH_2CO_2Et$, KNH_2 (b) 2-$PyCH_2Li$, $EtOCH_2COCl$	22.8% 20%		415
2-$PyCH_2CH_2CHCOMe$ Me	2-PyCH:CH_2, $CH_3COCH_2CH_3$, Na	28%	b.p. 101–2°/1 mm. $D_4^{25} = 0.9982$ $n_D^{20} = 1.5012$ semicarbazone, m.p. 153–54°	237
	2-PyCH:CH_2, $CH_3COCH_2CH_3$, "Triton B"	53.5%	b.p. 115–17°/2 mm.	407
2-$PyCH_2CH_2CHCOEt$ Me	2-PyCH:CH_2, $(CH_3CH_2)_2CO$, Na	53.4%	b.p. 142–44°/6 mm. $D_4^{29} = 0.9862$ $n_D^{20} = 1.4980$ semicarbazone m.p. 103–4°	237, 407
Me Me 2-$PyCH_2CH_2CCOCH(Me)_2$	2-PyCH:CH_2, $[(CH_3)_2CH]_2CO$, Na	71.9%	b.p. 146–48°/6 mm. picrate, m.p. 97–98°	407

(*continued*)

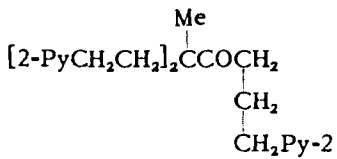
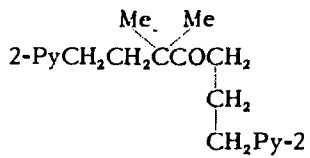
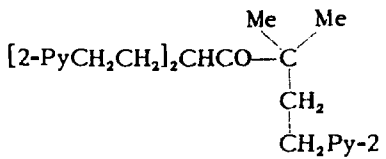
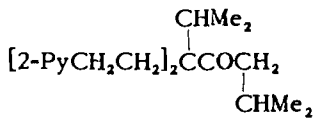
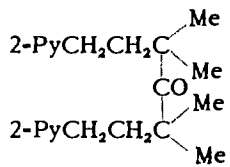
TABLE XIV-5. (*Continued*)

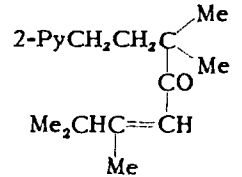
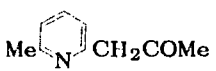
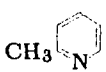
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-PyCH$_2$CH$_2$C(Me)$_2$COMe	2-PyCH : CH$_2$, CH$_3$COCH(CH$_3$)$_2$, Na	72%	b.p. 101–2°/0.5 mm.	407
	2-PyCH : CH$_2$, CH$_3$COCH(CH$_3$)$_2$, "Triton B"	72.2%	semicarbazone, m.p. 149–50°	
2-PyCH$_2$CH$_2$CH$_2$COCH$_2$CH(Me)$_2$	2-PyCH : CH$_2$, CH$_3$COCH$_2$CH(CH$_3$)$_2$, Na	19.6%	b.p. 134–35°/1.5 mm.	407
		32.5%	b.p. 138°/2 mm. D_4^{25} = 0.9664 n_D^{20} = 1.4950 semicarbazone, m.p. 65–66°	237
2-Py(CH$_2$)$_2$CH(CHMe$_2$)COCH$_2$CHMe$_2$	2-PyCH=CH$_2$, (Me$_2$CHCH$_2$)$_2$CO, Na	63.2%	b.p. 160–62°/6 mm. picrate, m.p. 99–100°	407
2-Py(CH$_2$)$_2$CH(Ph)COMe	2-PyCH=CH$_2$, MeCOCH$_2$Ph, Na	44.3%	b.p. 162–4°/2 mm. picrate, m.p. 67–8°	407
2-PyCH$_2$CH$_2$CH$_2$COCMe$_3$	2-PyCH : CH$_2$ + CH$_3$COC(CH$_3$)$_3$, Na	19.7%	b.p. 124–26°/2 mm. n_D^{20} = 1.4953 d_4^{25} = 0.9828	237

			semicarbazone, m.p. 153–54°	
		40%	pale orange oil, b.p. 170–80°/1 mm. $n_D^{23} = 1.5182$ picrate, m.p. 111–12°	39
	(a) 2-PyCH : CH_2, $CH_3COC_5H_{11}$, Na	38.6%	b.p. 155–56°/3–4 mm.	407
	(b) 2-PyCH : CH_2, "Triton B"	8.2%	semicarbazone, m.p. 155–56°	
$[2\text{-PyCH}_2CH_2]_2C(Me)COMe$	2-PyCH : CH_2, $CH_3COCH_2CH_3$, "Triton B"	34.0%	b.p. 189–93°/1.5–2 mm. distyphnate, m.p. 123–125°	407
$[2\text{-PyCH}_2CH_2]_2CHCOCH(Me)_2$	2-PyCH : CH_2, $CH_3COCH_2CH(CH_3)_2$, Na	34.3%	b.p. 208–10°/1.5 mm. dipicrate, m.p. 162–63°	407
	2-PyCH : CH_2, $(C_2H_5)_2CO$, Na	31.6%	b.p. 238–42°/6 mm. dipicrate, m.p. 149–50°	407

(*continued*)

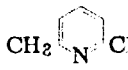
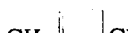
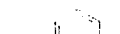
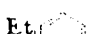
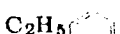
TABLE XIV-5. (*Continued*)

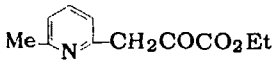
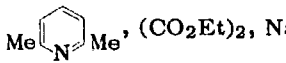
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	2-PyCH : CH_2, $CH_3COC_2H_5$, Na	15.5%	b.p. 268–70°/5 mm. tristyphnate, m.p. 90–91°	407
	2-PyCH : CH_2, $CH_3COCH(CH_3)_2$, Na	4–31%	b.p. 195–96°/0.5 mm. dipicrate, m.p. 137–38°	407
	2-PyCH : CH_2, $CH_3COCHMe_2$, Na	39%	b.p. 282–84°/5 mm. tripicrate, m.p. 155–57°	407
	2-PyCH : CH_2, $[(CH_3)_2CHCH_2]_2CO$, Na	14.1%	b.p. 242°/6 mm. chloroplatinate, m.p. 185–87°	407
	2-PyCH : CH_2, $[(CH_3)_2CH]_2CO$, Na	5.3%	b.p. 236–38°/6 mm. dipicrate, m.p. 148–49°	407

	2-PyCH : CH_2 + $CH_3COCH(CH_3)_2$, Na	3–6%	b.p. 153–55°/0.5 mm. picrate, m.p. 226–28°	407
$[2\text{-}PyCH_2CH_2]_2CCOMe$	2-PyCH : CH_2, $CH_3COC_5H_{11}$, Na	18.7%	b.p. 210–14°/1 mm. dipicrate, m.p. 91–92°	407
"Tripyridylethylated methyl *i*-butyl ketone"	2-PyCH : CH_2, $CH_3COCH_2CH(CH_3)_2$, Na	13.4%	b.p. 267–69°/1.5 mm.	407
2-$PyCH_2CH_2CHCOMe$ CO_2Et	2-PyCH : CH_2, $CH_3COCH_2CO_2Et$, HCl	50%	b.p. 138-50°/1 *mm.* n_D^{22} = 1.500	41,91
	 CH_2Li, CH_3CN	good	b.p. 96–98°/0.5 mm. b.p. 114–15°/9.5–10 mm. b.p. 119–20°/16 mm. picrate, m.p. 136–37.5° semicarbazone, m.p. 144–44.5°	58

(*continued*)

TABLE XIV-5. (*Continued*)

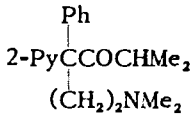
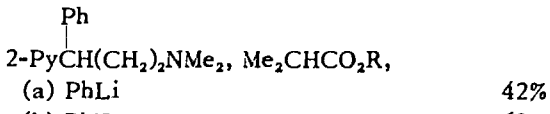
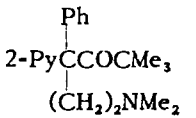
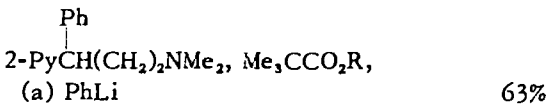
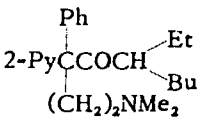
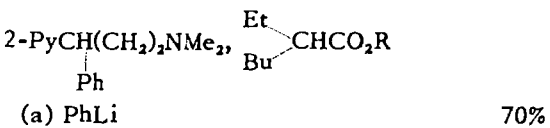
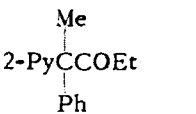
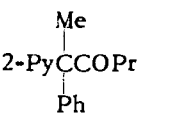
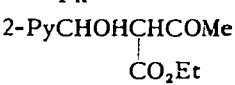
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
		41.6%	b.p. 105–106°/9.9 mm. monopicrate m.p. 137.7–38.3°	142
		46%	b.p. 114–15°/9.5 mm. monopicrate, m.p. 121.5–22.2°	142
		55.6%	b.p. 126–27°/ 10.3 mm. monopicrate, m.p. 124.4–24.9°	142
		61.9%	b.p. 119.5–20.5°/ 9.5 mm. monopicrate, m.p. 124.0–24.5°	142
		22%	b.p. 95°/0.3 mm. picrate, m.p. 108–109.5°	58
2-PyCHOHCH$_2$COMe	2-PyCHO, Me_2CO, Amberlite IRA 400 (OH^-) resin	70%	m.p. 75–6° hydrochloride, m.p. 120–1°	38
	2-PyCHO, Me_2CO, KOH	91.5%	m.p. 70–71° b.p. 98–100°/0.4 mm.	324

2-$PyCH_2COCO_2Et$	$(2\text{-}PyCH_2)_2Cd$, $(CO_2Et)_2$ (−70°)	10%	m.p. 82.5–83.5°	9
	 , $(CO_2Et)_2$, NaH	91%	obtained as 1-oxide, m.p. 56.5–58.5°	43
2-PyCH(Bu)COMe	2-PyCHLi(Bu), MeCN	10%	b.p. 138–42°/4 mm. semicarbazone, m.p. 126–126.5°	58
2-PyCH(Ph)COMe	2-$PyCH_2Ph$, CH_3CO_2Et, PhLi	93%	b.p. 145–50°/2.7 mm.	330
2-PyCH(Ph)COEt	2-$PyCH_2Ph$, $EtCO_2Et$:		b.p. 128–32°/0.28 mm.	330
	(a) PhLi	22–64%		
	(b) $NaN(i\text{-}Pr)_2$	82%	m.p. 76–78°	
	(c) PhNa	81%		
	(d) $LiN(i\text{-}Pr)_2$	54%		
2-PyCH(Ph)$COCHMe_2$	2-$PyCH_2Ph$, Me_2CHCO_2R, PhLi	81%	b.p. 133–5°/0.3 mm.	330
2-PyCH($(CH_2)_2NMe_2$)COMe	2-$Py(CH_2)_3NMe_2$, (a) PhLi CH_3CO_2R; (b) PhNa	35% 84%	b.p. 86–87°/0.33 mm. picrate, m.p. 179.7–180.4°	330
2-PyCH($(CH_2)_2NMe_2$)COEt	2-$Py(CH_2)_3NMe_2$, $EtCO_2R$, PhLi	49%	b.p. 90–91°/0.29 mm. picrate, m.p. 169–70°	330

(*continued*)

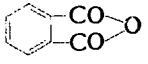
TABLE XIV-5. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-PyCHCOPr $(CH_2)_2NMe_2$	2-Py$(CH_2)_3NMe_2$, $PrCO_2R$, PhLi	44%	b.p. 95–96°/0.26 mm. picrate, m.p. 149.6–150.6°	330
2-PyCHCOCHMe$_2$ $(CH_2)_2NMe_2$	2-Py$(CH_2)_3NMe_2$, Me_2CHCO_2R, (a) PhLi (b) PhNa	48% 85%	b.p. 89–90°/0.28 mm. picrate, m.p. 155.8–156.7°	330
2-PyCHCOCMe$_3$ $(CH_2)_2NMe_2$	2-Py$(CH_2)_3NMe_2$, Me_3CCO_2R, PhLi	50%	b.p. 90–91°/0.29 mm. picrate, m.p. 171.3–172.5°	330
Ph 2-PyCCOMe $(CH_2)_2NMe_2$	Ph 2-PyCH$(CH_2)_2NMe_2$, CH_3CO_2R, (a) PhLi (b) PhNa	30% 67%	b.p. 151–2°/0.62 mm. picrate, m.p. 159.2–160.4°	330
Ph 2-PyCCOEt $(CH_2)_2NMe_2$	Ph 2-PyCH$(CH_2)_2NMe_2$, $EtCO_2R$, (a) PhLi (b) PhNa	32% 75%	b.p. 144–5°/0.27 mm. picrate, m.p. 142.2–145.3°	330
Ph 2-PyCCOPr $(CH_2)_2NMe_2$	Ph 2-PyCH$(CH_2)_2NMe_2$, $PrCO_2R$ (a) PhLi (b) PhNa	40% 69%	b.p. 152–3°/0.29 mm. picrate, m.p. 150.5–151.4°	330

			b.p. 145–6°/0.29 mm.	330
		(a) PhLi	42%	picrate, m.p. 159–60°
		(b) PhNa	69%	
			m.p. 65–67°	330
			b.p. 156–8°/0.25 mm.	
		(a) PhLi	63%	
		(b) PhNa	32%	picrate, m.p. 156.6–157.4°
			b.p. 176–7°/0.28 mm.	330
		(a) PhLi	70%	
		(b) PhNa	82%	
			m.p. 74°, b.p. 135–42°/0.3 mm.	308
			hydrochloride, m.p. 131°	
			m.p. 53–54°	308
			hydrochloride, m.p. 125–26°	
	2-PyCHO, $MeCOCH_2CO_2Et$, piperidine		m.p. 54–54.5°	253

(*continued*)

XIV-5. (*Continued*)

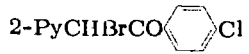
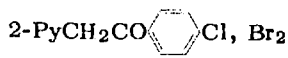
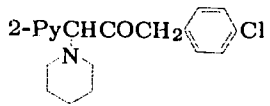
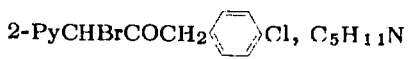
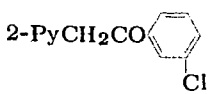
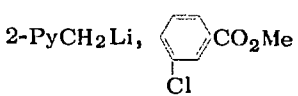
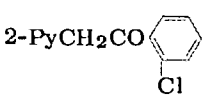
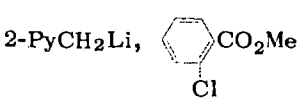
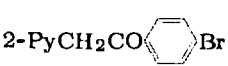
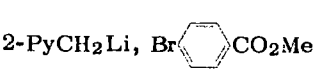
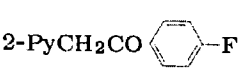
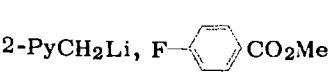
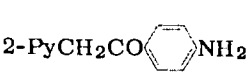
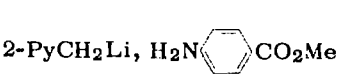
Compound	Method of preparation	Yield	Physical properties, derivatives	
=CHCOMe	2-PyCH=C(CO$_2$Et)COMe, (1) 2N—HCl (2) 	41.6%	b.p. 59–59.5°/ 0.05 mm. n_D^{20} = 1.5785	2
=CCOMe CO$_2$Et	2-PyCHOHCH(CO$_2$Et)COMe, dehydrated at reduced pressure	86.1%	m.p. 115–16°	2
	2-PyCHO, MeCOCH$_2$CO$_2$Et		m.p. 185–7°	3
HCH$_2$COMe	2-PyCHO, Me$_2$CO, NaOH (–20°)		m.p. 76–7°	2
=CHCOCMe$_3$	2-PyCHO, MeCOCMe$_3$, NaOH (–10°)	43%	b.p. 92°/0.1 mm. n_D^{20} = 1.5412	2
=CHCOCO$_2$H	2-PyCHO, MeCOCO$_2$H, KOH—MeOH	16%	dec. 136° oxime, dec. 169°	3
HCH$_2$COMe h	2-PyCH$_2$CN, PhCH=CHCOMe, KOH—MeOH		m.p. 109° phenylhydrazone, m.p. 150–1°	3
COPh	2-PyCH$_3$, PhCO$_2$Et		m.p. 56°	7
	2-PyC:CPh, 65% H$_2$SO$_4$	93%	m.p. 59° b.p. 159°/1 mm. oxime, m.p. 120°	4
	2-PyCH$_2$Li, PhCO$_2$Me	81.8%	b.p. 145–53°/2 mm. m.p. 52.5–54° m.p. 54° oxime, m.p. 120°	1 2

2-$PyCH_2Li$, PhCOCl	17.9%	b.p. 185–95°/10 mm.; m.p. 54°	30,206
		b.p. 185–95°/18 mm. m.p. 59° hydrobromide, m.p. 156–57° perchlorate, m.p. 207° (dec.)	223
2-$PyCH_2Li$, $(PhCO)_2O$	29.2%	m.p. 54° picrate, m.p. 179–80°	206
2-$PyCH_2Li$, $(PhCO)_2O$	14%	m.p. 61.5° hydantoin, m.p. 195.5–96°	379
2-$PyCH_2Li$, $PhCO_2Et$	27%	b.p. 158–70°/1 mm. m.p. 52.5–54° 2,4-dinitrophenylhydrazone m.p. 193–94°	420
2-$PyCH_2Li$, PhCN		m.p. 54° picrate, m.p. 178–80° ketimine, m.p. 53–54°	398

(*continued*)

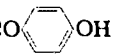
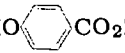
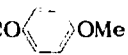
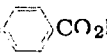
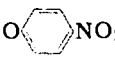
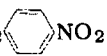
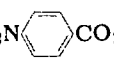
TABLE XIV-5. (*Continued*)

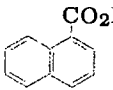
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	2-PyCHBrCHBrPh, KOH		chloroplatinate, m.p. 163–64°	226
			picrate, m.p. 176–77°	
			Enol-benzoate, hydrochloride, m.p. 128–129°	
			Enol-benzoate, picrate, m.p. 175–76°	
			Unstable form m.p. 75–76°	366
			stable form, m.p. 131°	
	2-PyMe, $PhCO_2Et$, (a) PhNa	80%	b.p. 148–155°/2 mm.	330
	(b) PhLi	80%		
2-PyCHCOPh (Br)	2-$PyCH_2COPh$, Br_2—AcOH		m.p. 93–94°	422
2-$PyCH_2CO$(C$_6$H$_4$)Cl	2-PyC⋮CC_6H_4Cl, 65% H_2SO_4	95%	m.p. 86–87° hydrochloride, m.p. 176–80°	356
	2-$PyCH_2Li$, Cl(C$_6$H$_4$)CO_2Me	80%	m.p. 89°	23

		95%	hydrobromide, m.p. 172–75°	356
		87%	m.p. 104–7° hydrochloride, m.p. 195–205°	356
		70%	m.p. 58°	23
		74%	n_D^{20} = 1.5990 picrate, m.p. 173°	23
		72%	m.p. 99°	23
		76%	m.p. 92.5°	23
		50%	m.p. 119.5°	23

(*continued*)

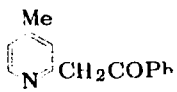
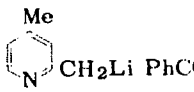
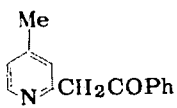
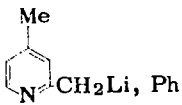
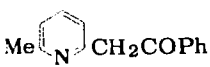
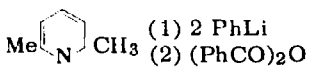
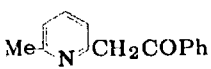
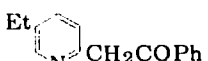
TABLE XIV-5. (*Continued*)

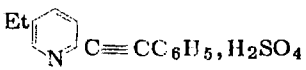
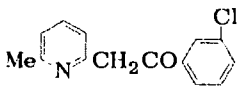
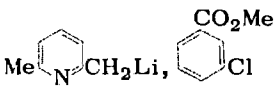
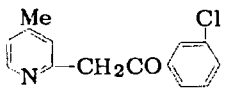
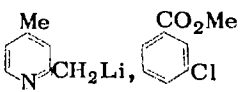
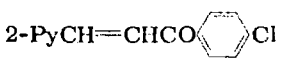
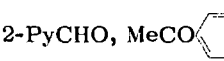
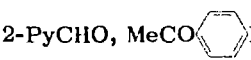
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-$PyCH_2CO$  OH	2-$PyCH_2Li$, HO  CO_2Me		m.p. 148°	23
2-$PyCH_2CO$  OMe	2-$PyCH_2Li$, MeO  CO_2Me	75%	m.p. 84.5°	23
2-$PyCH_2CO$  Me	2-$PyCH_2Li$, Me  CO_2Me	80%	m.p. 67°	23
2-$PyCH_2CO$  NO_2	2-$PyCHOHCH_2$  NO_2, CrO_3—AcOH		m.p. 160° hydrochloride, m.p. 218° chloroplatinate, m.p. 181° picrate, m.p. 175° oxime, m.p. 152° phenylhydrazone, m.p. 155°	209
	2-$PyCH_2Li$, O_2N  CO_2R		m.p. 166–7°	383

2-PyCH$_2$CO-  -Ph	2-PyCH$_2$Li, Ph-  -CO$_2$R		m.p. 129.5–130.5° copper complex, m.p. 206–8°	383
2-PyCH$_2$CO- 	2-PyCH$_2$Li, 	68%	m.p. 48°; m.p. 94–5° picrate, m.p.201–2° dec. copper complex, m.p. 179–82°	23,
2-PyCH$_2$COC$_6$H$_{11}$	2-PyCH$_2$Li, C$_6$H$_{11}$CO$_2$R		m.p. 50–52° b.p. 140–3°/3 mm. copper complex, m.p. 177–9°	383
2-PyCH$_2$COCH$_2$Ph	2-PyCH$_2$Li, PhCH$_2$CO$_2$R		b.p. 140–2°/3 mm. copper complex, m.p. 161–3°	383
2-PyCHCOCH$_2$Ph 	2-PyCHBrCOCH$_2$Ph, C$_4$H$_9$NO	50%	m.p. 110–11°	356
2-PyCHCOCH$_2$Ph N(Et$_2$)	2-PyCHBrCOCH$_2$Ph, Et$_2$NH	47.5%	m.p. 66–67° hydrochloride, m.p. 161–65°	356
2-PyCH$_2$COCH$_2$CH$_2$Ph	2-PyCH$_2$Li, PhCH$_2$CH$_2$CO$_2$R		b.p. 156–8°/3 mm.	383

(continued)

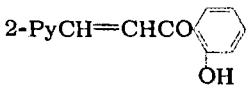
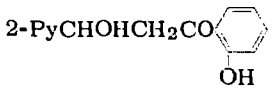
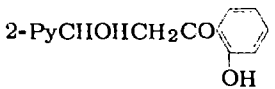
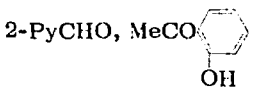
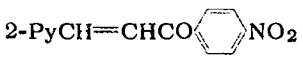
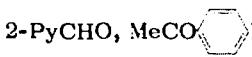
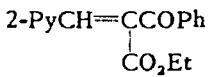
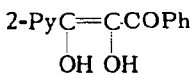
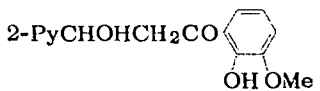
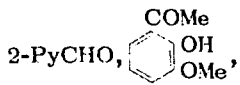
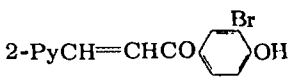
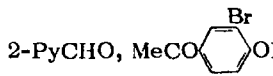
TABLE XIV-5. (*Continued*)

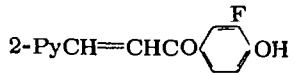
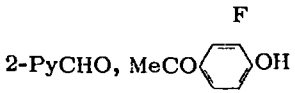
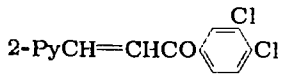
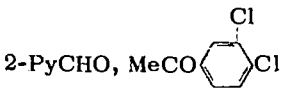
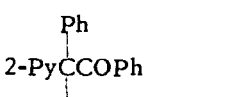
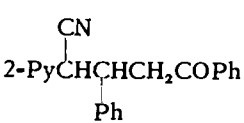
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			copper complex, m.p. 131–4°	
2-$PyCH_2COCH:CHC_6H_5$	2-$PyCH_2CHOHCH:CHC_6H_5$, Pd black, 150°		m.p. 110–11°	365
			picrate, m.p. 132–3°	
		89%	b.p. 159–60°/1.8 mm.	143
			picrate, m.p. 167–68°	
		65%	m.p. 53°	23
			picrate, m.p. 153°	
		small amount	picrate, m.p. 181–82°	206
		82%	m.p. 78.5°	23
		83%	b.p. 169–71°/1.8 mm.	143
			m.p. 64–65°	
			Cu Salt, m.p. 168–69° (dec.)	

			picrate, m.p. 163.8–64.2°	
			m.p. 68–69.4°	356
		85%	m.p. 53°	23
		78%	m.p. 84°	23
2-PyCH=CHCOPh	2-PyCHO, PhCOMe	52.6%	m.p. 53–54°	324
	2-PyCHOHCH$_2$COPh, SeO_2		m.p. 63–64°	102
	2-PyCHO, PhCOMe, NaOH	42%	m.p. 60–61°	251
			picrate, m.p. 190–2°	
	2-PyCHO, 		aldol, m.p. 83–4° m.p. 85–86°	251
	2-PyCHO, 	42%	m.p. 158–60°	251
			picrate, m.p. 170–1°	

(*continued*)

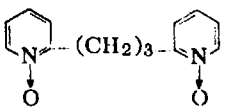
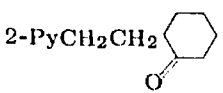
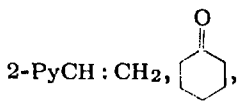
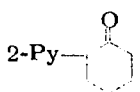
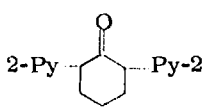
TABLE XIV-5. (*Continued*)

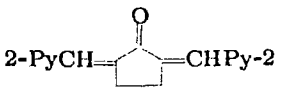
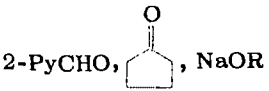
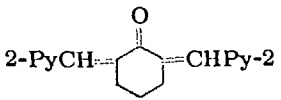
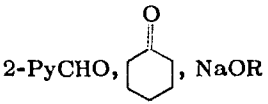
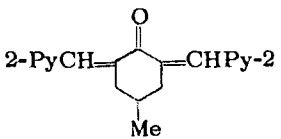
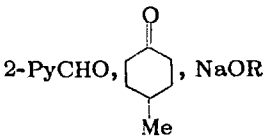
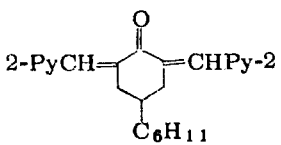
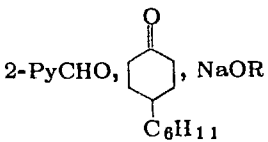
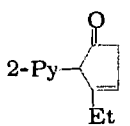
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 , Conc. HCl		m.p. 99–100°	38
	 , Amberlite IRA 400 (OH^-) resin	41%	m.p. 109–10°	38
	 , NaOH	89%	m.p. 148.5°	13
	2-PyCHO, $PhCOCH_2CO_2Et$, piperidine	58%	m.p. 98–9°	324
	2-PyCHO, PhCOCHO, KCN	35–45%	m.p. 93°	102
	 , Amberlite IRA 400 (OH^-) resin		m.p. 173–5° (dec.)	38
	 , base		m.p. 233°	60

			m.p. 216°	60
			m.p. 154°	60
	2-PyCH$_2$Ph, PhCO$_2$Et, (a) PhLi (b) PhNa (c) NaN(*i*-Pr)$_2$	60% 62% 82%	b.p. 190–195°/ 0.5 mm.; b.p. 180–185°/0.25 mm. m.p. 125–125.7°	330
	2-Py(CH$_2$)$_3$NMe$_2$, PhCO$_2$R (a) PhLi (b) PhNa	30% 66%	b.p. 132–133°/ 0.28 mm. picrate, m.p. 179.2–179.8°	330
	2-PyCH(CH$_2$)$_2$NMe$_2$, PhCO$_2$R, (a) PhLi (b) PhNa	68% 64%	m.p. 86–87.4° b.p. 200–205°/1 mm. picrate, m.p. 199–200.5°	330
	2-PyCH$_2$CN, PhCH=CHCOPh, KOH—MeOH	14%	m.p. 119°	33

(*continued*)

TABLE XIV-5. (*Continued*)

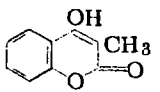
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-PyCOCH$_2$CH$_2$Py-2	 (1) Ac_2O (2) H_2SO_4 (3) Base	18%	b.p. 102–4°/0.1 mm. $n_D^{22.5}$ = 1.5972 picrate, m.p. 156.5–157.5° picrolonate, m.p. 203° methiodide, m.p. 180°	
2-PyCH=CHCOCH=CHPy-2	2-PyCHO, Me_2CO, aq. KOH	68%	m.p. 155–8°	324
		39.8%	b.p. 142–44°/1–1.5 mm. n_D^{20} = 1.5271 D_4^{25} = 1.0513 semicarbazone, m.p. 165°	237
			b.p. 99–100°/0.01 mm. dinitrophenylhydrazone, m.p. 148–9°	126
			b.p. 170–5°/0.05 mm. oxime, m.p. 114–16°	126

			dimethiodide, m.p. 254–6°	
			m.p. 197°	62
			m.p. 190°	62
			m.p. 151°	62
			m.p. 191°	62
	2-PyMe, $(EtCO)_2O$	12%	m.p. 86° semicarbazone, m.p. 201°	346
$2\text{-Py}(CH_2)_3COPh$	2-PyCH : CH_2, CH_3COPh, "Triton B"	11.3%	b.p. 174–76°/3 mm.	407
	2-PyCH : CH_2, CH_3COPh, Na	8.4%		407
	2-PyCH : CH_2, CH_3COPh, Na	29.2%	b.p. 178°/3 mm. $n_D^{20} = 1.5725$	237

(continued)

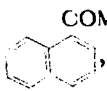
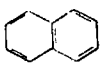
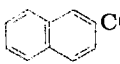
TABLE XIV-5. (*Continued*)

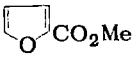
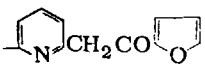
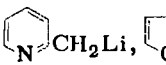
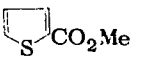
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	2-$PyCH_2CH_2OH$, CH_3COPh, Na		b.p. 165–69°/2 mm.	349
	2-$PyCH_2CH_2CHCOPh$ (COOEt), dil HCl	90%	b.p. 165–70°/2 mm. n_D^{20} = 1.5730 semicarbazone, m.p. 163–65° picrolonate, m.p. 181–84°	39
2-$Py(CH_2)_3CO$–C$_6$H$_4$–Me	2-$PyCH:CH_2$, CH_3CO–C$_6$H$_4$–CH_3, Na	30.7%	b.p. 187–89°/2 mm. n_D^{20} = 1.5685 D_4^{25} = 1.0723 semicarbazone m.p. 166–67°	237
	2-$PyCH_2CH_2OH$, CH_3CO–C$_6$H$_4$–CH_3, Na		b.p. 188–89°/3 mm.	349
2-$PyCH_2CH_2CHCOPh$ (Me)	2-$PyCH:CH_2$, PhCOEt, Na	81.2%	b.p. 174–76°/2 mm. n_D^{20} = 1.5615 d_4^{25} = 1.0712 semicarbazone m.p. 130–31°	237

	2-$PyCH_2CH_2OH$, EtCOPh, Na		b.p. 165–69°/2 mm.	349
	2-PyCH : CH_2, EtCOPh "Triton B"	59.2%	b.p. 189–90°/5 mm.	407
	2-PyCH : CH_2, EtCOPh, "Triton B"	42.7%		407
2-PyCHOHCH(Me)COPh	2-PyCHO, EtCOPh	40%	m.p. 95–96°	251
$[2\text{-}PyCH_2CH_2]_2CHCOPh$	2-PyCH : CH_2, MeCOPh	56.8%	b.p. 244–47°/3 mm. dipicrate, m.p. 173–74°	407
$[2\text{-}PyCH_2CH_2]_2\overset{Me}{\overset{\vert}{C}}COPh$	2-PyCH : CH_2, EtCOPh, "Triton B"	45.2%	b.p. 263–65°/4–5 mm. dipicrate, m.p. 73–74°	407
2-$Py(CH_2)_2CH(Me)CO$–C$_6$H$_4$–OH	2-PyCH : CH_2,  (1) pyridine (2) HCl	90%	b.p. 60°/0.03 mm. picrate, m.p. 93–94.5°	39
2-$Py(CH_2)_2\overset{CO_2Et}{\overset{\vert}{C}}HCOPh$	2-PyCH=CH_2, $PhCOCH_2CO_2Et$, Na	70%	pale orange oil, b.p. 170–5°/0.3 mm. n_D^{23} = 1.5526 picrolonate, m.p. 143.5–145°	39
2-$PyCH(CN)\text{—}CH(2\text{-}Py)CH_2COPh$	2-$PyCH_2CN$, 2-PyCH=CHCOPh, KOH—MeOH		m.p. 158°	33

(*continued*)

TABLE XIV-5. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-PyCH$_2$CH(2-Py)CH$_2$COPh			m.p. 99–100° 2,4-dinitrophenylhydrazone, m.p. 130–1°	33
2-Py(CH$_2$)$_3$CO– 	2-PyCH : CH$_2$,  , Na	19.6%	b.p. 232–35°/2 mm. n_D^{20} = 1.6240 semicarbazone, m.p. 183–84°	237
2-Py(CH$_2$)$_3$CO– 	2-PyCH : CH$_2$,  , Na	25.5%	m.p. 44° semicarbazone, m.p. 185–86°	237
2-PyCH$_2$CH(C$_6$H$_5$)COC$_6$H$_5$	2-PyMe, C$_6$H$_5$CH : CHCOPh, NaNH$_2$		m.p. 90–110° seems to contain dimer or trimer of m.p. 147.5–48.5°	398
2-PyCH$_2$C(OH)(CO$_2$Et)COPh	2-PyMe, C$_6$H$_5$COCO · CO$_2$Et	74%	m.p. 100–101°	244

2-$PyCH_2CO$ 	2-$PyCH_2Li$, 	48–57.8%	m.p. 50–51° picrate, m.p. 149–50° b.p. 141–3°/1 mm.; m.p. 52.5–54° 2,4-dinitrophenylhydrazone, m.p. 170–2°	23, 141, 157 420
Me 	Me 	78.6%	b.p. 136–7°/1.4 mm. picrate, m.p. 160.5–61.5°	142
2-$Py(CH_2)_3CO$ 	2-$PyCH{=}CH_2$, MeCO  , "Triton B"	5.3%	b.p. 162–5°/2 mm. picrate, m.p. 125–6°	407
2-$PyCH_2CO$ 	2-$PyCH_2Li$, 	73.5%	b.p. 167–72°/1 mm. pale yellow needles, m.p. 28.5–29.5° picrate, m.p. 154–5° 2,4-dinitrophenylhydrazone, m.p. 194.5–195.5°	141, 420

(*continued*)

TABLE XIV-5. (*Continued*)

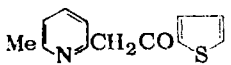
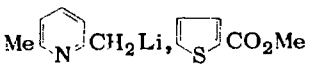
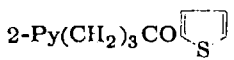
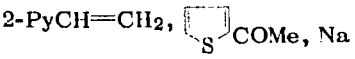
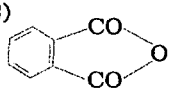
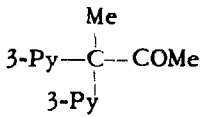
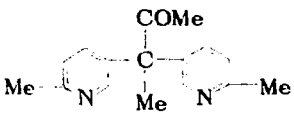
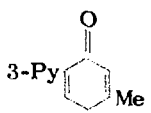
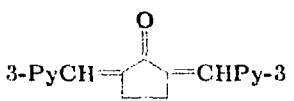
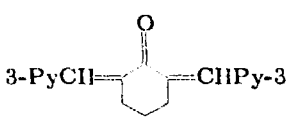
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
		82.9%	b.p. 156–7°/1.6 mm. picrate, m.p. 173–4°	142
		19.8%	b.p. 183–4°/2 mm. n_D^{20} = 1.5977 semicarbazone, m.p. 167–8°	237

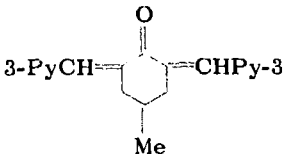
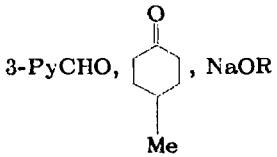
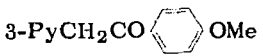
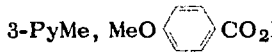
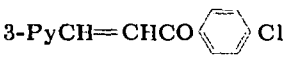
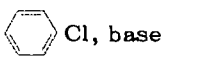
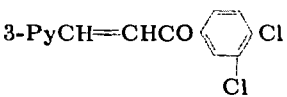
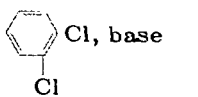
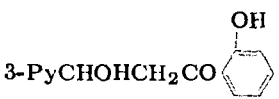
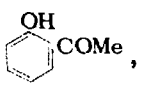
TABLE XIV-6. Preparation and Properties of 3- and 4-Pyridine Side-chain Ketones

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
3-$PyCH_2COMe$	3-$PyCH_2CO_2H$, Ac_2O, NaOAc	39.6%	b.p. 119–23°/1 mm. semicarbazone, m.p. 184.5–185° oxime, m.p. 117.5–119°	57
3-PyCHCOMe CN	3-$PyCH_2CN$, CH_3CO_2Et, NaOR	56%	m.p. 194.5–195.5°	57
3-$PyCHOHCH_2COMe$	3-$PyCOCH_2COMe$, Zn—AcOH		m.p. 115–7° gold salt, m.p. 143–5°	118
3-$PyCH{=}CHCOMe$ (trans)	3-PyCH=CCOMe (1) 2NHCl CO_2Et (2) 		b.p. 68.5–70°/0.05 mm.	253
3-PyCH=CCOMe CO_2Et	3-PyCHOHCHCOMe, dehydration CO_2Et at reduced pressure		b.p. 93°/0.07 mm. $n_D^{25} = 1.5442$	253
3-PyCHOHCHCOMe CO_2Et	3-PyCHO, $MeCOCH_2CO_2Et$, piperidine (– 20°)		m.p. 74°	253
Ph 3-PyCCOEt $(CH_2)_2NMe_2$	Ph 3-Py—C$(CH_2)_2NMe_2$, EtMgBr CN		b.p. 145–6°/0.05 mm. picrate, m.p. 192–4° hydrochloride, m.p. 133–6° (dec.)	283

(*continued*)

TABLE XIV-6. (*Continued*)

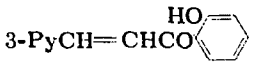
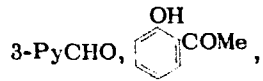
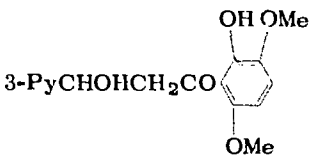
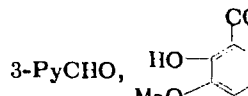
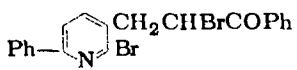
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
3-PyCH=CHCOCO$_2$H	3-PyCHO, MeCOCO$_2$H, KOH—MeOH	51%	dec. 169° oxime, dec. 176°	367
	3-PyCOMe (1) electrolytic or u.v. reduction (2) pinacol rearr.		m.p. 46–8° oxime, m.p. 146–8°	29
			m.p. 87–8°	29
3-PyCH=CHCOCH=CHPy-3	side product in preparation of 3-PyCH=CHCOMe	1.4%	m.p. 144°	253
	3-PyCHO, MeCOCH$_2$CO$_2$Et, piperidine (0°)	41%	b.p. 154°/12 mm. picrate, m.p. 111–2	447
	3-PyCHO,  , NaOR		m.p. 230°	62
	3-PyCHO,  , NaOR		m.p. 151°	62

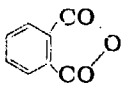
			m.p. 154°	62
$3\text{-PyCH}_2\text{COPh}$	3-PyMe, $PhCO_2R$, KNH_2	38.2%	b.p. 170–5°/3 mm. m.p. 48.6–49.5° picrate, m.p. 168.6–169.6° oxime, m.p. 154.2–155.2°	277
		31%	b.p. 174–9°/4 mm. m.p. 75–75.6° picrate, m.p. 168.8–169.6°	277
3-PyCH=CHCOPh	3-PyCHO, PhCOMe, NaOH	40%	m.p. 101–2° picrate, m.p. 180–81°	251
	3-PyCHO, 		m.p. 129°	60
	3-PyCHO, 		m.p. 145°	60
	3-PyCHO, 	43%	hydrochloride, m.p. 181–2° (dec.)	38

Amberlite IRA 400 (OH^-) resin

(continued)

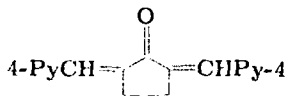
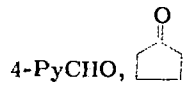
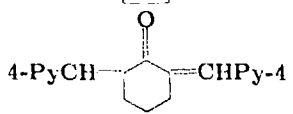
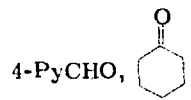
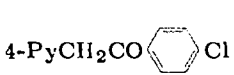
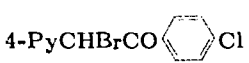
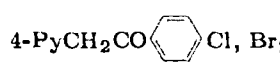
TABLE XIV-6. (*Continued*)

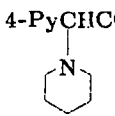
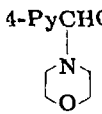
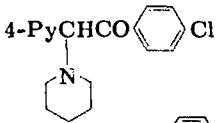
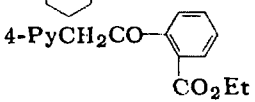
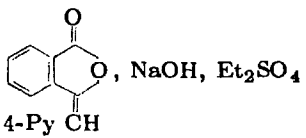
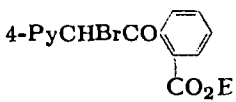
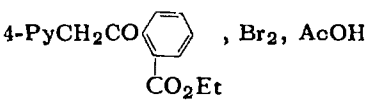
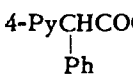
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 Amberlite IRA 400 (OH^-) resin	33%	m.p. 149–50°	38
	 Amberlite IRA 400 (OH^-) resin		m.p. 233–4°	38
3-PyCHCH$_2$COPh Ph	3-PyLi, PhCH=CHCOPh	10%	m.p. 190.5–191.5°	122
	PhCO(CH$_2$)$_2$CHCN(CH$_2$COPh, Br_2—AcOH		m.p. 151°	8
3-PyCH$_2$CO 	3-PyMe, 	35%	b.p. 157–160°/3 mm. picrate, m.p. 158–158.8°	277
3-PyCH$_2$CO 	3-PyMe, 	21.7%	b.p. 176–180°/4 mm. picrate, m.p. 150–150.5°	277
4-PyCH$_2$COMe	4-PyCH$_2$Li, MeCOCl 4-PyMe, CH_3CO_2Et, $NaNH_2$	45%	b.p. 96–102°/4 mm. b.p. 110–5°/3–4 mm. picrate, m.p. 167.5–168.1°	65 305

4-$PyCH_2COEt$	4-PyMe, $EtCO_2R$, $NaNH_2$		b.p. 86–88.5°/1 mm.	305
4-$PyCH_2COCHMe_2$	4-PyMe, Me_2CHCO_2R, $NaNH_2$		b.p. 95–97°/1 mm.	305
4-$PyCH_2COCMe_3$	4-PyMe, Me_3CCO_2R, $NaNH_2$		m.p. 41.8–42.4°	305
4-$PyCH_2COCO_2Et$	$(4\text{-}PyCH_2)_2Hg$, $(CO_2Et)_2$		m.p. 138–9°	9
4-PyCH=CHCOMe (trans)	4-PyCH=C(CO$_2$Et)—COMe (1) 2N—HCl (2) 		b.p. 86–87°/0.077 mm.	253
4-PyCH=C(CO$_2$Et)COMe	4-PyCHOHCH(CO$_2$Et)COMe, dehydration at reduced pressure		b.p. 113°/0.03 mm. $n_D^{25} = 1.5415$	253
4-$PyCH{=}CHCOCO_2H$	4-PyCHO, $MeCOCO_2H$, KOH—MeOH	24%	dec. 146.5°	367
Me 4-PyC—COMe 4-Py			m.p. 76–7°	29
4-$PyCH_2CH_2COMe$	4-$Py(CH_2)_2C{\equiv}CH$, HgO, H_2SO_4	60%	b.p. 143–4°/14 mm. semicarbazone, m.p. 202°	279,280
4-$Py(CH_2)_4COMe$	4-$Py(CH_2)_4C{\equiv}CH$, $HgSO_4$, H_2SO_4	62%	b.p. 129–30°/1 mm. semicarbazone, m.p. 158°	279
4-$Py(CH_2)_5COMe$	4-$Py(CH_2)_5C{\equiv}CH$, $HgSO_4$, H_2SO_4	60%	b.p. 151°/1.9 mm. semicarbazone, m.p. 143°	279,280

(*continued*)

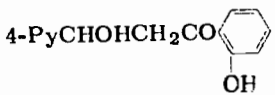
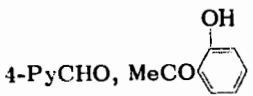
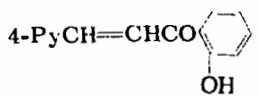
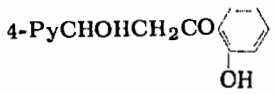
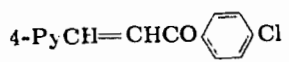
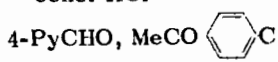
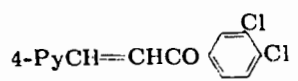
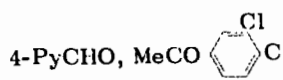
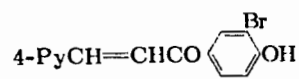
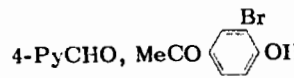
TABLE XIV-6. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
4-Py$(CH_2)_{10}$COMe	4-Py$(CH_2)_{10}$C≡CH, $HgSO_4$—H_2SO_4	52%	b.p. 177°/0.4 mm. m.p. 31° semicarbazone, m.p. 138°	279,280
			m.p. 238°	62
			m.p. 150°	62
4-PyCH$_2$COPh	4-PyMe, PhCN	very good	m.p. 100–5°	70
	4-PyMe, $PhCO_2Me$, $NaNH_2$		m.p. 112–113.4°	305
4-PyCHCOPh Me	(1) 4-PyEt, $PhCO_2R$, $NaNH_2$ (2) 4-PyC(Me)=C(OAc)Ph, Na_2CO_3	77%	m.p. 62.4–63° picrate, m.p. 152–152.5°	90,305
4-PyCHBrCOPh	4-PyCH$_2$COPh, Br_2, AcOH		hydrobromide, m.p. 221° (dec.)	422
	4-PyC≡CPh, H_2SO_4	100%	m.p. 94.5–96°	356
		100%	hydrobromide, m.p. 223–8°	356

	4-PyCHBrCOPh, $C_5H_{11}N$	93%	dihydrochloride hemihydrate, m.p. 170–80° (dec.)	356
	4-PyCHBrCOPh, C_4H_9NO	69.5%	dihydrochloride hemihydrate, m.p. 110–18° (dec.)	356
	4-PyCHBrCO  Cl, $C_5H_{11}N$	70%	hydrochloride, m.p. 199–203°	356
			m.p. 253.7–256.7°	422
			hydrobromide, m.p. 225.5° (dec.)	422
	4-PyCH$_2$Ph, $(CO_2Et)_2$, KOH	33%	m.p. 123–4° acid, m.p. ca 110°	354
4-PyCH=CHCOPh	4-PyCHO, MeCOPh, NaOH		m.p. 70–71° picrate, m.p. 198–9°	251

(*continued*)

TABLE XIV-6. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 , Amberlite IRA 400 (OH^-) resin	45%	m.p. 148–9°	38
	 ,		m.p. 124–5°	38
	conc. HCl 		m.p. 150°	60
			m.p. 164°	60
			m.p. 279°	60

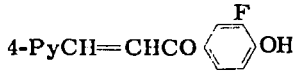
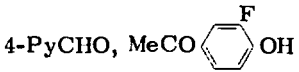
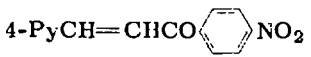
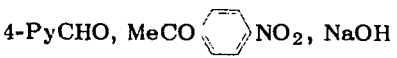
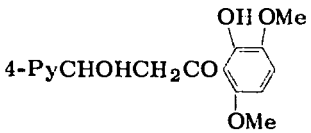
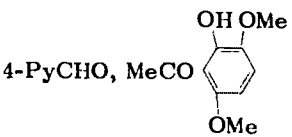
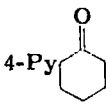
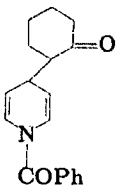
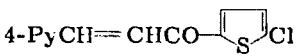
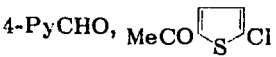
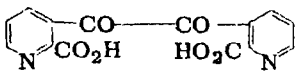
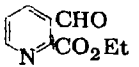
			m.p. 306°	60
		86.6%	m.p. 216°	13
			m.p. 124–5°	38
	Amberlite IRA 400 (OH^-) resin			
	 , I_2	33.9%	m.p. 107–108.5°	90
			m.p. 151°	60

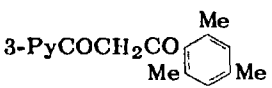
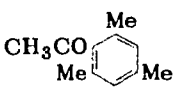
TABLE XIV-7. Preparation and Properties of Pyridine Polyketones

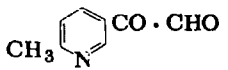
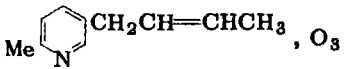
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
2-$PyCOCH_2COMe$	2-$PyCO_2Et$, Me_2CO, NaOMe or NaOEt	76–81%	b.p. 114–18°/4–6 mm.; 137–43°/15 mm.	236,272
			m.p. 49–50°	
2-$PyCOCH_2COMe_3$	2-$PyCO_2Et$, $MeCOMe_3$	74%	b.p. 134–6°/5 mm.	236
2-$PyCOCH_2COPh$	2-$PyCO_2C_2H_5$, $CH_3COC_6H_5$, $NaOCH_3$	73%	b.p. 184–90°/3 mm.	236
			m.p. 87–87.5°	
			picrate, m.p. 169–70.5°	
2-PyCOCOPh	2-$PyCHOH \cdot CHOHC_6H_5$, conc. HNO_3		hydrochloride, m.p. 124–25°	226
			picrate, m.p. 87–88°	
	2-$PyCH:CHC_6H_5$, SeO_2, 200–210°	31%	b.p. 168–73°	54,301
	2-$PyCH_2COPh$, SeO_2	59%	m.p. 72–72.5°	
2-PyCOCOPy-2	2-Py$C(OH)=C(OH)$—Py-2, tosyl chloride, pyridine		monoxime, m.p. 207°	101,301
			monoxime dimethiodide, m.p. 193°	
			dioxime: (a) m.p. 246; (b) 235°	
			dioxime dimethiodide, m.p. 274°	
			N,N'-dioxide, m.p. dec. 240–5°	
			thiosemicarbazone, m.p. 212	342

2-PyCOCOPy-3	2-$PyCOCH_2$Py-3, oxidation		m.p. 96–98°	301
3-PyCOCOPy-3			m.p. 79–80°	46,301
3-$PyCOCH_2COPy$-3	3-PyCOMe, 3-$PyCO_2Et$, NaOR	51%	m. p. 98° hydrochloride, m.p. 240–1°	224
	 (1) CN^- (2) OH^-, air		m.p. 220–1° (dec.)	46
4-PyCOCOPy-4	4-PyCHOHCOPy-4, HNO_3		m.p. 169–170.5°	301
3-$PyCOCH_2COMe$	3-$PyCO_2Et$, Me_2CO, NaOR	63%	m.p. 85°; 92° b.p. 171°/15 mm. hydrochloride, m.p. 92°, 154° chloroplatinate, m.p. 173–75° mercuric chloride (2 forms) (a) m.p. 123–25° (b) m.p. 107–10° Na derivative, m.p. 240° (dec.) dioxime, m.p. 79° monoxime, m.p. 164–65°	118,224
		34%	b.p. 132–34°/5 mm. m.p. 82.5–83.5°	236

(*continued*)

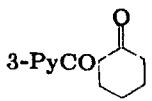
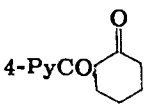
TABLE XIV-7. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
3-$PyCOCH_2COBu$	3-$PyCO_2Et$, MeCOBu, NaOR	46%	b.p. 165–68°/8 mm. hydrochloride, m.p. 122°	224
3-$PyCOCH_2CO(i\text{-}Bu)$	3-$PyCO_2Et$, $MeCOCH_2CHMe_2$, NaOR	70%	b.p. 134–35°/3 mm. m.p. 44° hydrochloride, m.p. 128–29°	224
3-$PyCOCH_2CO$(tert. Bu)	3-$PyCO_2Et$, $MeCO(t\text{-}Bu)$, NaOR,	42%	b.p. 135–36°/5 mm. m.p. 44–45° hydrochloride, m.p. 173°	224
	3-PyCOEt, $MeCO(t\text{-}Bu)$, $NaNH_2$	59.5%		236
3-$PyCOCH_2COC_5H_{11}$	3-$PyCO_2Et$, MeCOAm, NaOR	47%	b.p. 150–52°/2 mm. m.p. 29.5° hydrochloride, m.p. 114°	224
3- 	3-$PyCO_2Et$, 	60%	b.p. 186–90°/1 mm. m.p. 47.8° hydrochloride, m.p. 218–19°	224
3-$PyCOCH_2COCF_3$	3-PyCOMe, F_3CCO_2Et, NaOMe	88%	m.p. 173.5–74° copper chelate, m.p. 262–62.5°	235

			osazone, m.p. 191–93°	148
3-PyCOCH$_2$COPh	3-PyCO$_2$Et, MeCOPh	70%	b.p. 198–200°/3 mm. m.p. 121.5° hydrochloride, m.p. 211°	224
		30%	b.p. 177–80°/1 mm. m.p. 121–21.5°	236
4-PyCOCH$_2$COMe	4-PyCO$_2$Et, Me$_2$CO, NaOEt		colorless needles, m.p. 62° b.p. 145–47°/18 mm. chloroplatinate, 228° (dec.) monoxime, m.p. 164–65° anil, m.p. 103–104° monophenylhydrazone, m.p. 167° copper complex, m.p. 253° (dec.)	115,382
	4-PyCOEt, Me$_2$CO, NaOMe	51–56%	b.p. 118–20°/5 mm. m.p. 66.5–67°	236
4-PyCOCH$_2$COMe$_3$	4-PyCO$_2$Et, MeCO(*t*-Bu)	27%	b.p. 138–40°/5 mm. picrate, m.p. 191.5–92.5°	236
4-PyCOCH$_2$COCF$_3$	4-PyCOMe, F$_3$CCO$_2$Et, NaOMe	95%	m.p. 213–214.5° (sealed tube)	235

(*continued*)

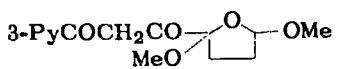
TABLE XIV-7. (*Continued*)

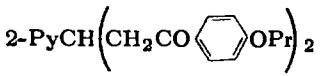
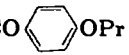
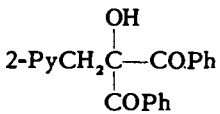
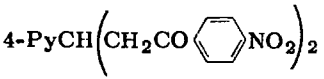
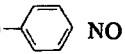
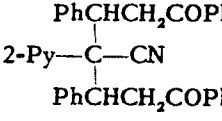
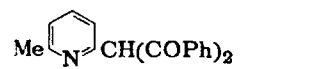
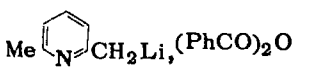
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
3-PyCOCH(CO$_2$C$_2$H$_5$)CH$_2$CHO	3-PyCOCH$_2$CO$_2$Et, EtOCHCl · CH$_2$Cl (NH$_4$OH or CH$_3$NH$_2$)		m.p. 116°	78
3-PyCOCH$_2$COCO$_2$C$_2$H$_5$	3-PyCOMe, (CO$_2$Et)$_2$, NaOEt	51%	m.p. 66°	329
	3-PyCO$_2$Me, cyclohexanone, NaH		m.p. 66–68°	47a,65
	4-PyCO$_2$Me, cyclohexanone, NaH		b.p. 108°/0.1 mm.	65
4-PyCOCH$_2$COCO$_2$Et	4-PyCOMe, (CO$_2$Et)$_2$		m.p. 96° free acid, m.p. 64°	181
4-PyCOCH$_2$COCOCH$_2$COPy-4	4-PyCOMe, (CO$_2$Et)$_2$, NaOAc	56%	m.p. 218° quinoxaline derivative with *o*-phenylenediamine, m.p. 281–3°	181
4-PyCOCH$_2$COPh	4-PyCO$_2$Et, MeCOPh, NaOMe	45–55%	m.p. 84.5–85.5° picrate, m.p. 207–8°	236
	4-PyCO$_2$Et, MeCOPh, NaOEt		m.p. 80° b.p. 233°/18 mm. isoxazole, m.p. 165°	118,382
4-PyCOCH$_2$COPy-4	4-PyCOMe, 4-PyCO$_2$Et, Na		m.p. 155–57°	115

4-PyCO(CH$_2$)$_3$COPy-4	(1) 4-PyCOCH$_2$CO$_2$Et, H$_2$CO (2) HCl		m.p. 92–93° monohydrochloride, dec. 254–6° dioxime, m.p. 197–8°	246
4-PyCOCH$_2$CH(Ph)CH$_2$COPy-4	4-PyCOCH(CO$_2$Et)CH(Ph)CH(CO$_2$Et)COPy-4, hydrolysis		monohydrate, m.p. 103°; anhydrous, m.p. 108–10°	246
4-PyCOCH(CO$_2$Et)CH(Ph)CH(CO$_2$Et)COPy-4	4-PyCOCH$_2$CO$_2$Et, PhCHO, piperidine		m.p. 102–3°	246
4-PyCOCH$_2$CH(3-NO$_2$C$_6$H$_4$)CH$_2$COPy-4			m.p. 151–2° dioxime, m.p. 258–60°	246
3-PyCOCH(2-ClC$_6$H$_4$N=N)CH$_2$CH(N=N-2-ClC$_6$H$_4$)COPy-3	3-PyCOCH=NNH(2-ClC$_6$H$_4$), H$_2$CO	23%	m.p. 203–5°	154
3-PyCOCH$_2$CO(2-thienyl)	3-PyCO$_2$Me, CH$_3$CO(2-thienyl), (NaNH$_2$)	59%	m.p. 133–34° picrate, m.p. 208–9°	235
4-PyCOCH$_2$CO(2-thienyl)	4-PyCO$_2$Me, MeCO(2-thienyl), NaOCH$_3$	64.8%	m.p. 152–52.5° picrate, m.p. 211–12.5°	235

(*continued*)

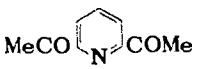
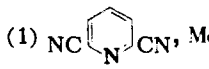
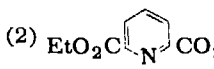
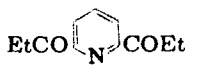
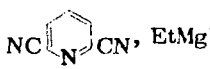
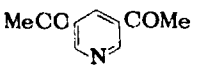
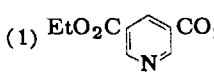
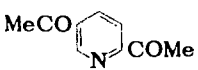
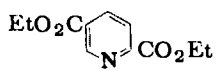
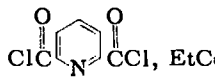
TABLE XIV-7. (*Continued*)

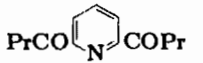
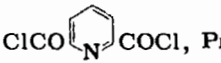
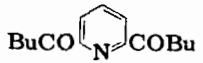
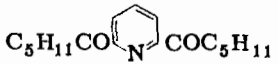
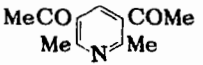
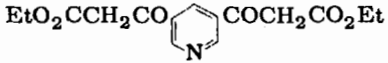
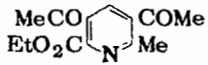
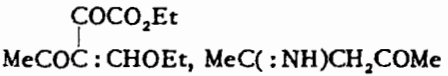
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
			b.p. 150–158°	429
2-PyCOCH$_2$ CHPh 2-PyCOCH$_2$	2-PyCOMe, PhCHO, 10% NaOH		m.p. 152° chloroplatinate, m.p. 206° mercuric chloride, m.p. 122°	110
2-PyCOCH$_2$ CHPh 2-PyCOCH CHPh 2-PyCOCH$_2$	2-PyCOMe, PhCHO, 10% NaOH		m.p. 215°	110
2-PyCOCHCOEt 2-PyCOCHCOEt	2-PyCO$_2$Et, diethyl succinate, NaOMe		m.p. 137° chloroplatinate, m.p. 217°	309
4-PyCOCHCO$_2$Et 4-PyCOCHCO$_2$Et	4-PyCOOEt, $\begin{matrix}\mathrm{CH_2CO_2Et}\\ \mid\\ \mathrm{CH_2CO_2Et}\end{matrix}$, NaOEt		m.p. 197°	309
3-PyCOCH$_2$CHPh 3-PyCOCH 3-PyCOCH$_2$CHPh	3-PyCOMe, PhCHO, $\mathrm{PhCH_2\overset{\oplus}{N}Me_3\cdot OH^-}$		"A" isomer, m.p. 240–1° "B" isomer, m.p. 203–5°	205

2-PyCH(COPh)$_2$	2-PyCH$_2$Li, (PhCO)$_2$O		m.p. 140°	206
2-PyCH(CH$_2$COPh)$_2$	2-PyCHO, MeCOPh, (NaOH)	66%	m.p. 119–21° picrate, m.p. 176–7°	251,324
	2-PyCHO, MeCO 		m.p. 105–6°	324
	(1) 2-PyMe, PhCOCOPh (2) 2-PyMe, PhCOCOCOPh	54% 16%	m.p. 110–11° m.p. 115–16°	244
2-PyCH$_2$CH$_2$CH(COMe)$_2$	2-PyCH:CH$_2$, (MeCO)$_2$CH$_2$, NaOEt	16%	b.p. 116–22°/0.05 mm. n_D^{22} = 1.5228 picrate, m.p. 117–8°	6,41
	4-PyCHO, MeCO  NO$_2$, NaOH	87%	m.p. 120°	13
2-PyCH$_2$CH$_2$CH(COMe)$_2$	2-PyCH=CH$_2$, MeCOCH$_2$COMe, Na		b.p. 118–9°/1 mm.	6
	2-PyCH$_2$CN, PhCH=CHCOPh KOH—MeOH	35%	m.p. 212–3°	33
			m.p. 138–9°	206

(continued)

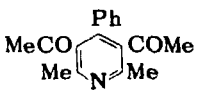
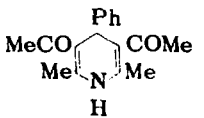
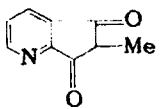
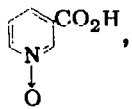
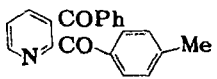
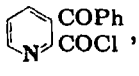
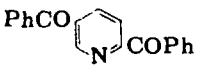
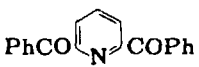
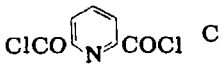
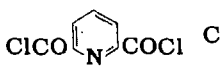
TABLE XIV-7. (*Continued*)

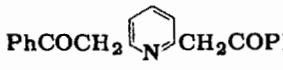
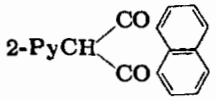
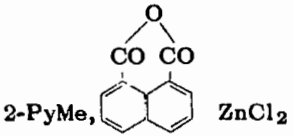
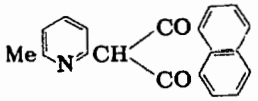
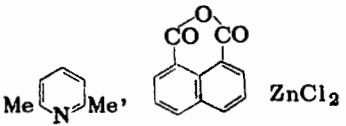
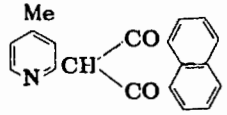
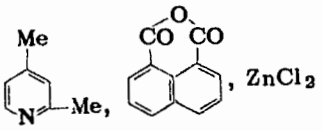
Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	(1)  , MeMgI	11%	b.p. 126°/6 mm. m.p. 79°; m.p. 44–6°	241,380
	(2)  (1) EtOAc, NaOAc (2) hydrol.	85.5%	disemicarbazone, m.p. 250° (dec.) dioxime, m.p. dec. 233.5° dihydrazone, m.p. 181°	
	 , EtMgBr	51%	b.p. 110°/0.8 mm. m.p. 62°	241
	(1)  , CH_3CO_2Et, KOEt (2) hydrolysis		m.p. 71–2° picrate, m.p. 147–147.5° dioxime, m.p. 194–5°	243
	 (1) Na, $CH_3CO_2C_2H_5$ (2) HCl		m.p. 81° dihydrazone m.p. 144°	321
	 , EtCdCl	22%	b.p. 120–25°/1 mm. dinitrophenylhydrazone, m.p. 272–73°	14

		40%	b.p. 143–46°/5 mm. dinitrophenylhydrazone, m.p. 254–55°	14
		39%	b.p. 163–70°/2 mm. dinitrophenylhydrazone, m.p. 234–35°	14
		33%	b.p. 190–204°/5 mm. dinitrophenylhydrazone, m.p. 194–95°	14
			base, m.p. 72° nitrate, m.p. 117° gold salt, m.p. 167° chloroplatinate, m.p. 179° diphenylhydrazone, nitrate salt, m.p. 232°	345
			m.p. 67.5–8.5° picrate, m.p. 76–8 monophenylhydrazone, nitrate salt, m.p. 180°	243
		27%	m.p. 96–97° free acid, m.p. 139–40° (dec.)	47

(*Continued*)

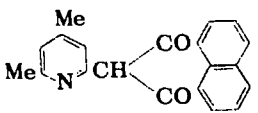
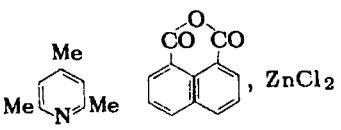
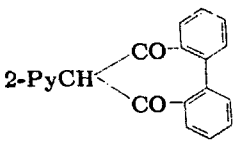
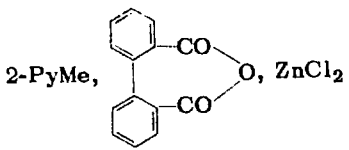
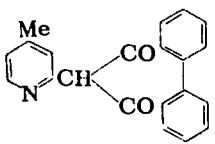
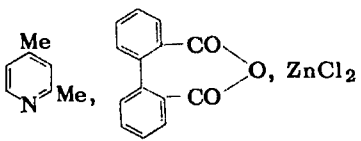
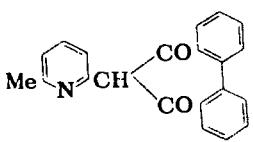
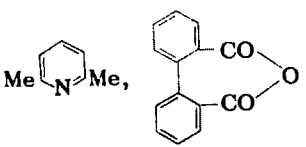
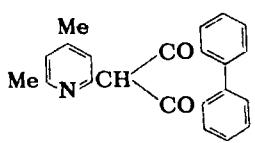
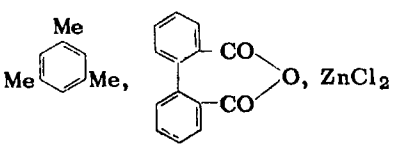
TABLE XIV-7. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
	 , dil. HNO_3 60°		m.p. 188°	208
	 , $(EtCO)_2O$		m.p. 160–1° 2,4-dinitrophenylhydrazone, m.p. 271–2° (dec.)	17
	 , PhMe, $AlCl_3$		m.p. 190–93°	183
	 C_6H_6, $AlCl_3$		m.p. 123° *bis*-phenylhydrazone, m.p. 129°	418
	 C_6H_6, $AlCl_3$		m.p. 108° *bis*-phenylhydrazone, m.p. 183°	418
	 C_6H_5CdCl	43%	m.p. 180° 2,4-dinitrophenylhydrazone, m.p. 236–37°	14

	 50% H_2SO_4	80–90%	m.p. 87°, 92° oxime, m.p. 188° sulfate, m.p. 197° hydrochloride, m.p. 223° (dec.) methyl-*p*-toluene sulfonate quat. salt, m.p. 224°	343,433
	 $ZnCl_2$	23%	m.p. 269° hydrochloride, m.p. 269° bromo derivative, m.p. 140° (dec.)	376
	 $ZnCl_2$	23.4%	m.p. 239–40° bromo derivative, m.p. 135–37° tribromo derivative, m.p. 205–206°	376
	 $ZnCl_2$	13.0%	m.p. 256–57° bromo derivative, m.p. 145–47° tribromo derivative, m.p. 150–60°	376

(*Continued*)

TABLE XIV-7. (*Continued*)

Compound	Method of preparation	Yield	Physical properties, derivatives	Ref.
		36.8%	m.p. 296–98° hydrochloride, m.p. 290° (dec.) bromo derivative, m.p. 210° (dec.)	376
		25%	m.p. 200°	377
		16%	m.p. 243–44°	377
		16%	m.p. 195°	377
		11%	m.p. 220°	377

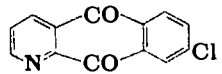
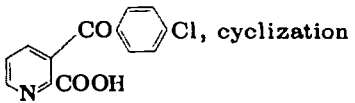
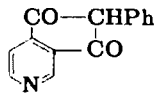
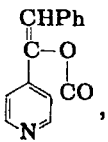
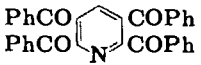
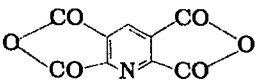
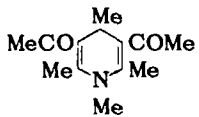
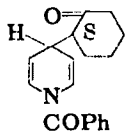
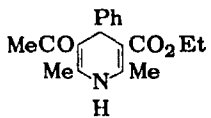
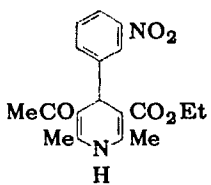
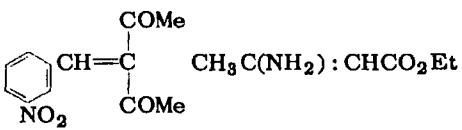
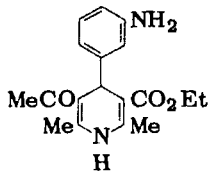
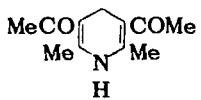
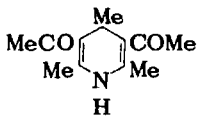
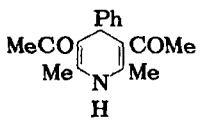
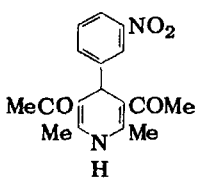
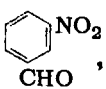
	 Cl, cyclization		m.p. 246° hydrochloride, m.p. 261°	214
	 , NaOMe	80%	dark violet-blue crystals	117
	 (1) $AlCl_3$, C_6H_6 (2) $SOCl_2$ (3) $AlCl_3$, C_6H_6		m.p. 165–70° (dec.)	245
	 C_6H_6, $AlCl_3$		m.p. 186–87°	183

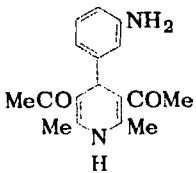
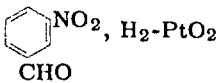
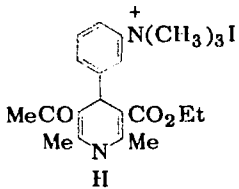
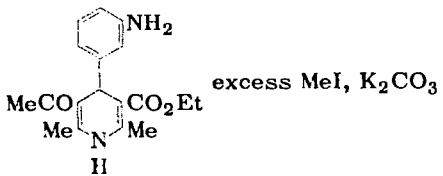
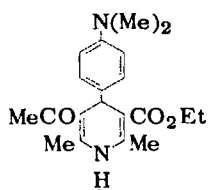
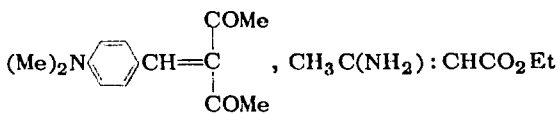
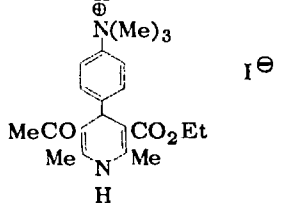
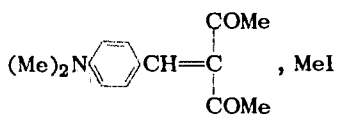
TABLE XIV-8. Preparation and Properties of Hydropyridine Ketones

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
	$MeC{=}C(COMe)_2$, $MeCOC(Me){=}NMe$		m.p. 118°	208
	pyridine, cyclohexanone, C_6H_5COCl (25°, 1 month	34%	m.p. 81–83°	90
	(a) $PhCH{:}C(CO_2Et)(COMe)$ + $CH_3COCH_2C(Me){:}NH$		m.p. 167°; b.p. 210–30°/25–30 mm.	208
	(b) $PhCH{:}C(COMe)_2$, $MeC(NH_2){:}CHCO_2Et$			
		80%	m.p. 168–69°	313

	above product, H_2-PtO_2	84%	m.p. 168–69°	313
	$CH_3COCH_2COCH_3$, H·CHO, NH_4OH (trace piperidine)		m.p. 198°	345
	$CH_3C:C(COMe)_2$, $CH_3COCH_2C(Me):NH$		m.p. 152°; b.p. 220–30°/20 mm.	208
	(1) $CH_3COCCOCH_3$, $CH_3COCH_2C(:NH)Me$ ·· CHPh		b.p. 225–35°/ 25 mm.; m.p. 180°; 182–3	208, 313
	(2) PhCHO, $MeCOCH_2COMe$, NH_4OH	32%		
	 , $CH_3COCH_2COCH_3$, NH_4OH	50%	m.p. 211–12°	313

(*Continued*)

TABLE XIV-8. (*Continued*)

Compound	Method of Preparation	Yield	Physical Properties, Derivatives	Ref.
		70%	m.p. 213–14°	313
	 excess MeI, K_2CO_3	100%	m.p. 185–86°	313
		35%	m.p. 168–69°	313
		85%	m.p. 196–97°	313

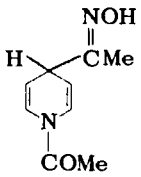
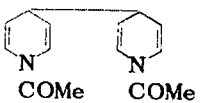
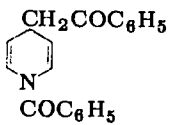
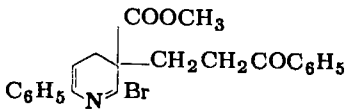
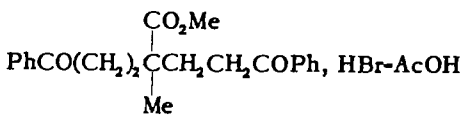
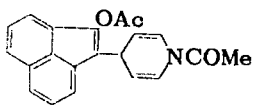
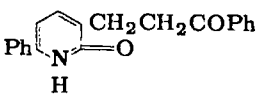
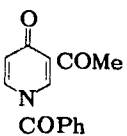
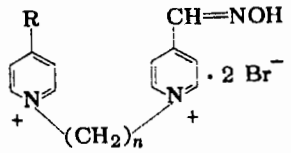
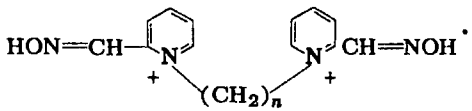
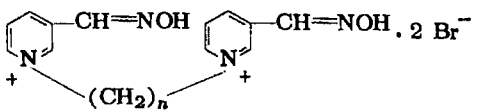
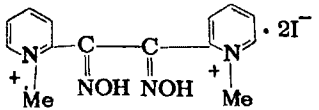
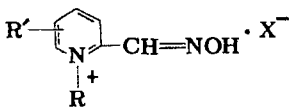
	 , NH_2OH, CH_3OH		m.p. 121–22°	107
	pyridine, MeCOPh, C_6H_5COCl	13.3%	m.p. 108–11° (dec.) sublimes 180°/0.5 mm.	90
			m.p. 144°	8
	pyridine, Ac_2O, acenaphthenone		m.p. 140–45° (dec.); m.p. 145–47°	90, 135
	$C_6H_5CO(CH_2)_2CHCN(CH_2)_2COC_6H_3$, conc. H_2SO_4		m.p. 141°	8
	$CH_3COCH_2N(CH_2)_2CH(OEt)_2$, HCl COC_6H_5	5%	m.p. 160°	5

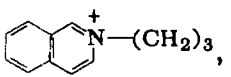
TABLE XIV-9. Properties of Pyridinium Aldoxime and Ketoxime Salts

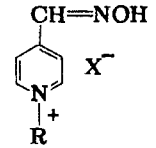
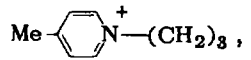
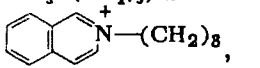
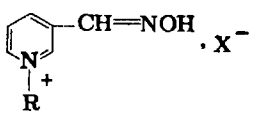
Compound	R, n =	Properties	Relative Reactivation Potency of Dialkylphosphorylacetocholinesterase		Ref.
			Diethyl ester	Di-*i*-propyl ester	
	H, 3	m.p. 212	8	11	32,176
	H, 4		6.7	10	176
	H, 5		7.5	11	176
	—CH=NOH, 1		2.8		176
	—CH=NOH, 2	m.p. 285°; 300°	17	22	32,176, 316, 323
	—CH=NOH, 3	m.p. 222°; 242°; 238-41° (dec.)	22	52	32,176, 316, 323
	—CH=NOH, 4	m.p. 245-6°; 240°; 239-41° (dec.)	18	38	32,176, 316, 323
	—CH=NOH, 5	m.p. 210°	16	36	176,316, 323
	—CH=NOH, 6	m.p. 212-14°			32
	—CH=NOH, 10	m.p. 210-2°; 219-23 (dec)			32,316

	3	m.p. 226–8°; 234°			32,323
	4	m.p. 268°; 260°			323
	5	m.p. 208–9°			323
	6	m.p. 204–5°			32
	3	m.p. 203°			32
	6	m.p. 240°			32
		(a) m.p. 246° (b) m.p. 274° (active)			310
	Me, I	m.p. 181–3° "A" configuration, m.p. 105–6° "B" configuration, m. p. 224–5°	1	1	176,427 140
	Me, Cl	"B" configuration, m.p. 226–7°			140
	Et, I	m.p. 176–7°	0.54		176,316

(*Continued*)

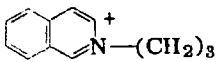
TABLE XIV-9. (*Continued*).

Compound	R, R′, X = R′ = H unless specified	Properties	Relative Reactivation Potency of Dialkylphosphorylacetocholinesterase		Ref.
			Diethyl ester	Di-*i*-propyl ester	
	Allyl, Br	m.p. 300°			316
	Pr, I		0.63		176
	Bu, I		0.87		176
	i-Pr, I		0.46		176
	$HO(CH_2)_2$, Br	m.p. 197–200° (dec.)			316
	Me, I R′ = 3-Me	"B" configuration, m.p. 214°			140
	Me, I R′ = 3-OH	"B" configuration, m.p. 214°			140
	Me, I R′ = 3-OMe	"B" configuration, m.p. 178–9°			140
		m.p. 219°			32

		*anti*-oxime, m.p. 169–72°		176,316, 427
	Me, I	*syn*-oxime, m.p. 182–3°	0.06	
	Et, I		0.03	140
	Allyl, Br	m.p. 183–7° (dec.)		316
	$Br(CH_2)_3$, Br		1.9	176
	$Br(CH_2)_4$, Br		0.25	176
	$Br(CH_2)_9$, Br		0.94	176
	$HO(CH_2)_2$, Br	m.p. 187–90° (dec.)		316
	Bu, Br	m.p. 138–9° (dec.)		316
	 2 Br	m.p. 212°		32
	$Et_3\overset{+}{N}(CH_2)_3$, 2 Br	deliquescent		32
	 2 Br	m.p. 215–6°		32
	Me, I	m.p. 173–5° (dec.)	0.0003	176
	Me, I	"A" isomer, oil "B" isomer,		140

(*Continued*)

TABLE XIV-9. (*Continued*).

Compound	Properties	Relative Reactivation Potency of Dialkylphosphorylacetocholinesterase		Ref.
		Diethyl ester	Di-*i*-propyl ester	
 2 Br	m.p. 154–5° deliquescent			32
2-Acetylpyridine ketoxime methiodide	m.p. 213–14°			427

D. BIBLIOGRAPHY

1. Adams and Miyano, *J. Am. Chem. Soc.*, **76**, 3168 (1954).
2. Abramovitch, Seng and Notation, *Can. J. Chem.*, **38**, 761 (1960).
2a. Adams and Reifschneider, *J. Am. Chem. Soc.*, **81**, 2537 (1959).
3. Adkins, Wolff, Pavlik, and Hutchinson, *J. Am. Chem. Soc.*, **66**, 1293 (1944).
4. Akagi and Paretsky, *J. Org. Chem.*, **24**, 1526 (1959).
5. Albers, Kallischnigg, and Schmidt, *Ber.*, **77B**, 617 (1944).
6. Albertson, *J. Am. Chem. Soc.*, **72**, 2594 (1950).
7. Allan and Allan, *J. Org. Chem.*, **23**, 639 (1958); Allan, Allan, and Thomson, *ibid.*, 112 (1958).
8. Allen and Bell, *Can. J. Research*, **11**, 40 (1934); *C.A.*, **29**, 1502 (1935).
9. Amstutz and Besso, *J. Org. Chem.*, **25**, 1687 (1960).
10. Anderson, Duca, and Scudi, *J. Am. Chem. Soc.*, **73**, 4967 (1951).
11. Angyal, Barlin, and Wailes, *J. Chem. Soc.*, **1953**, 1740.
12. Arnold, *Experientia*, **15**, 415 (1959); *Coll. Czech. Chem. Communs.*, **25**, 1308 (1960); Czech 97162; *C.A.*, **56**, 3466c (1962).
13. Ariyan and Suschitsky, *J. Chem. Soc.*, **1961**, 2242.
14. Bachmann and Jenkins, *J. Am. Pharm. Assoc.*, **40**, 44 (1951); *C.A.*, **48**, 9368b (1954).
15. Bachman and Schisla, *J. Org. Chem.*, **22**, 858 (1957); *ibid.*, 1302.
16. Badger and Pettit, *J. Chem. Soc.*, **1953**, 2774.
17. Bain and Saxton, *J. Chem. Soc.*, **1961**, 5216.
18. Basu, *J. Indian Chem. Soc.*, **12**, 289 (1935); *Chem. Zentr.*, **1935**, II, 3384.
19. Basu and Banerjee, *J. Indian Chem. Soc.*, **12**, 665 (1935); *C.A.*, **30**, 2194 (1936).
20. Baumgarten and Dornow, *Ber.*, **73**, 353 (1940).
21. Baumgarten and Krieger, *J. Am. Chem. Soc.*, **77**, 2438 (1955).
22. Beckett and Kerridge, *J. Chem. Soc.*, **1954**, 2948.
23. Beckett, Kerridge, Clark, and Smith, *J. Pharm. and Pharmacol.*, **7**, 717 (1955).
24. Beets, *Rec. trav. chim.*, **63**, 120 (1944).
25. Beets and Wibaut, *Rec. trav. chim.*, **60**, 909 (1941).
26. Benary, *Ber.*, **60**, 914 (1927).
27. Benary, *Ber.*, **59**, 2198 (1926).
28. Benary and Psille, *Ber.*, **57**, 828 (1924).
29. Bencze and Allen, *J. Am. Chem. Soc.*, **81**, 4015 (1959); U.S. 2,966,493; *C.A.*, **55**, 7442a (1961).
30. Bergmann and Rosenthal, *J. prakt. Chem.*, **135**, 267 (1932).
31. Bernthsen and Mettegang, *Ber.*, **20**, 1208 (1887).
32. Berry, Davies, and Green, *Brit. J. Pharmacol*, **14**, 186 (1959).
33. Beyer and Leverenz, *Chem. Ber.*, **94**, 263 (1961).
34. Beyerman, Eveleens, and Muller, *Rec. trav. chim.*, **75**, 63 (1956).
35. Biemann, Buechi, and Walker, *J. Am. Chem. Soc.*, **79**, 5558 (1957).

36. Bloom, Breslow, and Hauser, *J. Am. Chem. Soc.*, **67**, 2206 (1945).
37. Bobbitt and Scola, *J. Org. Chem.*, **25**, 560 (1960).
38. Boehm and Koo, *J. Org. Chem.*, **26**, 3589 (1961).
39. Boekelheide and Agnello, *J. Am. Chem. Soc.*, **72**, 5005 (1950).
40. Boekelheide and Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954).
41. Boekelheide and Rothschild, *J. Am. Chem. Soc.*, **71**, 879 (1949).
42. Borsch and Hahn, *Ann.*, **537**, 219 (1939).
43. Boekelheide and Windgassen, *J. Am. Chem. Soc.*, **81**, 1456 (1959).
44. Borsche and Hartmann, *Ber.*, **73**, 839 (1940).
45. Bottari and Carboni, *Gazz. Chim. Ital.*, **86**, 990 (1956).
46. Bottari and Carboni, *Gazz. Chim. Ital.*, **87**, 1281 (1957).
47. Bottorff, Jones, Kornfield, and Mann, *J. Am. Chem. Soc.*, **73**, 4380 (1951).
48. Bourbon, Malbosc, and Ping, *Compt. rend.*, **250**, 4179 (1960).
49. Bowden and Jones, *J. Chem. Soc.*, **1946**, 953.
50. Boyer and Goebel, *J. Org. Chem.*, **25**, 304 (1960).
51. Braun, *J. Pharm. Exptl. Therap.*, **95**, 58 (1949).
52. Bryans and Pyman, *J. Chem. Soc.*, **1929**, 549.
53. Buehler, Addleburg, and Glenn, *J. Org. Chem.*, **20**, 1350 (1955).
54. Buehler, Harris, and Arendale, *J. Am. Chem. Soc.*, **72**, 4953 (1950).
55. Burger, Alfriend, and Deinet, *J. Am. Chem. Soc.*, **66**, 1327 (1944).
56. Burger, Clements, Dawson, and Henderson, *J. Org. Chem.*, **20**, 1383 (1955).
57. Burger and Walter, *J. Am. Chem. Soc.*, **72**, 1988 (1950).
58. Burger and Ullyot, *J. Org. Chem.*, **12**, 342 (1947).
59. Burrus and Powell, *J. Am. Chem. Soc.*, **67**, 1468 (1945).
60. Buu-Hoï, Xuong, and Trien, *Bull. Soc. Chim. France*, **1961**, 584.
61. Buu-Hoï and Xuong, *Bull. Soc. Chim. France*, **1961**, 1377.
62. Buu-Hoï and Xuong, *Compt. rend.*, **251**, 2725 (1960).
63. Callighan and Wilt, *J. Org. Chem.*, **26**, 4912 (1961).
64. Castle and Burger, *J. Am. Pharm. Assoc.*, **43**, 163 (1954).
65. Čejka, Ferles, Chládek, Labský, and Zelinka, *Coll. Czech. Chem. Communs.*, **26**, 1429 (1961).
66. *Chem. Eng. News*, **34**, 1446 (1956).
67. Chichibabin, *Ber.*, **37**, 1370 (1904).
68. Chichibabin, *J. Russ. Phys. Chem. Soc.*, **33**, 700 (1901); *Chem. Zentr.*, **1902**, I, 206.
69. Chichibabin, *J. Prakt. Chem.*, (2) **75**, 526 (1907); *Chem. Zentr.*, **1907**, II, 542.
70. Chichibabin, *Rec. trav. chim.*, **57**, 582 (1938); *Chem. Zentr.*, **1938**, II, 1774.
71. Chichibabin, *Ber.*, **36**, 2711 (1903).
72. Chichibabin and Benewolenskaja, *Ber.*, **61**, 547 (1928).
73. Chichibabin and Knunjanz, *Ber.*, **62**, 3048 (1929).
74. Chichibabin, Kuindshi, and Benewolenskaja, *Ber.*, **58**, 1580 (1925).
75. Childs, Davies, Green, and Rutland, *Brit. J. Pharmacol.*, **1955**, 462.
76. Claisen and Haase, *Ber.*, **36**, 3674 (1903).

77. Clemo and Hoggarth, *J. Chem. Soc.*, **1941**, 41.
78. Clemo and Holmes, *J. Chem. Soc.*, **1934**, 1739.
79. Clemo, Holmes, and Leitch, *J. Chem. Soc.*, **1938**, 753.
80. Clemo, Morgan, and Roper, *J. Chem. Soc.*, **1937**, 965.
81. Clemo, Ramage, and Raper, *J. Chem. Soc.*, **1932**, 2959.
82. Coppage, Island, Smith, and Liddle, *J. Clin. Invest.*, **38**, 2101 (1959); *C.A.*, **54**, 1044e (1960).
83. Craig, *J. Am. Chem. Soc.*, **55**, 2854 (1933).
84. Craig, *J. Am. Chem. Soc.*, **56**, 1144 (1934).
85. Craig and Hixon, *J. Am. Chem. Soc.*, **53**, 4367 (1931).
86. Cramer and Krum, *Chem. Ber.*, **86**, 1586 (1953).
87. Crook and McElvain, *J. Am. Chem. Soc.*, **52**, 4006 (1930).
88. Denton, Turner, Neier, Lawson, and Schedl, *J. Am. Chem. Soc.*, **71**, 2048 (1949).
89. Diels and Alder, *Ann.*, **505**, 103 (1933).
90. Doering and McEwen, *J. Am. Chem. Soc.*, **73**, 2104 (1951).
91. Doering and Weil, *J. Am. Chem. Soc.*, **69**, 2461 (1947).
92. Dornow, *Ber.*, **72**, 1548 (1939).
93. Dornow, *Ber.*, **73**, 156 (1940).
94. Dornow, *Ber.*, **73**, 185 (1940).
95. Dornow and Bormann, *Ber.*, **82**, 216 (1949).
96. Dornow and Machens, *Ber.*, **73**, 355 (1940).
97. Dummel and Mosher, *J. Org. Chem.*, **24**, 1007 (1959).
98. Dornow and Schacht, *Chem. Ber.*, **82**, 117 (1949).
99. Dyson and Hammick, *J. Chem. Soc.*, **1939**, 781.
100. Eistert and Munder, *Chem. Ber.*, **88**, 215 (1955).
101. Eistert and Munder, *Chem. Ber.*, **88**, 226 (1955).
102. Eistert and Munder, *Chem. Ber.*, **91**, 1415 (1958).
103. Eistert and Schade, *Chem. Ber.*, **91**, 1411 (1958).
104. Eistert and Schade, *Chem. Ber.*, **91**, 1404 (1958).
105. Elming, *Acta Chem. Scand.*, **11**, 1496 (1957).
106. Elslager, Benton, Short, and Tendick, *J. Am. Chem. Soc.*, **78**, 3453 (1956).
107. Emmert and Wolpert, *Ber.*, **74**, 1015 (1941).
108. Engler, *Ber.*, **24**, 2539 (1891).
109. Engler and Bauer, *Ber.*, **24**, 2530 (1891).
110. Engler and Engler, *Ber.*, **35**, 4061 (1902).
111. Engler and Kiby, *Ber.*, **22**, 597 (1889).
112. Engler and Majmon, *Ber.*, **24**, 2536 (1891).
113. Engler and Rosumoff, *Ber.*, **24**, 2527 (1891).
114. Evstigneeva and Preobrazhenskii, *Zhur. Obshchei Khim.*, **28**, 3085 (1958); *C.A.*, **53**, 10215 (1959).
115. Fabrini, *Il Farmaco (Pavia)*, **9**, 603 (1954).
116. Fand and Lutomski, *J. Am. Chem. Soc.*, **71**, 2931 (1949).
117. Fels, *Ber.*, **37**, 2137 (1904).

118. Ferenczy, *Monatsh.*, **18**, 673 (1897); *Chem. Zentr.*, **1898**, I, 250.
119. Frank and Phillips, *J. Am. Chem. Soc.*, **71**, 2804 (1949).
120. Frank and Weatherbee, *J. Am. Chem. Soc.*, **70**, 3482 (1948).
121. Frankenburg, Gottscho, Mayaud, and Tso, *J. Am. Chem. Soc.*, **74**, 4309 (1952).
122. French and Sears, *J. Am. Chem. Soc.*, **73**, 469 (1951).
123. Freund, *Monatsh.*, **18**, 447 (1897).
124. Fulda, *Monatsh.*, **20**, 762 (1899).
125. Fulda, *Monatsh.*, **21**, 981 (1900).
126. Funk and Rissi, *Compt. rend.*, **239**, 713 (1954).
127. Furst, *J. Am. Chem. Soc.*, **71**, 3550 (1949).
128. Furukawa, *Yakugaku Zasshi*, **78**, 957 (1958); *C.A.*, **53**, 3219 (1959).
129. Furukawa and Kuroiwa, *Pharm. Bull. (Tokyo)*, **3**, 233 (1955).
130. Fuson and Miller, *J. Am. Chem. Soc.*, **79**, 3477 (1957).
131. Gautier and Miocque, *Bull. Soc. Chim. France*, **1961**, 431.
132. Gardner, Smith, Wenis, and Lee, *J. Org. Chem.*, **16**, 1121 (1951).
133. Gardner, Wenis, and Lee, *J. Org. Chem.*, **20**, 976 (1955).
134. Geissman, Schlatter, Webb, and Roberts, *J. Org. Chem.*, **11**, 741 (1946).
135. Ghigi, *Ber.*, **75**, 764 (1942).
136. Ghigi, *Ber.*, **75**, 1316 (1942).
137. Gilman and Broadbent, *J. Am. Chem. Soc.*, **70**, 2755 (1948).
138. Gilman, Tolman, and Massie, *J. Am. Chem. Soc.*, **68**, 2399 (1946).
139. Gilman and Towle, *Rec. trav. chim.*, **69**, 428 (1950).
140. Ginsburg and Wilson, *J. Am. Chem. Soc.*, **79**, 481 (1957).
141. Goldberg, Barkley, and Levine, *J. Am. Chem. Soc.*, **73**, 4301 (1951).
142. Goldberg and Levine, *J. Am. Chem. Soc.*, **74**, 5217 (1952).
143. Goldberg and Levine, *J. Am. Chem. Soc.*, **77**, 3647 (1955).
144. Gold'farb and Karaulova, *Doklady Akad. Nauk. S.S.S.R.*, **65**, 843 (1949); *C.A.*, **43**, 6626e (1949); *Chem. Zentr.*, **1949**, E 415.
145. Gough and King, *J. Chem. Soc.*, **1933**, 350.
146. Graef, Fredericksen, and Burger, *J. Org. Chem.*, **11**, 257 (1946).
147. Graf, Langer, and Háumeda, *J. prakt. Chem.*, **150**, 156 (1938).
148. Graf, Langer, and Haumeda, *J. prakt. Chem.*, **150**, 153 (1938).
149. Graf and Laszlo, *J. prakt. Chem.*, **138**, 231 (1933).
150. Graf, *J. prakt. Chem.*, **146**, 88 (1936).
151. Graf and Weinberg, *J. prakt. Chem.*, **134**, 177 (1932).
152. Hagenbach and Gysin, *Experientia*, **8**, 184 (1952).
153. Hahn, *Roczniki Chem.*, **33**, 627 (1959); *C.A.*, **54**, 523e (1960).
154. Hahn and Zielinski, *Lodz Towarz. Nauk. Wydzial III*, No. 6, 23 (1961); *C.A.*, **55**, 21113 (1961).
155. Haines and Eisner, *J. Am. Chem. Soc.*, **72**, 1719 (1950).
156. Haines, Eisner, and Woodward, *J. Am. Chem. Soc.*, **67**, 1258 (1945).
157. Halla, *Monatsh.*, **32**, 747 (1911).
158. Hanania and Irving, *Nature*, **183**, 40 (1959).

159. Hardegger and Nikles, *Helv. Chim. Acta*, **40**, 1016 (1957).
160. Harries and Lenart, *Ann.*, **410**, 1 (1915).
161. Harris, Heyl, and Folkers, *J. Am. Chem. Soc.*, **66**, 2088 (1944).
162. Harris, Heyl, and Folkers, *J. Biol. Chem.*, **154**, 315 (1944).
163. Hart, *J. Chem. Soc.*, **1952**, 4540.
164. Hartmann and Bosshard, *Helv. Chim. Acta*, **24**, 28 E (1941).
165. Heinert and Martell, *Tetrahedron*, **3**, 49 (1958); *J. Am. Chem. Soc.*, **81**, 3933 (1959).
166. Hawthorne and Wilt, *J. Org. Chem.*, **25**, 2215 (1960).
167. Henry, Kirby, and Shaw, *J. Chem. Soc.*, **1945**, 524.
168. Hensel, *Angew. Chem.*, **65**, 491 (1953).
169. Henze, *Ber.*, **67**, 750 (1934).
170. Henze and Knowles, *J. Org. Chem.*, **19**, 1127 (1954).
171. Hesse and Schroedel, *Angew. Chem.*, **68**, 438 (1956).
172. Hey and Williams, *J. Chem. Soc.*, **1950**, 1678.
173. Heyl, *J. Am. Chem. Soc.*, **70**, 3434 (1948).
174. Heyl, Luz, Harris, and Folkers, *J. Am. Chem. Soc.*, **73**, 3430 (1951).
175. Heyl, Luz, and Harris, *J. Am. Chem. Soc.*, **73**, 3437 (1951).
176. Hobbiger, Pitman, and Sadler, *Biochem. J.*, **75**, 363 (1960).
177. Howton and Golding, *J. Org. Chem.*, **15**, 1 (1950).
178. Hughes, Lions, and Ritchie, *J. Proc. Roy. Soc. N.S. Wales*, **72**, 209 (1939); *C.A.*, **33**, 6838[5] (1939).
179. Huntress and Walter, *J. Am. Chem. Soc.*, **70**, 3702 (1948).
180. Hurd and Webb, *J. Am. Chem. Soc.*, **49**, 546 (1927).
181. Janculev and Jančevska, *Bull. sci. Conseil acad. R.P.F. Yougoslavie*, **6**, 1 (1961); *C.A.*, **55**, 27305 (1961).
182. Jaunin and Godat, *Helv. Chim. Acta*, **44**, 95 (1961).
183. Jephcott, *J. Am. Chem. Soc.*, **50**, 1189 (1928).
184. Jephcott, *Trans. Roy. Soc. Can.*, **III(3)19**, 28 (1925); *C.A.*, **20**, 764[8] (1926); *Chem. Zentr.*, **1926**, II, 30.
185. Jerchel and Heider, *Ann.*, **613**, 153 (1958).
186. Johnson, *J. Chem. Soc.*, **1947**, 1626.
187. Jonge, den Hertog, and Wibaut, *Rec. trav. chim.*, **70**, 989 (1951).
188. Just, *Monatsh.*, **18**, 452 (1897).
189. Kaegi, *Helv. Chim. Acta*, **24**, 141E (1941).
190. Kato, Hamaguchi, and Oiwa, *Yakugaku Zasshi*, **78**, 422 (1958); *C.A.*, **52**, 14603e (1958).
191. Kahn, Petrow, Rewald, and Sturgeon, *J. Chem. Soc.*, **1949**, 2128.
192. Koelsch, *J. Am. Chem. Soc.*, **65**, 2460 (1943).
193. Kakimoto and Yamamoto, *J. Pharm. Soc. Japan*, **74**, 997 (1954); *C.A.*, **49**, 11650 (1955).
194. Kao and Robinson, *J. Chem. Soc.*, **1955**, 2865.
195. Kaplan and Ciotti, *J. Am. Chem. Soc.*, **76**, 1713 (1954).
196. Karrer and Visconti, *Helv. Chim. Acta*, **30**, 52 (1947).

197. Katritzky, *J. Chem. Soc.*, **1955**, 2586.
198. Katritzky, *J. Chem. Soc.*, **1956**, 2404.
199. Kaufmann and Vallette, *Ber.*, **45**, 1736 (1912); *ibid.*, **46**, 49 (1913).
200. Kegelman and Brown, *J. Am. Chem. Soc.*, **75**, 4649 (1953).
201. Kipnis, Levy, and Ornfelt, *J. Am. Chem. Soc.*, **70**, 4265 (1948).
202. Kirpal, *Monatsh.*, **30**, 355 (1909).
203. Kirpal, *Monatsh.*, **31**, 295 (1910); Jeiteles, *ibid.*, **17**, 515 (1896); Mettegang, *Ber.*, **20**, 1208 (1887).
204. Kirpal and Kunze, *Ber.*, **60**, 138 (1927).
205. Kloetzel and Chubb, *J. Am. Chem. Soc.*, **79**, 4226 (1957).
206. Kloppenburg and Wibaut, *Rec. trav. chim.*, **65**, 393 (1946).
207. Klosa, *J. prakt. Chem.* [4], **10**, 335 (1960).
208. Knoevenagel and Ruschhaupt, *Ber.*, **31**, 1025 (1898).
209. Knick, *Ber.*, **35**, 1162 (1902).
210. Knudsen, *Ber.*, **28**, 1762 (1895).
211. Knudsen, *Ber.*, **25**, 2985 (1892).
212. Koenings, Mensching, and Kirsch, *Ber.*, **59**, 1717 (1926).
214. Kogan and Shchukina, *J. Appl. Chem.* (*U.S.S.R.*), **19**, 925 (1946); *C.A.*, **42** 572c (1948).
215. Kolloff and Hunter, *J. Am. Chem. Soc.*, **63**, 490 (1941).
216. Koenig, Siefken, and Offe, *Chem. Ber.*, **87**, 825 (1954).
217. Korytnyk and Kris, *Chem. & Ind.* (*London*), **1961**, 1834.
218. Krause and Busch, *J. Am. Chem. Soc.*, **82**, 4830 (1960).
219. Krasnek, Durinda, and Szucs, *Chem. Zvesti*, **15**, 558 (1961); *C.A.*, **56**, 12847g (1962).
220. Kröhnke, *Ber.* **68**, 1177 (1935).
221. Krönhnke, Leister, and Vogt, *Chem. Ber.*, **90**, 2792 (1957).
222. Kröhnke and Gross, *Chem. Ber.*, **92**, 22 (1959).
223. Kröhnke, *Ber.*, **68**, 1177 (1935).
224. Kuick and Adkins, *J. Am. Chem. Soc.*, **57**, 143 (1935).
225. Kuhn and Muenzing, *Ber.*, **85**, 29 (1952).
226. Ladenburg and Kroener, *Ber.*, **36**, 119 (1903).
227. LaForge, *J. Am. Chem. Soc.*, **50**, 2477 (1928).
228. LaForge, *J. Am. Chem. Soc.*, **50**, 2484 (1928).
229. Laiblin, *Ann.*, **196**, 160 (1879).
230. Lautenschlaeger and Onsager, *Ber.*, **51**, 602 (1918).
231. Lenart, *Ber.*, **47**, 808 (1914).
232. Legrand and Lozach, *Bull. Soc. Chim. France*, **1955**, 79.
233. Levelt and Wibaut, *Rec. trav. chim.*, **48**, 466 (1929); *C.A.*, **23**, 2976 (1929).
234. Levine and Raynolds, *J. Org. Chem.*, **25**, 530 (1960).
235. Levine and Sneed, *J. Am. Chem. Soc.*, **73**, 4478 (1951).
236. Levine and Sneed, *J. Am. Chem. Soc.*, **73**, 5614 (1951).
237. Levine and Wilt, *J. Am. Chem. Soc.*, **74**, 342 (1952).
239. Linsker and Evans, *J. Am. Chem. Soc.*, **68**, 907 (1946).

240. Liu and Liu, *J. Am. Chem. Soc.*, **83**, 2615 (1961).
241. Lukés and Pergal, *Chem. Listy*, **52**, 68 (1958); *C.A.*, **52**, 16346e (1958).
242. Lyle, Leone, Troscianiec, and Warner, *J. Org. Chem.*, **24**, 330 (1959).
243. Lukés and Vaculic, *Chem. Listy*, **51**, 1510 (1957); *C.A.*, **52**, 1163c (1958).
244. McElvain and Johnson, *J. Am. Chem. Soc.*, **63**, 2213 (1941).
245. Machek, *Monatsh.*, **59**, 175 (1932); *C.A.*, **26**, 2457[3] (1932).
246. Magidson, *Zhur. Obschei Khim.*, **29**, 165 (1959); *C.A.*, **54**, 530d (1960).
247. Malan and Dean, *J. Am. Chem. Soc.*, **69**, 1797 (1947).
249. Mariella and Zelko, *J. Org. Chem.*, **25**, 647 (1960).
250. Marion, *Can. J. Chem.*, **29**, 347 (1951).
251. Marvel, Coleman and Scott, *J. Org. Chem.*, **20**, 1785 (1955).
252. Marvel and Stille, *J. Org. Chem.*, **21**, 1313 (1956).
253. Marvel and Stille, *J. Org. Chem.*, **22**, 1451 (1957).
254. Massie, *Iowa State Coll. J. Sci.*, **21**, 41 (1946); *C.A.*, **41**, 3044b (1947).
255. Mathes, Sauermilch, and Klein, *Chem. Ber.*, **87**, 1870 (1954).
256. Mathes and Sauermilch, *Ann.*, **618**, 152 (1958).
257. Mathes and Sauermilch, *Chem. Ber.*, **84**, 648 (1951).
258. Mathes and Sauermilch, *Ber.*, **89**, 1515 (1956).
259. Mathes and Sauermilch, *Chemiker-Ztg.*, **76**, 518 (1952).
260. Mathes and Sauermilch, *Chem. Ber.*, **87**, 1868 (1954).
261. Mathes and Sauermilch, *Chemiker-Ztg.*, **80**, 475 (1956).
262. Mathes and Sauermilch, *Chem. Ber.*, **90**, 758 (1957).
263. Mathes and Sauermilch, *Chem. Ber.*, **85**, 1008 (1952).
264. Mathes and Sauermilch, *Chem. Ber.*, **86**, 109 (1953).
265. Mathes and Sauermilch, *Chem. Ber.*, **88**, 1276 (1955).
266. Mathes and Sauermilch, *Chem. Ber.*, **93**, 286 (1960).
267. Mathes, Sauermilch, and Klein, *Ber.*, **86**, 584 (1953).
268. Mathes, Sauermilch, and Klein, *Ber.*, **84**, 452 (1951); D.B. patent 837,535.
269. Menassé, Klein, and Erlenmeyer, *Helv. chim. Acta*, **38**, 1289 (1955).
270 Michalski, Wojaczynski, and Zajac, *Bull. Acad. Polon Sci. Ser. Sci. Chim.*, **8**, 285 (1960); *C.A.*, **56**, 7263 (1962).
271. Merz and Stolte, *Arch. Pharm.*, **292**, 496 (1959).
272. Micko, *Monatsh.*, **17**, 442 (1896).
273. Micovic and Mihailovic, *Rec. trav. chim.*, **71**, 970 (1952).
274. Miescher and Kägi, *Helv. Chim. Acta*, **24**, 1471 (1941).
275. Miller, *J. Am. Chem. Soc.*, **75**, 4849 (1953).
276. Mills, Palmer, and Tomkinson, *J. Chem. Soc.*, **125**, 2365 (1924).
277. Miller, Osuch, Goldberg, and Levine, *J. Am. Chem. Soc.*, **78**, 674 (1956).
278. Mingoia and Ferriera, *Anais fac. farm.e. odontol. Univ. Sao Paulo*, **11**, 9 (1953); *C.A.*, **49**, 7566a (1955).
279. Miocque, *Bull. Soc. Chim. France*, **1960**, 322.
280. Miocque, *Compt. rend.*, **247**, 1470 (1958).
281. Mizzoni, R. H., unpublished work.
283. Mosher and Tessieri, *J. Am. Chem. Soc.*, **73**, 4925 (1951).

284. Mueller and Dorfman, *J. Am. Chem. Soc.*, **56**, 2787 (1934).
285. Mumm and Bergell, *Ber.*, **45**, 3040 (1912).
286. Mumm and Boehme, *Ber.*, **54**, 726 (1921).
287. Mumm and Hingst, *Ber.*, **56**, 2301 (1923).
288. Neu, *Chem. Ber.*, **90**, 2638 (1957).
289. Nakashima, *Yakugaku Zasshi*, **77**, 1298 (1957); *C.A.*, **52**, 6345g (1958).
290. Niemann, Lewis, and Hays, *J. Am. Chem. Soc.*, **64**, 1678 (1942).
290a. Nienburg, *Ber.*, **67**, 874 (1934).
291. Nishimoto and Nakashima, *Yakugaku Zasshi*, **81**, 88 (1961); *C.A.*, **55**, 13420 (1961).
292. Noller and Azima, *J. Am. Chem. Soc.*, **72**, 17 (1950).
293. Noller and Wunderlich, *J. Am. Chem. Soc.*, **74**, 3835 (1952).
294. Nunn and Schofield, *J. Chem. Soc.*, **1952**, 583.
295. Ochiai and Ikuma, *Ber.*, **69**, 1147 (1936).
296. Ochiai, Miyaki, and Sato, *Ber.*, **70**, 2018 (1937).
297. Ochiai, Tsuda, and Ikuma, *Ber.*, **68**, 1551 (1935).
298. Ochiai, Tsuda, and Ikuma, *Ber.*, **68**, 1710 (1935).
299. Ochiai, Tsuda, and Ikuma, *Ber.*, **69**, 2238 (1936).
300. Ockenden and Schofield, *J. Chem. Soc.*, **1953**, 3440.
301. Oda, *Nippon Kagaku Zasshi*, **82**, 478 (1961); *C.A.*, **56**, 10089b (1962).
302. Oparina, *J. Russ. Phys. Chem. Soc.*, **61**, 2011 (1929); *C.A.*, **24**, 4785[7] (1930).
303. Oparina, *J. Russ. Phys. Chem. Soc.*, **57**, 319 (1925); *Chem. Zentr.*, **1926**, 3336.
304. Oparina, *Khim. Farm. Prom.*, **1934**, No. 4, 1215; *Chem. Zentr.*, **1935** I, 2536; *C.A.*, **29**, 1820[6] (1935).
305. Osuch and Levine, *J. Org. Chem.*, **22**, 939 (1957).
306. Overhoff and Wibaut, *Rec. trav. chim.*, **52**, 55 (1933).
307. Panizzon, *Helv. Chim. Acta*, **24**, 24E (1941).
308. Panizzon, *Helv. Chim. Acta*, **29**, 324 (1946).
309. Pinner, *Ber.*, **34**, 4234 (1901).
310. Pitman and Sadler, *J. Chem. Soc.*, **1961**, 759.
311. Pitha and Ernest, *Coll. Czech. Chem. Communs.*, **24**, 2632 (1959).
312. Philips, *Ber.*, **27**, 1923 (1894).
313. Philips, *J. Am. Chem. Soc.*, **73**, 2248 (1951).
314. Plieninger and Suehiro, *Chem. Ber.*, **87**, 882 (1954).
315. Popp and McEwen, *J. Am. Chem. Soc.*, **80**, 1181 (1958).
316. Poziomek, Hackley, and Steinberg, *J. Org. Chem.*, **23**, 714 (1958).
317. Poziomek, Kramer, and Mosher, *J. Org. Chem.*, **25**, 2135 (1960).
318. Prelog, Heimbach, and Seiwerth, *Ber.*, **72**, 1319 (1939).
319. Preobrazhenskii and Beer., *J. Gen. Chem. U.S.S.R.*, **15**, 667 (1945); *C.A.*, **40**, 5724[3] (1946).
320. Prostenik and Balling, *Archiv Kemi.*, **18**, 10 (1946); *C.A.*, **42**, 3399g (1948).
321. Prostenik and Filliporic, *Archiv Kemi.*, **18**, 3 (1946); *C.A.*, **42**, 3398a (1948).
322. Profft, *Chem. Tech. (Berlin)*, **6**, 484 (1954); *C.A.*,**50**, 332 (1956).

323. Profft and Krueger, *Wiss. Z. Tech. Hochsch. Chem. Leuna-Mersburg*, **2**, 281 (1959-60); *C.A.*, **55**, 1607e (1961); *J. prakt. Chem.*, **12**, 86 (1960).
324. Profft, Schneider, and Beyer, *J. prakt. Chem.* [4], **2**, 147 (1950).
325. Rabe and Jantzen, *Ber.*, **54**, 925 (1921).
326. Rapaport, Windgassen, Hughes, and Onak, *J. Am. Chem. Soc.*, **82**, 4404 (1960).
327. Räth, *Ann.*, **486**, 95 (1931).
328. Räth, *Ber.*, **57**, 840 (1924).
329. Räth and Schiffmann, *Ann.*, **487**, 127 (1931).
330. Raynolds and Levine, *J. Am. Chem. Soc.*, **82**, 1152 (1960); Levine and Raynolds, *J. Org. Chem.*, **25**, 530 (1960).
331. Ried and Gick, *Ann.*, **581**, 16 (1956).
332. Ried, Gick, and Oertel, *Ann.*, **581**, 29 (1953).
333. Risaliti, *Ricerca Sci.*, **28**, 561 (1958); *C.A.*, **52**, 18416a (1958).
334. Rodwell, Volcani, Ikawa and Snell, *J. Biol. Chem.*, **233**, 1548 (1958).
335. Rojann and Schulten, *Arch. Pharm.*, **264**, 348 (1925); *C.A.*, **20**, 2587 (1926).
336. Rubtsov, *J. Gen. Chem. U.S.S.R.*, **13**, 702 (1943); *C.A.*, **39**, 706^5 (1945).
337. Rubtsov, *J. Gen. Chem. U.S.S.R.*, **16**, 461 (1946); *C.A.*, **41**, 762d (1947).
338. Rubtsov, Nikitskaya, and Yanina, *Zhur. Obshchei Khim.*, **24**, 1648 (1954); *C.A.*, **49**, 13241h (1955).
339. Rubtsov, Nikitskaya, and Yanina, *Zhur. Obshchei Khim.*, **23**, 963 (1953); *C.A.*, **48**, 8781 (1954); *Doklady Akad. Nauk. S.S.S.R.*, **89**, 81 (1953); *C.A.*, **48**, 4532 (1954).
340. Runti and Stener, *Boll. sci. fac. chim. ind. Bologna*, **12**, 153 (1954).
341. Sauermilch and Wolf, *Arch. Pharm.*, **292**, 38 (1959).
342. Sadler, *J. Org. Chem.*, **26**, 1315 (1961).
343. Scheuing and Winterhalder, *Ann.*, **473**, 126 (1929).
344. Schmelkes and Joiner, *J. Am. Chem. Soc.*, **61**, 2562 (1939).
345. Scholtz, *Ber.*, **30**, 2295 (1897).
346. Scholtz and Fraude, *Ber.*, **46**, 1069 (1913).
347. Schulte-Frohlinde, *Ann.*, **622**, 43 (1959).
348. Schwenk and Papa, *J. Org. Chem.*, **11**, 798 (1946).
349. Shono, Yasumura, and Oda, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **57**, 900 (1954); *C.A.*, **49**, 11643 (1955).
350. Sen, *Chem. & Ind. (London)*, **1958**, 562.
351. Siemeatycki, *Compt. rend.*, **241**, 63 (1955); *C.A.*, **50**, 10092e (1956).
352. Seyhan, *Chem. Ber.*, **87**, 1124 (1954).
353. Shivers, Dillon, and Hauser, *J. Am. Chem. Soc.*, **69**, 119 (1947).
354. Singh, *J. Chem. Soc.*, **127**, 2445 (1925).
355. Skraup and Cobenzl, *Monatsh.*, **4**, 436 (1883).
356. Smith, Stewart, Roth, and Northey, *J. Am. Chem. Soc.*, **70**, 3997 (1948).
357. Snell, Guirard, and Williams, *J. Biol. Chem.*, **143**, 519 (1942).
358. Snell and McElvain, *J. Am. Chem. Soc.*, **56**, 1612 (1934).
359. Solomon, *J. Chem. Soc.*, **1946**, 934.

360. Späth and Galinovsky, *Ber.*, **71**, 721 (1938).
361. Sperber, Fricano, and Papa, *J. Am. Chem. Soc.*, **72**, 3068 (1950).
362. Sperber, Papa, Schwenk, and Sherlock, *J. Am. Chem. Soc.*, **71**, 887 (1949).
363. Spielman, Swadesh, and Mortenson, *J. Org. Chem.*, **6**, 780 (1941).
364. Späth and Bretschneider, *Ber.*, **61**, 327 (1928).
365. Späth, Kubiczek, and Dubensky, *Ber.*, **74**, 873 (1941).
366. Stanek and Zuerina, *Chem. Listy*, **47**, 471 (1953).
367. Strell and Kopp, *Chem. Ber.*, **91**, 1621 (1958).
368. Strell and Kopp, *Chem. Ber.*, **91**, 2854 (1958).
369. Steinberg, Poziomek and Hackley, *J. Org. Chem.*, **26**, 368 (1961).
370. Strong and McElvain, *J. Am. Chem. Soc.*, **55**, 816 (1933).
371. Sugasawa and Kirisawa, *Pharm. Bull. (Tokyo)*, **3**, 190 (1955); *C.A.*, **50**, 9415f (1956).
372. Sugasawa and Matsuo, *Chem. Pharm. Bull. (Tokyo)*, **8**, 819 (1960).
373. Supniewski, Bany, and Krupinska, *Bull. Acad. Polon. Sci. Class II*, **3**, 55 (1955); *C.A.*, **50**, 7800d (1956).
374. Suzuki, *Pharm. Bull. (Tokyo)*, **4**, 479 (1956).
375. Takeda, Maejima, and Namekata, *Japan J. Tuber.*, **2**, 184 (1954); *C.A.*, **49**, 13243 (1955).
376. Taurins, *J. prakt. Chem.*, **153**, 177 (1939).
377. Taurins, *J. prakt. Chem.*, **153**, 189 (1939).
378. Teague, *J. Am. Chem. Soc.*, **69**, 714 (1947).
379. Teague, Ballentine, and Rushton, *J. Am. Chem. Soc.*, **75**, 3429 (1953).
380. Terent'ev, Rukhadze, Mochalina, and Rode, *Zhur. Vsesoyuz. Khim. Obshchestva im. D.I. Mendeleeva*, **6**, 116 (1961); *C.A.*, **55**, 14450i (1961).
381. Tilford, Shelton, and Van Campen, *J. Am. Chem. Soc.*, **70**, 4001 (1948).
382. Tscherne, *Monatsh.*, **22**, 615 (1901); *Chem. Zentr.*, **1901**, II, 780.
382a. Tschugaeff, *Ber.*, **39**, 3382 (1906).
383. Uhlemann, *J. prakt. Chem.* [4], **14**, 281 (1961).
384. Vanags, Grens, and Stankevich, *Izvest. Vysshikh Ucheb Zavedenii, Khim. i Khim. Teknol.*, **2**, 210 (1959); *C.A.*, **54**, 529d (1960).
385. Van der Meer, Kofman, and Veldstra, *Rec. trav. chim.*, **72**, 236 (1953).
386. Villani and King, *Org Syntheses*, **37**, 6 (1927).
387. Van Zyl, De Vries, Decker, and Niles, *J. Org. Chem.*, **26**, 3373 (1961).
388. Villani and Papa, *J. Am. Chem. Soc.*, **72**, 2722 (1950).
389. Visconti, Ebnother, and Karrer, *Helv. Chim. Acta*, **34**, 1834 (1951).
390. Wada and Yamasaki, *J. Am. Chem. Soc.*, **76**, 155 (1954).
391. Walker, *J. Org. Chem.*, **25**, 1047 (1960).
392. Webb and Corwin, *J. Am. Chem. Soc.*, **66**, 1456 (1944).
393. Webb and Webb, *J. Am. Chem. Soc.*, **71**, 2285 (1949).
394. Weygand, *Angew, Chem.*, **67**, 357 (1955).
395. Wibaut and Beets, *Rec. trav. chim.*, **59**, 653 (1940).
396. Wibaut and Heeringa, *Rec. trav. chim.*, **74**, 1003 (1955).
397. Wibaut and Huls, *Rec. trav. chim.*, **71**, 1021 (1952); Wibaut and van der Voort, *ibid.*, 798.

398. Wibaut and De Jong, *Rec. trav. chim.*, **68**, 485 (1949).
399. Wibaut and Kloppenburg, *Rec. trav. chim.*, **65**, 100 (1946).
400. Wibaut, Kloppenburg, and Beets, *Rec. trav. chim.*, **63**, 134 (1944).
401. Wibaut, Kooyman, and Boer, *Rec. trav. chim.*, **64**, 30 (1945).
402. Wibaut and van der Voort, *Rec. trav. chim.*, **71**, 798 (1952).
403. Wibaut, Wallingford, Rang, and Kettenes, *Rec. trav. chim.*, **74**, 1049 (1955).
404. Wilson, *J. Chem. Soc.*, **1931**, 1936.
405. Wilson and Ginsburg, *Biochem. et Biophys. Acta*, **18**, 168 (1955).
406. Wilson and Harris, *J. Am. Chem. Soc.*, **73**, 4693 (1951).
407. Wilt and Levine, *J. Am. Chem. Soc.*, **75**, 1368 (1953).
408. Wingfield, Harland, and Hanmer, *J. Am. Chem. Soc.*, **74**, 5796 (1952).
409. Winterfeld and Holschneider, *Ann.*, **499**, 109 (1932).
410. Winterfeld and Holschneider, *Ber.*, **66**, 1751 (1933).
411. Winterfeld and Holschneider, *Arch. Pharm.*, **277**, 192 (1939); *Chem. Zentr.*, **1939**, II, 2431.
412. Winterfeld and Holschneider, *Arch. Pharm.*, **277**, 221 (1939); *Chem. Zentr.*, **1939**, II, 3577.
413. Winterfeld and Holschneider, *Arch. Pharm.*, **273**, 305 (1935); *Chem. Zentr.*, **1935**, II, 1711.
414. Winterfeld and Mueller, *Ann.*, **581**, 77 (1953).
415. Winterfeld and Schneider, *Ann.*, **581**, 66 (1953).
416. Winterfeld and Van Cosel, *Arch. Pharm.*, **278**, 80 (1940); *C.A.*, **34**, 5847[9] (1940).
417. Wunderlich, *J. prakt. Chem.* [4], **2**, 302 (1955).
418. Wolffenstein and Hartwich, *Ber.*, **48**, 2043 (1915).
419. Work, *J. Chem. Soc.*, **1942**, 429.
420. Zelinsky and Benilda, *J. Am. Chem. Soc.*, **73**, 696 (1951).
421. Zymalkowski, *Arch. Pharm.*, **289**, 52 (1956).
422. U.S. 2,414,398; *C.A.*, **41**, 5904 (1947).
423. U.S. 2,526,231; *C.A.*, **45**, 2975c (1951).
424. U.S. 2,624,740; *C.A.*, **49**, 2524 (1955).
425. U.S. 2,670,352; *C.A.*, **49**, 2523 (1955).
426. U.S. 2,685,584; *C.A.*, **49**, 10381 (1955).
427. U.S. 2,816,113; *C.A.*, **52**, 10212h (1958).
428. U.S. 2,862,928; *C.A.*, **54**, 5801 (1960).
429. U.S. 2,921,078.
430. U.S. 2,723,270; *C.A.*, **50**, 3504f (1956).
431. British 312,919; *C.A.*, **24**, 862[9] (1930); German 55,240; *Friedl.*, **19**, 1149.
432. British 783,420; *C.A.*, **52**, 4696i (1958).
433. German 594,849; *C.A.*, **28**, 4541[8] (1934); *Friedl.*, **19**, 1147.
434. German 697,759; *C.A.*, **35**, 6270[9] (1941).
435. German 741,320; *C.A.*, **40**, 1180[5] (1946).
436. German 1,065,417; *C.A.*, **55**, 21150d (1961).
437. German 1,008,294; *C.A.*, **53**, 18968e (1959).
438. German 1,116,668; *C.A.*, **56**, 5939b (1962).

439. Swiss 350,462; *C.A.*, **55**, 21150 (1961).
440. Japanese 10,719; *C.A.*, **52**, 15595i (1958).
441. Chap. VII, Table 18 (p. 461).
442. U.S. 2,834,787; *C.A.*, **52**, 15595a (1958).
443. Case and Butte, *J. Org. Chem.*, **26**, 4415 (1961); Case and Kasper, *J. Am. Chem. Soc.*, **78**, 5842 (1956).
444. Feilelson and Petrov, *J. Chem. Soc.*, **1952**, 228.
445. Mills, Palmer, and Tomkinson, *ibid.*, 2365.
446. Kato, *J. Pharm. Soc. Japan*, **75**, 1228 (1955); *C.A.*, **50**, 8664c, i (1956).
447. Beyer, Lässig, and Schudy, *Chem. Ber.*, **90**, 592 (1957).
448. Harris, Heyl, and Folkers, *J. Am. Chem. Soc.*, **70**, 3429 (1948).

CHAPTER XV

Sulfur and Selenium Compounds of Pyridine

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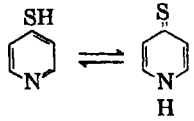
A. PYRIDINETHIOLS AND PYRIDINETHIONES

1. Structure

Of the three isomeric pyridinethiols, only the 2- and 4-isomers can exist in the tautomeric pyridinethione form (XV-1). The earlier



(XV-1)

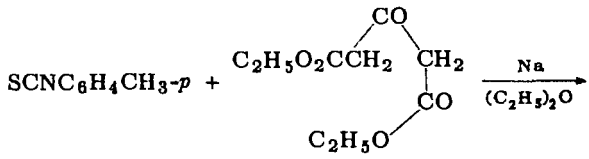
workers in this field designated compounds of these types as possessing either the thiol or the thione structure, but proof was lacking. In recent years, Renault (*141*), Ross (*147*), Spinner (*296*), Jones and Katritzky (*301*), and Albert and Barlin (*331*) investigated the absorption spectra and ionization constants of a number of pyridinethiols in an effort to determine the predominant tautomeric forms. Although their data favor the thione form, in this chapter, compounds of these types will be referred to as pyridenethiols to follow the practice of *Chemical Abstracts*. With 1-substituted derivatives, *e.g.*, 1-methyl-2(1*H*)-pyridinethione (XV-2), tautomerism is no longer possible, and the pyridinethione nomenclature will be used.

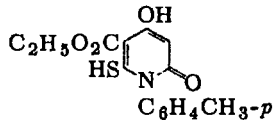
(XV-2)

2. Preparation

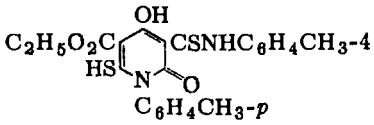
a. Nuclear Synthesis

The reaction of one equivalent each of an aryl isothiocyanate and ethyl acetonedicarboxylate was reported by Worrall (*203,204*) to give complex pyridine derivatives (XV-3). With two equivalents of isothiocyanate, the reaction was more complex and gave (XV-4), which reacted with bromine in acetic acid to give (XV-5).

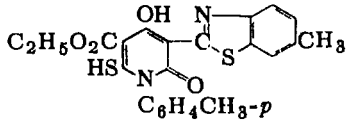




(XV-3)



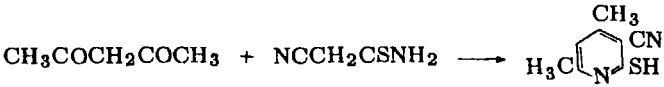
(XV-4)



(XV-5)

From the reaction of butyraldehyde and aniline, Craig *et al.* (*38*) obtained a compound, $C_{18}H_{25}N$, which, when heated with sulfur, gave a compound of m.p. 127°, believed to be 3,5-diethyl-1-phenyl-6-propyl-2(1*H*)-pyridinethione.

Cyanothioacetamide and β-diketones gave 3-cyano-2-thiopyridones (XV-5a) (*307*). 4-Thiopyrones and monoalkylamines gave



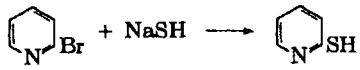
(XV-5a)

1-alkyl-4-thiopyridones (*305*). Benzylidene bis(phenylphenacylthioether) and ammonium acetate gave 2,4,6-triphenyl-3,5-bis(phenylthio) 1,4-dihydropyridine; the latter, with nitrous acid, gave 2,4,6-triphenyl-3,5-bis(phenylthio) pyridine (*328*). 1,1,3,3-Tetracyanopropene and methylisothiourea gave 2-amino-3,5-dicyano-6-methylthiopyridine (*329*).

b. From Halopyridines

These are the most widely used precursors of pyridinethiols. Sodium or potassium hydrosulfide have been reacted with a variety of substituted and unsubstituted halopyridines, generally in methanol or ethanol at reflux or in sealed tubes at higher temperatures

(XV-6). In ethanol, 2-bromopyridine, and potassium hydrosulfide yielded, in addition to 2-pyridinethiol, a small amount of 2-(ethyl-



(XV-6)

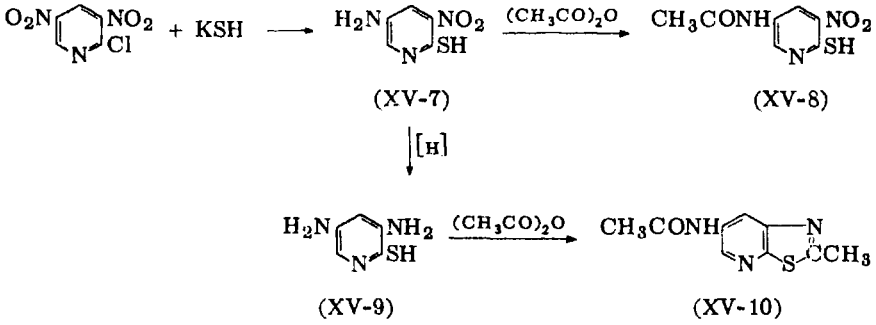
thio)pyridine (*10*). Disulfide formation has also been reported (*29*). Recently, propylene glycol has been used as a high boiling solvent for the reaction of potassium hydrosulfide with 2-bromopyridine (*192*) and 3-bromopyridine (*205*); in the latter case copper catalyst was used and the yield of purified mercaptan was only 14%.

Alkyl groups do not interfere, as shown by the reaction of 4-chloro-2,6-lutidine with potassium hydrosulfide to give 2,6-dimethyl-4-pyridinethiol (*107*). Halogen in the 3 position is inert under the relatively mild conditions required for the replacement of 2- or 4-halogen; a number of di- and trihalopyridines have thus been converted to halopyridinethiols (*42,86,136*).

3- and 5-Nitro groups are also usually inert. For example, 2-chloro-5-nitropyridine has been converted to 5-nitro-2-pyridinethiol by means of sodium sulfide in ethanol (*57*), potassium hydrosulfide in ethanol (*98,127*), thioacetamide (*365*), and potassium hydrosulfide in methanol (*36,136*). In the last case, the formation of bis(5-nitro-2-pyridyl) sulfide has also been observed (*175*). On the other hand, 2-chloro-3-nitropyridine gave 3-nitro-2-pyridinethiol together with some of the corresponding disulfide (rather than the sulfide) (*150*). Several 2,3-dihalo-5-nitropyridines have been converted normally to the 3-halo-5-nitrothiol (*136*).

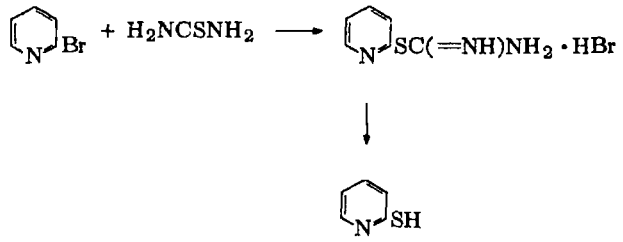
Reduction of a nitro group has however been observed with 2-chloro-3,5-dinitropyridine, which reacted with potassium hydrosulfide in methanol to give an aminonitropyridinethiol. Apparently the 5-nitro group was reduced, since the product (XV-7) gave an *N*-acetyl derivative (XV-8) rather than a thiazole, whereas the corresponding diamine (XV-9) gave a thiazole (XV-10) (*188*).

2-Chloronicotinic acid reacts normally to give 2-mercaptonicotinic acid (*51*). Similarly 2,6-dichloroisonicotinic acid (*15*) and 2,4,6-trichloronicotinic acid (*148*) have been converted to the corresponding di- and trimercapto acids. Nitrile groups are sometimes inert, as in the conversion of 6-chloronicotinonitrile to 6-mercaptonicotinonitrile (*56,86*), but have also been observed to add a molecule of



hydrogen sulfide; the result is the conversion of a halonitrile to a mercaptothioamide (*136*).

Thiourea has also been reacted with numerous halogenated pyridines, generally in refluxing methanol or ethanol; the resulting *S*-pyridylthiuronium halide is decomposed with aqueous alkali metal hydroxide or carbonate to the pyridinethiol (XV-11). Small amounts



(XV-11)

of 2-pyridinethiol were obtained directly when the mixture of 2-bromopyridine, thiourea, and ethanol was refluxed for 24 hours rather than the usual 2-3 hours (*16*). Renault (*141*) reported that the decomposition of *S*-(2-pyridyl)thiuronium bromide with aqueous sodium carbonate on the steam bath gave equal amounts of 2-pyridinethiol and bis(2-pyridyl) sulfide. When *S*-(1-oxido-4-pyridyl)-thiuronium chloride was decomposed with cold aqueous sodium hydroxide, 1-hydroxy-4(1*H*)-pyridinethione was obtained; however, when the decomposition was carried out with aqueous ammonia on the steam bath, bis(1-oxido-4-pyridyl) sulfide was the product (*72, 156,211*).

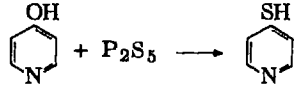
Forrest and Walker (*56*) decomposed *S*-(5-nitro-2-pyridyl)thiuronium chloride with aqueous sodium hydroxide and obtained,

in addition to 5-nitro-2-pyridinethiol, a small amount of bis(5-nitro-2-pyridyl) disulfide.

Table XV-1 lists the known *S*-pyridylthiuronium halides (p. 382).

c. From Pyridinols

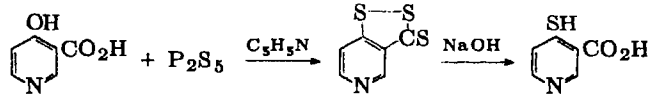
Phosphorus pentasulfide reacts with 2- and 4-pyridinols to give the corresponding thiols (*66,302,319*). 4-Pyridinethiol has been prepared in this manner in 86% yield by fusion at 60–70° (XV-12) (*80*),



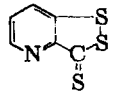
(XV-12)

and 2-pyridinethiol in 70–75% yield at 160° (*141*). The 3,5-diiodo derivatives of both 2-pyridinol and 4-pyridinol react smoothly in high yield with phosphorus pentasulfide in pyridine solution (*84,85*). An earlier attempt to react 5-iodo-2-pyridinol, apparently without solvent, gave a resinous product from which only bis(2-pyridyl) disulfide was isolated, the iodine having been lost (*136*).

4-Hydroxynicotinic acid reacts with phosphorus pentasulfide in pyridine to give the dithiolethione (XV-13); this was found highly resistant to hydrolysis but could be converted to 4-mercaptonicotinic acid (XV-14) in refluxing 30% sodium hydroxide (*245*). Subse-



(XV-13) (XV-14)



(XV-15)

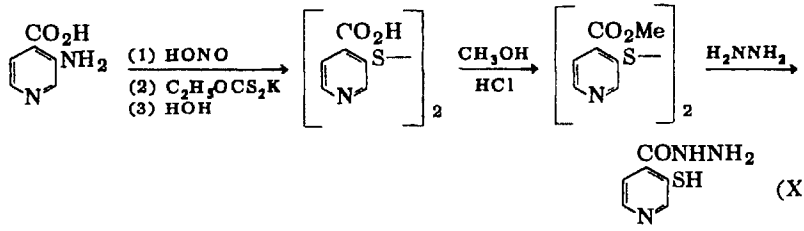
quently, the 2,3-isomer (XV-15) (m.p. 178°) was prepared from phosphorus pentasulfide and bis(2-carboxy-3-pyridyl) disulfide (*248, cf. 307*).

Substitution on the ring nitrogen does not appear to interfere with the conversion of pyridones to thiopyridones. Thus, this re-

action has been successfully performed with a series of 1-alkyl-2(1*H*)-pyridones (*141–144*), with 1-(4-pyridyl)-4(1*H*)-pyridone (*7*), and with 1-phenylchelidamic acid diethyl ester (*8*), giving the corresponding 1-substituted pyridinethiones.

d. From Aminopyridines

The conversion of amines to mercaptans by means of diazotization followed by reaction with a sulfur compound has thus far found little application in the pyridine series. As might be expected, it seems to be limited to the 3-amines. Diazotized 3-aminopicolinic acid and 3-aminoisonicotinic have been successfully reacted with sodium sulfide (*169*); the use of potassium ethyl xanthate, followed by hydrolysis of the resulting xanthate ester (Leuckart reaction), gave the corresponding disulfides. After esterification, the disulfide linkage was then reduced with hydrazine, which also aminolyzed the ester group to give the mercaptohydrazides. (XV-16) (*245*).



(XV-16)

According to a brief report in a patent, the xanthate reaction has also been applied to the conversion of 5-amino-2-pyridinol to 5-mercapto-2-pyridinol (*86*).

e. From Pyridinesulfonyl Chlorides

3-Pyridinethiol has been prepared by the reduction of 3-pyridinesulfonyl chloride with stannous chloride in concentrated hydrochloric acid (*165,166*).

f. From Pyridylpyridinium Chlorides

1-(4-Pyridyl)pyridinium chlorides (*cf.* Chapter III, pp. 11 ff.) react with hydrogen sulfide in pyridine to give 4-pyridinethiols (*279*).

3. Properties

The pyridinethiols are generally obtained as colored crystalline solids; for example, 2-pyridinethiol forms deep yellow, 2,6-dimethyl-4-pyridinethiol yellow-brown, and 5-nitro-2-pyridinethiol red-brown crystals. The pyridinethiols are insoluble in water, ether, and ligroin, and soluble in ethanol, acetone, and benzene. They are amphoteric substances, being soluble both in mineral acid and in aqueous alkali metal hydroxides and carbonates; they are precipitated from the latter by the addition of acetic acid. In alkaline solution, pyridinethiols are susceptible to oxidation. Nothing is known of the effect of structure and substitution in the pyridine ring upon the acidity of the —SH group. The only reports concerning the effects of structure and substitution upon the basicity of the pyridinethiols are that 2,6-dimethyl-4-pyridinethiol forms a stable hydrochloride, m.p. 258°, while 2-pyridinethiol forms an oily, readily dissociated hydrochloride and forms no salt with picric acid (*107,141*). The pyridinethiols form highly insoluble salts with the heavy metals, *e.g.*, mercury, copper, and silver.

Penfold (*247*) determined the crystal structure of 2-pyridinethiol by means of electron-density projections on the (001) and (010) planes. 2-Pyridinethiol molecules are linked in pairs across centers of symmetry by what appear to be weak hydrogen bonds between nitrogen and sulfur atoms.

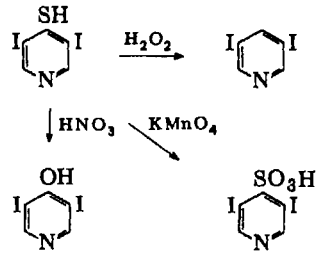
4. Reactions

a. Oxidation and Reduction

Pyridinethiols generally undergo the normal oxidation reactions of mercaptans to disulfides, sulfonic acids, and sulfonyl chlorides; these will be discussed in detail in the sections of the chapter devoted to these classes of compounds. 5-Nitro-2-pyridinethiol reacts with chlorine in carbon tetrachloride to give 5-nitro-2-pyridinesulfenyl chloride, m.p. 116–118° C. (*57*); this seems to be the only representative of this class of compounds in the pyridine series.

Interesting anomalies were observed by Dohrn and Diedrich (*42*) in the oxidation of 3,5-dihalo-2- and -4-pyridinethiols: Hydrogen peroxide removed the sulfur reductively, giving the 3,5-dihalopyridine. Nitric acid removed the sulfur hydrolytically, giving the di-

halopyridone. Potassium permanganate gave the expected dihalopyridinesulfonic acid (XV-17). The attempted oxidation, on the



(XV-17)

other hand, of 5-nitropyridine-2-thiol to the corresponding sulfonic acid failed completely, but its reduction product 5-acetamido-2-pyridinethiol reacted with hydrogen peroxide to give an excellent yield of sulfonic acid (*21*).

b. Acylation and Alkylation

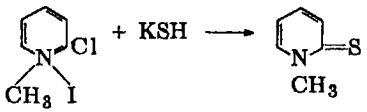
Two reports were found on the acylation of a pyridinethiol; these were the esterification of 3-pyridinethiol and dimethylcarbamyl chloride (*205*) and 3-amino-5-bromo-4-pyridinethiol with *p*-nitrobenzoyl chloride (*276*).

Pyridinethiols engage readily in the normal alkylation reactions of mercaptans to sulfides. Not only the 3-thiol, but also the 2- and 4-isomers seem to give S-alkylation exclusively; this contrasts with 2- and 4-pyridones, which tend to favor *N*-alkylation under normal conditions. Typical of such alkylation reactions are the following: 2-pyridinethiol with ethanol and hydrochloric acid or with ethyl iodide (*37*), with ethyl bromide (*10*), with allyl bromide and powdered sodium hydroxide (*191*) with 1-bromo-4-diethylamino-2-butanone hydrobromide in glacial acetic acid (*251*); 4-pyridinethiol with methyl iodide in ethanol (*80*) or with chloroacetic acid (*80*); 5-nitro-2-pyridinethiol with diazomethane (*175*). 3,5-Diiodopyridine-4-thiol reacted normally with alkaline chloroacetic acid solution, but the isomeric 2-thiol lost sulfur under these conditions, giving 3,5-diiodo-2-pyridinol; the silver salt of the 2-thiol also lost sulfur when treated with ethyl bromoacetate in refluxing ethanol, giving the pyridone-1-acetic ester (*83*).

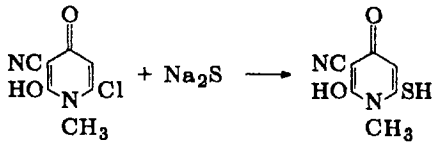
Preferential *S*- as against *O*-alkylation has been reported in the reaction of 2-mercaptoricinic acid with chloroacetic acid (*155*; see also ref. *203*).

2-Pyridinethiol reacts with 2-chloropyridine in xylene to give bis(2-pyridyl) sulfide (*37*).

The *N*-substituted pyridinethiones, which are *not* obtainable by *N*-alkylation reactions, are prepared by the reaction of phosphorus pentasulfide with the corresponding *N*-substituted pyridone (*7,8, 141–144*), or from hydrosulfides and an *N*-substituted halopyridone (XV-18, XV-19) (*114*). These compounds are reported to react



(XV-18)



(XV-19)

readily with ammonia to give 1-alkyl-1,2-dihydro-2-iminopyridines (*224*). 1-Methyl-2(1*H*)-pyridinethione has been quaternized with various alkyl halides; 2-(methylthio)pyridine methiodide has been pyrolyzed to 2-(methylthio)pyridine (*60,114,250*).

Pyridinethiols may be arylated to the aryl sulfide by reaction with an active aryl halide such as 2-chloropyridine (*37*) or with an aromatic diazo compound (*36*).

The only known pyridine derivatives containing more than one mercaptan group are certain di- and trimercaptopyridinecarboxylic acids, prepared from the corresponding halogenated acids and potassium hydrosulfide; see Table XV-2 (p. 383) (*15,148*).

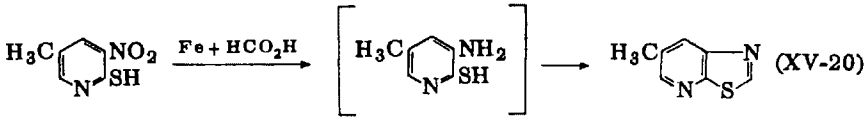
5. Sustituted Pyridinethiols

Most substitution products are prepared by application of the syntheses described above to appropriately substituted starting materials, and require no special comment. In a few cases, however, the substitution modifies the chemistry significantly.

The mercaptan group in 5-nitro-2-pyridinethiol is highly activated and can be replaced by hydroxy, methoxy, amino, or chloro

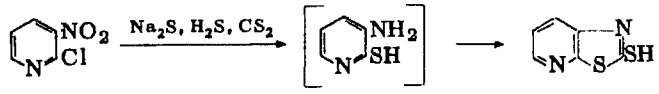
groups; oxidation to the sulfonic acid could not be effected unless the nitro group was first converted to acetamido (*21*).

o-Aminopyridinethiols are readily converted into pyridothiazoles. For example, a solution of 3-amino-6-chloro-2-pyridinethiol in aqueous sodium hydroxide was treated with a stream of carbon dioxide saturated with carbon disulfide, giving 5-chloropyrido [3,2-*d*] thiazole-2-thiol (*213,214*). The aminothiol may be formed *in situ* from the corresponding nitrothiol, as in the reaction of 5-methyl-3-nitro-2-pyridinethiol with 85% formic acid and iron filings to give 6-methylpyrido[3,2-*d*]thiazole (XV-20) (*29*). Instead of a nitromer-



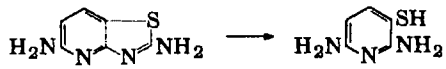
(XV-20)

captan, a nitrohalo compound has also been used: 2-chloro-3-nitropyridine reacted with sodium sulfide and hydrogen sulfide in carbon disulfide to give pyrido[3,2-*d*]thiazole-2-thiol (XV-21) (*213,214*).



(XV-21)

2,6-Diamino-3-pyridinethiol has been obtained by alkaline hydrolysis of 2,5-diaminopyrido [2,3-*d*] thiazole (XV-22) (*187*).



(XV-22)

The known isomeric pyridinethiols are listed in Tables XV-2–XV-5 (pp. 383 ff.). The known 1-substituted 2(1*H*)-pyridinethiones are listed in Table XV-6 (p. 386).

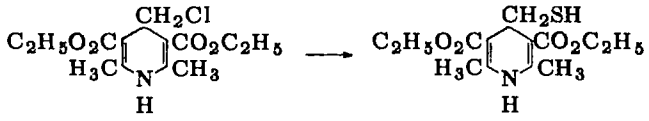
B. PYRIDYLALKYLTHIOLS

The few known representatives of this class of compounds have been prepared by one of two methods:

1. From Pyridylalkyl Halides

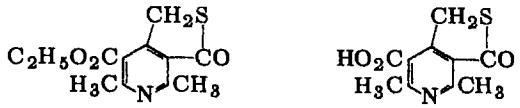
Benary (*13*) reacted diethyl 4-chloromethyl-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate with ethanolic potassium hydro-

sulfide and obtained (XV-23), which was unaffected by hot aqueous



(XV-23)

sodium hydroxide or hydrochloric acid. Under the same conditions, diethyl 4-iodomethyl-2,6-dimethyl-3,5-pyridinedicarboxylate and ethanolic potassium hydrosulfide gave (XV-24) which was hydrolyzed to (XV-25) by potassium hydroxide in ethanol. 3-Pyridine-

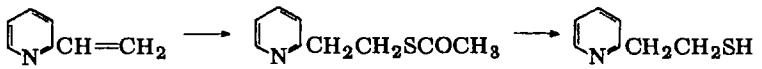


(XV-24) (XV-25)

methanethiol was prepared *via* the decomposition of the isothiuronium chloride with aqueous sodium hydroxide (*256*). 2-Methyl-4,5-bis(bromomethyl)-3-pyridinol hydrobromide, *via* the isothiuronium salt, gave 6-methyl-7-hydroxythieno[3,4-*c*]pyridine (*302*).

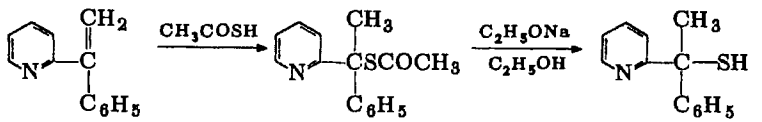
2. From 2-Vinylpyridine

This is converted to 2-pyridineethanethiol either directly by the addition of hydrogen sulfide (*236*), thiolacetic acid followed by hydrolysis (XV-26) (*238*), or thiourea followed by hydrolysis (*323*).



(XV-26)

Shelton and Tilford (*233*) utilized the same procedure for preparing α-methyl-α-phenyl-2-pyridinemethanethiol (XV-27); it will be noted



(XV-27)

that in this reaction the thiolacetic acid added to the unsaturated double bond in the reverse manner to that shown in (XV-26).

3. From Alcohols

Pyridoxol and carbon disulfide in ethanolic sodium hydroxide gave 4-pyridoxthiol (*304*); a "thiopyridoxal" has been reported (*315, 316*).

The known pyridylalkylthiols are given in Table XV-7, pyridine thiolactones in Table XV-8 (p. 387).

C. PYRIDYL THIOKETONES

Kahn and Petrow (*225*) heated 3,3′-methylenebis(6-dimethylaminopyridine) and sulfur in cymene and obtained bis(6-dimethylamino-3-pyridyl) thioketone; this is hydrolyzed by acid to the corresponding ketone.

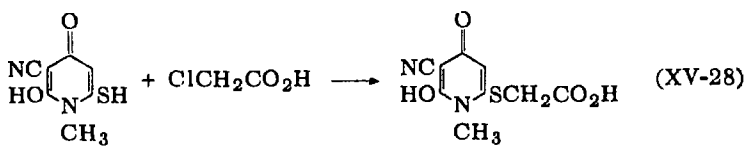
D. PYRIDYL SULFIDES

1. Preparation

a. From Pyridinethiols

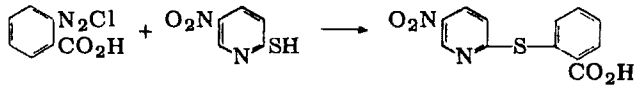
As has been pointed out (p. 354), pyridinethiols are readily alkylated to sulfides with typical alkylating agents. The most frequently used solvents seem to be methanol and ethanol, with or without added base. Normal *S*-alkylation has been observed with a variety of substituted pyridinethiols, such as 2,6-dimethyl-4-pyridinethiol (*107*), 3-amino-6-ethoxy-2-pyridinethiol (*187*), 5-amino-3-nitro-2-pyridinethiol (*188*), 6-mercaptonicotinonitrile (*56*), and 2,6-diamino-3-pyridinethiol (*187*). On the other hand, 3-amino-6-chloro-2-pyridinethiol could not be methylated with dimethyl sulfate; its *N*-acetyl derivative reacted normally (*187*).

Anomalies have been observed with other thiols: 3,5-diiodo-2-pyridinethiol, as well as its silver salt, is reported to lose sulfur under alkylating conditions, giving derivatives of the corresponding 2-pyridone (*83*). Preferential alkylation of the sulfur rather than oxygen is reported in the reaction of chloroacetic acid with 2-mercaptoricinic acid to give the *S*-acetic acid (XV-28) (*155*). 5-Nitro-2-pyridinethiol



(XV-28)

has been arylated by reaction with diazotized anthranilic acid (XV-29) (*36*).



(XV-29)

The ultraviolet spectra of the 2-, 3-, and 4-methylpyridyl sulfides have been studied (*348*).

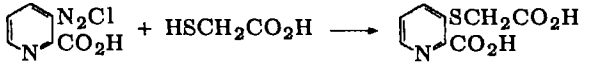
b. From Halopyridines

These have been converted to sulfides by reaction with a variety of thiols (generally in the form of metal salts), including thiophenol (*133,177,17,291*), *p*-thiocresol (*126*), *p*-nitrothiophenol (*11,140*), and thioglycolic acid (*35*). The desired sulfide was not, however, obtained in the reaction of *p*-nitrothiophenol with 4-chloropyridine (*20*) or of thiophenol with 2-chloro-3,5-dinitropyridine (*188*). The reaction of 4-chloro-3,5-diiodopyridine with thiosalicylic acid gave a complex mixture of products (*5*).

The preparation of symmetrical dipyridyl sulfides is exemplified by the reaction of 2-chloro-5-nitropyridine with sodium sulfide in ethanol, giving bis(5-nitro-2-pyridyl) sulfide; this preparation is improved by the use of thiourea instead of sodium sulfide (*171*). Bis-(2-pyridyl) sulfide has been prepared from 2-pyridinethiol and 2-chloropyridine (*37*).

c. From Aminopyridines

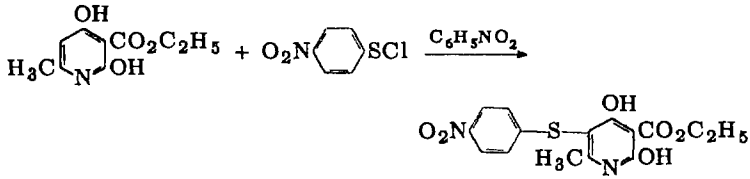
Diazotized 3-aminopicolinic acid reacts with thioglycolic acid to give the sulfide (XV-30) (*131*).



(XV-30)

d. From a Sulfenyl Halide

Direct substitution by *p*-nitrobenzensulfenyl chloride, reported by Burton and Davy (*20*), could presumably be extended to other highly activated pyridine derivatives (XV-31).



(XV-31)

e. From a Pyridylpyridinium Chloride

1-(4-Pyridyl)pyridinium chloride reacts with thiophenol to give 4-(phenylthio)pyridine, with hydrogen sulfide and allyl chloride to give 4-(allylthio)pyridine, and with sodium sulfide to give bis(4-pyridyl) sulfide (*279*).

f. From Phenacyl Thioethers and Aldehydes

Phenyl phenacyl thioether, benzaldehyde, and ammonium acetate give 2,4,6-triphenyl-3,5-bis(phenylthio)-1,4-dihydropyridine (*328*).

2. Properties

The pyridyl sulfides are obtained as colorless oils or yellow-colored crystalline solids, insoluble in cold water but soluble in alchol. They form stable salts with picric acid, chromic acid, and the mineral acids, and highly insoluble double salts with chloroplatinic acid. While pyridyl sulfides quaternized at the pyridine nitrogen atom are known, no sulfonium derivatives have been prepared, although one is postulated as an intermediate (*37*).

The known monopyridyl sulfides are listed in Tables XV-9–XV-12, dipyridyl sulfides in Table XV-13 (pp. 388 ff.).

Anomalous instability has been observed in (3,5-diiodo-4-pyridylthio)acetic and -propionic acids, which lose the side chain under mild conditions to give bis(3,5-diiodo-4-pyridyl) disulfide (*83*). Longer chain *S*-aliphatic acids were found to be stable (*5*).

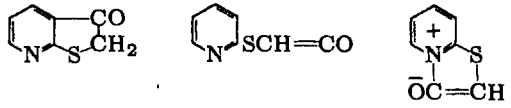
Mangini and Passerini (*99,100*) have investigated the ultraviolet spectra of certain 3-nitropyridyl sulfides.

3. Reactions

Pyridine sulfides are oxidized normally to sulfoxides and sulfones; these reactions are discussed in detail in the sections of this chapter devoted to these compounds.

2-Pyridylthioacetic acid loses the elements of water when heated with acetic anhydride; the product was assigned the structure (XV-32) by Koenigs and Geisler (*87*). Chichibabin and Vorozhtzov (*28*), by an unequivocal synthesis of (XV-32), showed that the compound in question had a different structure, for which they proposed (XV-33). More recently, Duffin and Kendall (*47*), on the basis of a study

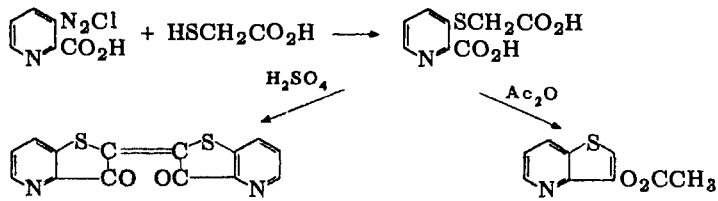
of the 2-quinoline analog, have favored the sydnone structure (XV-34). The preparation of a 6-membered analog has been reported



(XV-32) (XV-33) (XV-34)

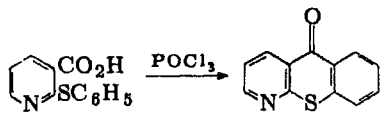
by Colonna (*35*). 2-Methylthio-4,6-dimethylnicotinonitrile, zinc and acetic acid gave 4,6-dimethylnicotinonitrile (*318*).

The pyridine analog (XV-35) of thioindigo has been prepared from 3-(carboxymethylthio)picolinic acid; it is described as somewhat deeper in shade than thioindigo itself (*131*). The same starting material, on treatment with acetic anhydride, gives the cyclization product 3-thieno-(3,2-*b*)-pyridyl acetate (XV-36) (*157*). 2-Vinylpyridine and H_2S gave trace amounts of thieno[3,2-*b*]pyridine (*317*).



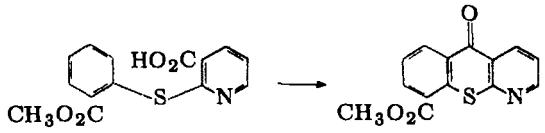
(XV-35) (XV-36)

Appropriately substituted pyridyl aryl sulfides can be condensed to tricyclic systems, the sulfur atom entering into the new ring. Thus 2-(phenylthio)nicotinic acid has been cyclized with phosphorus oxychloride to give 9-thia-1-azaanthrone (XV-37) (*101*); 2-(*o*-carboxy-



(XV-37)

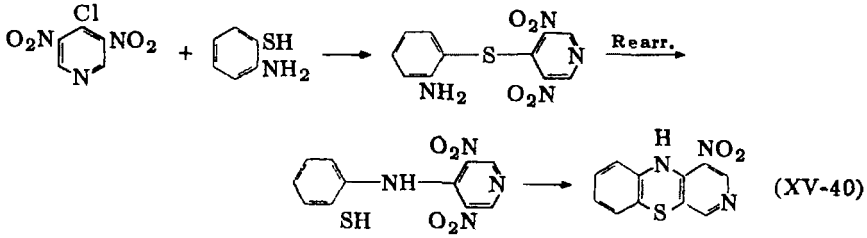
phenylthionicotinic acid did not react with phosphorus oxychloride but its monomethyl ester (XV-38) gave 8-carbomethoxy-9-thia-1-azaanthrone (XV-39). 3-(Phenylthio)isonicotinic acid gave 9-thia-2-azaanthrone, 3-(phenylthio)picolinic acid gave 9-thia-4-azaanthrone



(XV-38) (XV-39)

(*253*), and 4-(phenylthio)nicotinic acid gave 9-thia-3-azaanthrone (*254*).

1-Nitro-3-azaphenothiazine has been prepared from 4-chloro-3,5-dinitropyridine by the steps shown (XV-40) (*232*), one of which in-

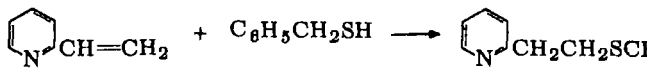


(XV-40)

volves a Smiles rearrangement (*246*); a related series of reactions led to other azaphenothiazines (*261,283,299*).

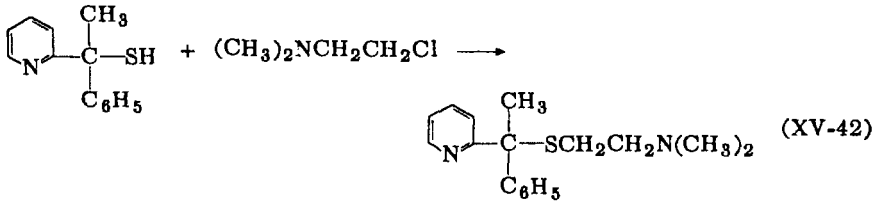
E. PYRIDYLALKYL SULFIDES

Prill *et al.* (*132*), Thompson *et al.* (*236*), Profft (*280,295*), and Vinton (*237*) added various aliphatic, aromatic, and aralkylthiols to 2-vinylpyridine and obtained a series of sulfides (XV-41). Shelton



(XV-41)

and Tilford (*233*) reacted the sodium salt of α-methyl-α-phenyl-2-pyridinemethanethiol with 2-dimethylaminoethyl chloride in toluene and obtained 2-[α-(2-dimethylaminoethylthio)-α-methylbenzyl]pyridine (XV-42). Table XV-14 (p. 402) lists the known pyridylalkyl sulfides.



(XV-42)

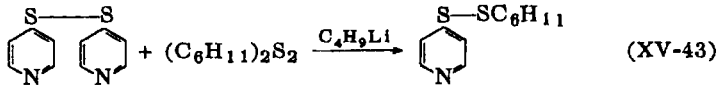
F. PYRIDYL DISULFIDES

1. Preparation

Pyridinethiols are readily oxidized to disulfides with a variety of oxidizing agents. Thus 2- and 4-pyridinethiol have been oxidized to the disulfide with iodine in the presence of aqueous sodium hydroxide (90,107); this method has also been used with 3,5-diiodo-4-pyridinethiol (*83*). 4-Pyridinethiol has also been oxidized with chlorine or hydrogen peroxide (*80*); the latter reagent has been used as well with 5-nitro-2-pyridinethiol (*136*) and 5-acetamido-2-pyridinethiol (*21,136*). Ferric chloride has been used to oxidize 3-amino-6-chloro-2-pyridinethiol to the disulfide (*213,215*); 2-methyl-4-pyridinethiol and potassium ferricyanide also gave the disulfide (*321*). Air has been used in the oxidation of 2,6-diamino-3-pyridinethiol (*187*).

Saikachi (*150*) reports the formation of bis(3-nitropyridyl) disulfide from 2-chloro-3-nitropyridine and the lead salt of 3-nitropyridinethiol in ethylene glycol.

Methyl 2-pyridyl disulfide has been prepared from 2-pyridinethiol and dimethyl sulfide; mixed disulfides are also prepared by an exchange reaction from bis(4-pyridyl) disulfide (XV-43) (*81,82*).



(XV-43)

Bis(3,5-diiodo-4-pyridyl) disulfide is formed by the spontaneous decomposition of (3,5-diiodo-4-pyridylthio)acetic and -propionic acids (*83*).

The known pyridyl disulfides are listed in Tables XV-15 and XV-16 (pp. 403 f.).

2. Reactions

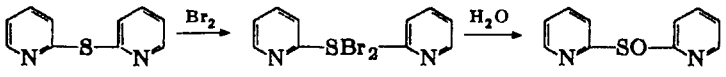
These compounds undergo the normal oxidation and reduction reactions of their class. For example, reduction with hydrazine to the thiol has been reported by Katz (*245*).

An unusual oxidation to thiolsulfinic esters is disclosed in a patent (*24*) that does not however give any detailed examples in the

pyridine series. Bis(2-pyridyl) disulfide and hydrogen peroxide are reported to give 2-pyridyl 2-pyridylthiosulfinate 1,1′-dioxide (*344*).

G. PYRIDYL SULFOXIDES

These are prepared by oxidation of the sulfide. Hydrogen peroxide has been used to convert methyl 2-pyridyl sulfide (*37*) and 6-(methylthio)nicotinamide (*56*) to the respective sulfoxides. Bromine oxidation of 2-pyridyl sulfide gave a dibromide which could be hydrolyzed to the sulfoxide (XV-44) (*37*). In the perbenzoic



(XV-44)

acid oxidation of benzyl 2-pyridyl sulfide, the sulfoxide was obtained instead of the expected 1-oxide (*156*).

The known pyridyl sulfoxides are listed in Table XV-17 (p. 404).

H. PYRIDYL SULFONES

1. Preparation

a. From Pyridyl Sulfides

These compounds are readily oxidized to sulfones. Potassium permanganate has been commonly used, for example, with 2-(methylthio)pyridine (*37*), 4-(methylthio)pyridine, 2,6-dimethyl-4-(methylthio)pyridine (*107*), bis(2,6-dimethyl-4-pyridyl) sulfide (*107*), 6-(methylthio)nicotinonitrile (*56*), 2,6-diacetamido-3-(methylthio)pyridine (*187*), and 5-nitro-2-(4-nitrophenylthio)pyridine (*178,240*).

Hydrogen peroxide oxidation has been used with 2-(5-nitro-2-pyridylthio)benzoic acid (*139*) and 3-(2,4-dinitrophenylthio)-6-nitropyridine (*11*). Dichromate oxidation has been used with 2-(5-nitro-2-pyridylthio)benzoic acid (*36*), and bis(5-nitro-2-pyridyl) sulfide (*35, 170*).

b. From Halopyridines

Active halides react with benzenesulfinic acid salts to give sulfones (*11,44,333*); several sulfones have been made in this way from

4-chloropyridine (*20*). Similarly, 3-pyridinesulfinic acid salts also give sulfones (*273*).

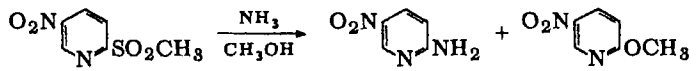
An unusual preparation of 5-nitro-2-pyridyl *p*-tolyl sulfone involved the reaction of 2-chloro-5-nitropyridine and *p*-tolylsulfonylhydrazide (*333*).

2. Properties

The pyridyl sulfones are colorless oils or crystalline solids. The effect of nuclear methylation on the basic properties seems to be similar to that observed in the pyridinethiols. Methyl 2-pyridyl sulfone, for example, is a viscous oil, easily soluble in water, and without basic properties; it forms no salts with hydrochloric acid, picric acid, platinum tetrachloride, or gold chloride; with mercuric chloride it forms a double salt. In contrast, 2,6-dimethyl-4-pyridyl methyl sulfone forms a chloroplatinate, a bichromate, and a picrate.

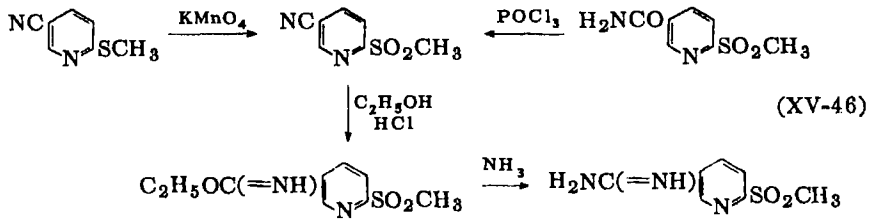
3. Reactions

Cleavage of a sulfone group has been reported by Forrest and Walker (*56*); methyl 5-nitro-2-pyridyl sulfone reacted with ammonia in methanol to give a mixture of 2-amino-5-nitropyridine and 2-methoxy-5-nitropyridine (XV-45). In general, however, the group



(XV-45)

is unaffected by ordinary reaction conditions. Thus 6-(methylsulfonyl)nicotinamide was converted successively to the nitrile, imido ether, and amidine (XV-46). The stability of the sulfone group to



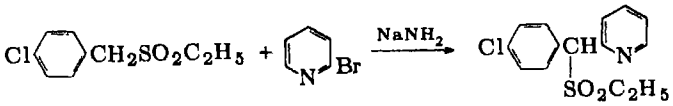
(XV-46)

reducing conditions makes it possible to reduce nitrated pyridyl aryl sulfones to the corresponding amines (*44,140,170,178,240*). This reduction can also be done catalytically (*55,56*).

The known 2-pyridyl sulfones are listed in Table XV-18, 3-pyridyl sulfones in Table XV-19, 4-pyridyl sulfones in Table XV-20, and dipyridyl sulfones in Table XV-21 (pp. 405 ff.). The only known pyridine disulfone is 6-methyl-2,4-bis(*p*-acetamidophenylsulfonyl)-pyridine, m.p. 275–276 (*20*).

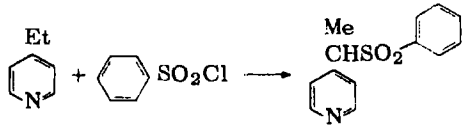
I. PYRIDYLALKYL SULFONES

Most of the known compounds of this class have been prepared by reaction (XV-47). The reaction of 2- and 4-vinylpyridine with



(XV-47)

various benzenesulfinic acids gave a number of pyridylethyl phenyl sulfones; 4-chloromethylpyridine and sodium *p*-toluenesulfinate gave 4-pyridylmethyl *p*-tolyl sulfone (*274*). 1-(4-Pyridyl)pyridinium chloride and benzenesulfinic acid gave phenyl 4-pyridyl sulfone (*290*). The reaction of 4-methyl- and 4-ethylpyridine with arylsulfonyl chlorides has now been shown to involve attack at the alkyl group and not in the nucleus (XV-47a) (*309*). These compounds are listed in Table XV-22 (p. 409).



(XV-47a)

J. PYRIDINESULFINIC ACIDS

4- and 3-Pyridinesulfonic acid hydrazide and carbonyl compounds containing three or more carbon atoms, *e.g.*, acetone, reacted to give 4- and 3-pyridinesulfinic acid, m.p. 140–141 and 161–163°, respectively (*273,326*). Sulfoxides were prepared (*a*) by reaction of the acid with 2- or 4-vinylpyridine or (*b*) by reaction of the alkali metal salt of the acid with another compound containing an active halogen atom. 2-Pyridinesulfonyl chloride and zinc dust gave 2-pyridinesulfinic acid (*249*). The dry distillation of 3-cyano-4,6-dimethylpyridinesulfinic acid sodium salt gave 4,6-dimethylnicotinonitrile (*308*).

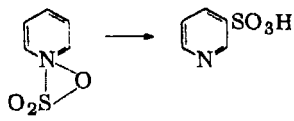
K. PYRIDINESULFONIC ACIDS

1. Preparation

a. Sulfonation of Pyridine and its Derivatives

(a) Pyridine. The earlier literature on the sulfonation of pyridine to the 3-sulfonic acid is rather confusing. Thus, Fischer and his collaborators (*53–55*) obtained a 50% yield by heating pyridine and concentrated sulfuric acid for extended periods of time (30–40 hours to several days or weeks) at 320–330° in sealed tubes. Weidel and Murmann (*202*) used the procedure of Fischer, but added small amounts of various metal sulfates, of which aluminum sulfate proved the most effective catalyst, although with it the yields were only 45–50%. Mayer and Ritter (*113*) and Craig (*239*) reported that vanadyl sulfate also exerted a beneficial effect on the yield obtained by distilling a mixture of dry pyridine sulfate and 100% sulfuric acid. Von Gastel and Wibaut (*63*) heated a mixture of pyridine sulfate and fuming sulfuric acid at 350–390° and obtained a 13% yield. By adding mercuric sulfate to the same mixture and operating at 300–350°, these authors obtained a mixture of the 3- (5% yield) and 2-sulfonic acids (2% yield); at 340–350°, the same sulfonating mixture gave a 1% yield of the 2-isomer. Subsequently, other workers (*79,96,195,196,206*) used mercury or its salts in the sulfonation. den Hertog, Van der Plas, and Buurman obtained mainly 3-sulfonic acid at 275°, some of the 4-isomer and 4-pyridinol at 330° (*287*).

McElvain and Goese (*102*) in a classical paper, reported a detailed study of the sulfonation reaction and found that the yield was dependent upon (*a*) the catalyst (mercuric sulfate), (*b*) the presence of one equivalent of sulfur trioxide in the fuming sulfuric acid, and (*c*) the duration of heating at 225–230°. From these studies, optimum conditions were developed which gave 71% yields of 3-pyridinesulfonic acid. This procedure has been used successfully by others (*74,201,218,310*). Recently, Hope and deLeon (*71*) have reported a 76.3% yield by heating a mixture of pyridine, fuming sulfuric acid and mercuric sulfate at 225–230° under pressure. A British patent (*134*) claims a 63% yield by the rearrangement of the pyridine-sulfur trioxide addition product at 180–200° (XV-48).



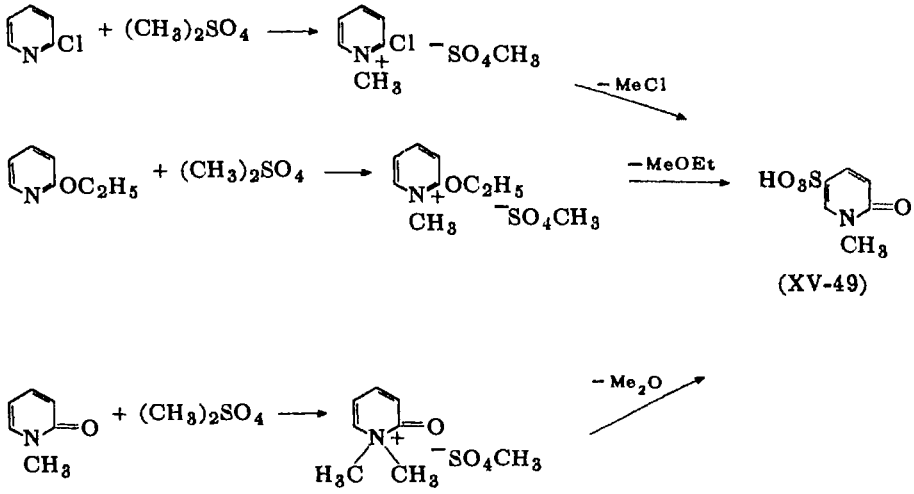
(XV-48)

Piperidine and sulfuric acid are reported to give small amounts of 3-pyridinesulfonic acid; 3,5-pyridinedisulfonic acid has also been obtained (*70,97*).

(b) Alkylpyridines. The sulfonation of α-picoline gave mainly 2-methyl-5-pyridinesulfonic acid along with some of the isomeric 3-sulfonic acid (*102,125,197,206,207,210*); β-picoline gave 3-methyl-5-pyridinesulfonic acid (*102*); and γ-picoline gave 4-methyl-3-pyridinesulfonic acid (*46,102,199,201,206,210*). 5-Ethyl-2-methylpyridine is reported to give 5-ethyl-2-methyl-3-pyridinesulfonic acid (*79, 206,210*), but this could not be reproduced (*268*). 2,6-Lutidine sulfonates in the 3-position (*370*). Morel and Stoll (*116*) have reported that 2-(2-methoxybenzyl)pyridine and 75% sulfuric acid at reflux gave a monosulfonic acid of uncertain structure. The use of chlorosulfonic acid has also been reported (*278*). Brown and Kanner (*18*) found that 2,6-di-*tert*-butylpyridine and sulfur trioxide in liquid sulfur dioxide at – 10° gave a sulfonic acid believed to be a 4-isomer. Under the same conditions, 2,6-lutidine gave only the sulfur trioxide addition compound. The ease of substitution was attributed to the blocking of the nitrogen atom by the *tert*-butyl groups; since coordination was not possible, the reagent attacked the heterocyclic nucleus. Van der Plas and den Hertog (*277,297,310*) and Muller and Wallace (*294*) have since shown that the product is actually the 3-sulfonic acid; Van der Plas (*310*) has extended this reaction to other 2,6-dialkylpyridines.

(c) Aminopyridines. The sulfonation product of 2-aminopyridine has been assigned the 5-sulfonic acid structure (*26,119,226*). The sulfonation product of 3-aminopyridine is not the 5-sulfonic acid (which has been prepared by reducing 3-nitro-5-pyridinesulfonic); it can be diazotized and reduced to 2-pyridinesulfonic acid. Plazek (*129,130*) inferred that the structure was 3-amino-2-pyridinesulfonic acid, but the evidence does not seem to exclude the 6-sulfonic acid. 4-Aminopyridine has been sulfonated to 4-amino-3-pyridinesulfonic acid, which can be diazotized and reduced to 3-pyridinesulfonic acid (*88*). Sulfonation of 4-amino-2,6-lutidine gave only sulfone (*370*).

(d) Pyridinols. 4-Pyridinol has been sulfonated to 4-hydroxy-3-pyridinesulfonic acid at 200° in a mixture of concentrated and fuming sulfuric acid; the same product was obtained by diazotizing 4-amino-3-pyridinesulfonic acid (*88*). Plazek (*128–130*) assumed that 3-pyridinol sulfonated in the 2 position. 2-Pyridinol has apparently not been sulfonated directly, but its sulfonic acid is obtained by diazotizing 2-aminopyridinesulfonic acid; the sulfo group is believed to be in the 5-position (*119,26,27*). A number of 1-methyl-2(1*H*)-pyridones have been sulfonated with chlorosulfonic acid (*153*). Haack (*67*) reports the preparation of the same compound, 1-methyl-2(1*H*)-pyridone-5-sulfonic acid, by the reaction of methyl sulfate with 1-methyl-2(1*H*)-pyridone, 2-ethoxypyridine, or 2-chloropyridine (XV-49).

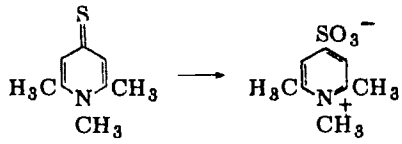


(e) Pyridine 1-Oxide. Pyridine 1-oxide sulfonates principally in the 3-position (*349*); the product may be hydrogenated over Raney nickel to 3-pyridinesulfonic acid (*258*). Since the sulfonation conditions for the oxide are as severe as for pyridine itself, there does not seem to be any preparative advantage in this procedure.

b. From Pyridinethiols

The oxidation of pyridinethiols is advantageous in the preparation of 2- and 4-pyridinesulfonic acids, which are not accessible by direct sulfonation. Thus, hydrogen peroxide has been used to oxi-

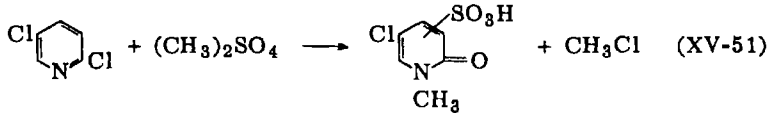
dize 2-pyridinethiol (*80*), 4-pyridinethiol (*370*), 5-acetamido-2-pyridinethiol (*21*), and 2,6-dimethyl-4-pyridinethiol (*107*). Nitric acid has been used to oxidize 2-pyridinethiol (*107,287,370*) and 4-pyridinethiol (*90,287*). Nitric acid has also been used to prepare 3-sulfopicolinic acid from 3-mercaptopicolinic acid or its disulfide (*169*). 5-Nitro-2-pyridinethiol (*98*), 2-mercaptonicotinic acid (*169*), and several 3,5-dihalo-4-pyridinethiols (*42,43*) have been oxidized to the corresponding sulfonic acids with alkaline permanganate. 2,6-Dimercaptoisonicotinic acid has been oxidized to 2,6-disulfoisonicotinic acid with fuming nitric acid (*15*). Hypochlorite oxidation of 1,2,6-trimethyl-4(1*H*)-pyridinethione gave a betaine (XV-50) (*114*); related products have also been described (*305*).



(XV-50)

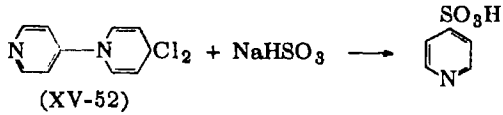
c. From Halopyridines

Aqueous sodium sulfite has been to prepare sulfonic acids directly from various 4-chloropyridines, including 4-chloropyridine itself (*370*), 4-chloro-2-picoline, 4-chloro-2,6-lutidine (*244*), and 4-chloro-3,5-dibromopyridine (*42,43*). 2,5-Dichloropyridine and methyl sulfate gave a 5-chloro-1-methyl-2(1*H*)-pyridone-*x*-sulfonic acid (XV-51); 2-chloropyridine gave 1-methyl-2(1*H*)-pyridone-5-sul-



(XV-51)

fonic acid (*67*). 4-Pyridinesulfonic acid has been obtained from (XV-52) (*194*).



(XV-52)

3-Chloropyridine is inert to aqueous sodium sulfite, but the *N*-oxide reacts (*370*).

Aqueous sodium bisulfite converts 4-pyridinol to the 4-sulfonic acid in low yield; the reaction of sodium sulfite with 1-(4-pyridyl)-pyridinium chloride hydrochloride is suitable for large-scale preparative purposes (*370*).

2. Properties

The pyridinesulfonic acids are obtained as high melting crystalline solids, generally soluble in water and insoluble in ethanol. In the free state they exist as inner salts. Crystallographic (*6*) and ultraviolet absorption data (*287*) have been reported.

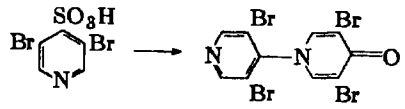
The known pyridinesulfonic acids are listed in Tables XV-23–XV-26 (pp. 410 ff.).

3. Reactions

The sulfonic acids of the pyridine series show the normal functional reactions of sulfonic acids. They form sulfonyl chlorides with phosphorus pentachloride; this class of compounds is discussed below. 4-Pyridinesulfonic acid can be esterified directly with ethanol and hydrogen chloride; the ethyl ester reacts with ammonia to give 4-pyridinesulfonamide (*193*). With dimethyl sulfate, the sulfonic acids form *N*-methylbetaines (*275*). Hydrogen peroxide in acetic acid gives the *N*-oxides (*370*).

The normal replacement reactions of aromatic sulfonic acids are observed in the pyridine series. Thus alkaline fusion gives pyridinols (*46,108,207–209*); this reaction is discussed in Chapter XII (p. 592). Sodium cyanide and sodium 3-pyridinesulfonate give nicotinonitrile (*53,102,158*); 4-methylnicotinonitrile has been obtained similarly (*201*).

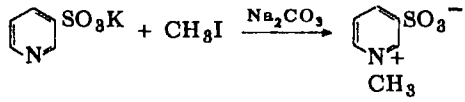
4-Pyridinesulfonic acid, concentrated aqueous ammonia and zinc chloride, at 150–160°, gave 4-aminopyridine (*338*). The sulfo group of 3,5-dibromo-4-pyridinesulfonic acid has also been replaced by amino and anilino groups; refluxing with water gave 1-(3,5-dibromo-4-pyridyl)-3,5-dibromo-4(1*H*)-pyridone (XV-53) (*42*). The sulfo



(XV-53)

group of 5-nitro-2-pyridinesulfonic acid has been replaced by ethoxy and methylamino groups. 2-Pyridinesulfonic acid reacts with hydrazine to give 2-pyridylhydrazine (*98*).

Potassium 3-pyridinesulfonate reacts with methyl iodide to give the betaine (XV-54); this proved inert to mineral acids and gave no



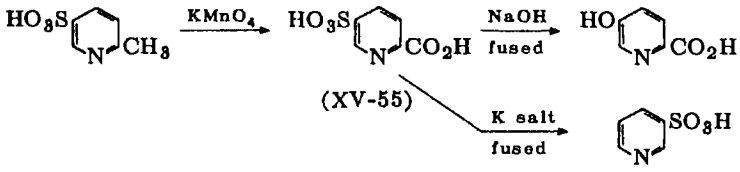
(XV-54)

complex with platinum tetrachloride, but did react with bases, presumably liberating methylamine (*68,111,112*).

4. Substituted Pyridinesulfonic Acids

The applicability of general synthetic methods to the preparation of various substituted sulfonic acids has been indicated above.

Carboxypyridinesulfonic acids may be obtained by the oxidation of alkylpyridinesulfonic acids. Thus, the permanganate oxidation of 6-methyl-3-pyridinesulfonic acid gives 5-sulfopicolinic acid (XV-55), which may be converted to 5-hydroxypicolinic acid or 3-pyridinesulfonic acid (XV-56) (*46*). Oxidation of 4-methyl-3-pyridine-



(XV-56)

sulfonic acid with barium permanganate gives 3-sulfoisonicotinic acid (*199*).

3-Amino-4-hydroxy-2-pyridinesulfonic acid is obtained by dithionite reduction of 3-nitro-4-pyridinol (*371*).

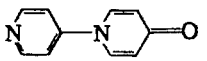
2-Amino-5-pyridinesulfonic acid is reported to brominate and nitrate in the 3-position, and to give a small yield of 3-nitro-2-pyridinol when treated with 45% phosphoric acid at 150° (*136,226*). However, Czuba (*325*) has recently shown that nitration actually gives the *N*-nitro derivative, and has described the preparation of

the 3-nitro compound. 2-Amino-3-nitro-5-pyridinesulfonic acid gives some 3-nitro-2-pyridinol when treated with phosphoric acid at 150–200° (*226*).

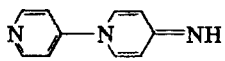
5. Pyridinesulfonyl Chlorides

a. Preparation

(a) From Pyridinesulfonic Acids. 3-Pyridinesulfonic acid and phosphorus pentachloride give the sulfonyl chloride, which may be reacted further *in situ* (*92,97,145,218*) or isolated as the hydrochloride (*138*). 2-Pyridinesulfonyl chloride has been prepared by the reaction of an alkali metal 2-pyridinesulfonate with benzotrichloride; sodium 3-pyridinesulfonate did not react (*92*). The sulfonyl chloride could not, however, be obtained from sodium 4-pyridinesulfonate and phosphorus pentachloride; the product reacted with water to give 1-(4-pyridyl)-4(1*H*)-pyridone (XV-57) and with ammonia to give the corresponding pyridonimine (XV-58) (*80*). The sulfonyl chloride could likewise not be obtained from 5-acetamido-2-pyridinesulfonic acid (*21*). 3,5-Pyridinedisulfonic acid and phosphorus pentachloride gave the disulfonyl chloride, which proved unusually stable to hydrolysis (*97*).

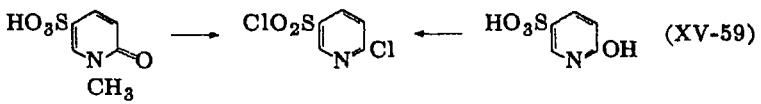


(XV-57)



(XV-58)

Pyridonesulfonic acids react with phosphorus pentachloride to give the chloropyridinesulfonyl chloride. This is seen in the formation of 2-chloro-5-pyridinesulfonyl chloride from 2-hydroxy-5-pyridinesulfonic acid (*27,119,136*) and 1-methyl-2(1*H*)-pyridone-5-sulfonic acid (*1,154*) (XV-59).



(XV-59)

(b) From Pyridinethiols. 2-Pyridinethiol and 5-nitro-2-pyridinethiol are oxidized by hypochlorite directly to 2-pyridinesulfonyl chloride and 5-nitro-2-pyridinesulfonyl chloride, respectively (*249,*

22); 5-acetamido-2-pyridinethiol reacts similarly (*21*). However, the reaction failed with 4-pyridinethiol: chlorine gave 4-chloropyridine and bis(4-pyridyl) sulfide, while bromine gave bis(4-pyridyl) disulfide (*80*).

(c) From Aminopyridines. Bis(5-amino-2-pyridyl) sulfide, when tetrazotized and treated with sulfur dioxide, gave the bis-sulfonyl chloride derivative (*358*).

b. Reactions

Concentrated hydrochloric acid in ether has been used to hydrolyze 2-chloro-5-pyridinesulfonyl chloride to the sulfonic acid (*136*). Kinetics of hydrolysis have been studied by Linetskay and Sapozhnikova (*227*). The kinetics of the hydrolysis of 3-pyridinesulfonyl chloride in aqueous dioxane have also been studied (*335*). A good many pyridinesulfonyl chlorides have been reacted with amines to obtain pyridinesulfonamides; these are further discussed below.

3-Pyridinesulfonyl chloride has been reduced with sulfur dioxide and hydriodic acid to bis(3-pyridyl) disulfide (*65*), and with stannous chloride one stage further to 3-pyridinethiol (*165,166*). 2-Pyridinesulfonyl chloride and zinc dust in water gave 2-pyridinesulfinic acid (*249*).

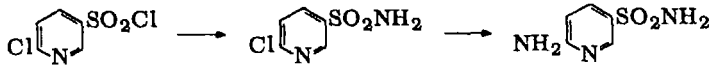
The known pyridinesulfonyl chlorides are listed in Table XV-27 (p. 413).

6. Pyridinesulfonamides and Pyridinesulfohydrazides

These compounds are prepared from pyridinesulfonyl chlorides and amines or hydrazine. Thus, 3-pyridinesulfonyl chloride reacts with aqueous ammonia (*97*), hexadecylamine (*218–221*), 2-aminopyridine (*105*), 2-aminothiazole (*145*), and ethyl *p*-aminobenzoate (*138*). 3,5-Pyridinesulfonyl chloride reacts with diethylamine to give the bis(sulfondiethylamide) (*97*). A variety of amines have been reacted with 2-amino-5-pyridinesulfonyl chloride (*50*). 2-Pyridinesulfohydrazide in water or ethanol decomposes to 2,2′-dipyridyl disulfite with the evolution of nitrogen (*282*).

Stepwise replacement of chlorine is shown in the reaction of ammonia with 6-chloro-3-pyridinesulfonyl chloride. Fusion with ammonium carbonate effected ammonolysis of the more reactive sul-

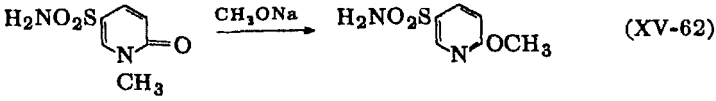
fonyl chlorine, giving 6-chloro-3-pyridinesulfonamide (XV-60); the nuclear chlorine was then displaced in concentrated aqueous ammonia and a trace of copper sulfate at 145°, giving 6-amino-3-pyridinesulfonamide (XV-61) (*27,117–119,136*). In other cases, 6-chloro-



(XV-60) (XV-61)

3-pyridinesulfonyl chloride has reacted with 3-amino-6-(ethylthio)-pyridine or 3,5-dibromoaniline to give the *N*-substituted 6-chloro-3-pyridinesulfonamide; the chlorine was then hydrolyzed, giving the corresponding 6-hydroxy-3-pyridinesulfonamide (*181*).

1-Methyl-2(1*H*)-pyridone-5-sulfonamide isomerizes in the presence of sodium methoxide in methanol, giving 2-methoxy-5-pyridinesulfonamide (XV-62) (*1*).



(XV-62)

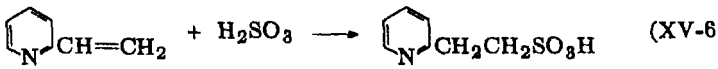
3-Pyridinesulfonamide methiodide is reduced by aqueous sodium hydrosulfite to 1-methyl-1,6-dihydro-3-pyridinesulfonamide; this reduces cold aqueous silver nitrate (*75*).

Tables XV-28, XV-29, and XV-29a (pp. 414 ff.) list the known pyridinesulfonamides and pyridinesulfohydrazides. Table XV-30 (p. 421) lists pyridinedisulfonamides.

7. Side-Chain Sulfonic Acids

The known side-chain sulfonic acids of pyridine fall into three classes:

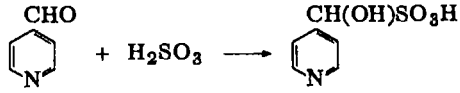
a. 2-Vinylpyridine reacts with aqueous sodium bisulfite to give pyridineethanesulfonic acid (XV-63) (*41*); Cislak has described similar addition reactions with 2-vinylpyridine, 4-vinylpyridine, and 6-



(XV-63)

methyl-2-vinylpyridine (*34*). The 2-ethanesulfonic acid has also been obtained by nitric acid oxidation of the hydrochloride of 2-pyridineethanethiol (*323*).

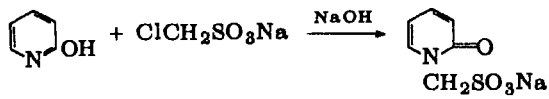
b. Picolinaldehyde, isonicotinaldehyde and 6-methylpicolinaldehyde react with aqueous sulfur dioxide to give the α-hydroxypyridinemethanesulfonic acids (XV-64) (*109,229*).



(XV-64)

c. Allardt and von Schickh (*3*) found that 2-pyridinol reacted with compounds like sodium chloromethanesulfonate in the presence of sodium hydroxide to give 1-alkylsulfonic acids. Some *O*-alkylation occurred if sodium iodomethanesulfonate was used. Only 5-iodo-2-pyridinol gave both *N*- and *O*-alkylation with sodium chloromethanesulfonate.

Compound XV-65 reacts with iodine monochloride or bromine to give the 3,5-dihalo derivative.



(XV-65)

The known pyridylalkane- and pyridylalkanolsulfonic acids are listed in Table XV-31 (p. 421).

L. PYRIDYLDITHIOCARBAMIC ACID AND PYRIDYLALKYLDITHIOCARBOXYLIC ACID DERIVATIVES

Salts of pyridyldithiocarbamic acids have been prepared from an aminopyridine, carbon disulfide and a tertiary amine; these, with an alkyl halide, form alkyl pyridyldithiocarbamic acid esters (*361*). One derivative of 4-pyridinedithiobutyric acid has been reported (*368*). See Table XV-35 (p. 424).

M. THIOCYANATOPYRIDINES

1. Preparation

a. From Halopyridines

Various nitrohalopyridines react with potassium thiocyanate to give the corresponding thiocyanato compounds. For example, 2-chloro-3-nitropyridine gives 3-nitro-2-thiocyanatopyridine (*172,189*). 2-Chloro-5-nitropyridine (*189*), 2-chloro-3,5-dinitropyridine (*188*), and 4-chloro-3-nitropyridine react similarly; in the last case the desired product was obtained in a mixture of acetic acid and potassium acetate at room temperature, while steam bath temperature gave 4-amino-3-nitropyridine (*241,242*). It has not been possible to convert 2-bromopyridine to 2-thiocyanatopyridine (*91,124*). The structure of 2-pyridyl isothiocyanate has recently been elucidated (*320, 322*). Pyridylalkylisothiocyanates are also known (*360*).

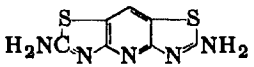
b. From Diazo Compounds

Diazotized 3-aminopyridine reacts with potassium and copper thiocyanates to give 3-thiocyanatopyridine together with some bis(3-pyridyl) sulfide. Diazotized 2-aminopyridine does not react (*124*). The reported thiocyanato derivatives of 2-aminopyridine and 2-amino-5-iodopyridine (*91*) are actually amine thiocyanate salts (*124*).

c. Direct Thiocyanation

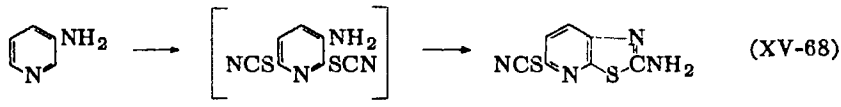
2,6-Diaminopyridine reacts with one equivalent of potassium thiocyanate and bromine in acetic acid to give 2,5-diaminopyrido [2,3-*d*]thiazole (XV-66) directly; the intermediate thiocyanato derivative was not isolated. Two equivalents of potassium thiocyanate and bromine gave 2,6-diaminopyrido[2,3-*d*; 6,5-*d'*]bisthiazole (XV-67) (*14,228*). Yamamoto (*212*) has reported that 3-aminopyri-

(XV-66)



(XV-67)

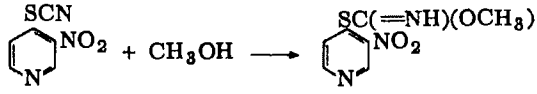
dine, potassium thiocyanate, and bromine in acetic acid gave 5-thiocyanatopyrido[3,2-*d*]thiazole (XV-68).



(XV-68)

2. Reactions

Thiocyanatopyridines are readily hydrolyzed to the corresponding mercaptans or disulfides; they add alcohols to give substituted thiocarbamates (XV-69) (*241,242*). The spontaneous cyclization of



(XV-69)

o-aminothiocyanates to aminothiazoles has been noted above, and is also seen in the reduction of 3-nitro-2-thiocyanatopyridine (*189*) or 3,5-dinitro-2-thiocyanatopyridine (*188*).

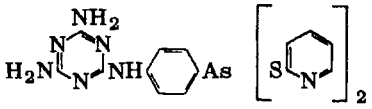
The known monocyclic thiocyanatopyridines are listed in Table XV-32, and *S*-pyridyl-*O*-alkylthiocarbamates in Table XV-33. Condensed thiocyanatopyridines and aminopyridothiazoles are listed in Table XV-34 (p. 423).

N. BIOLOGICAL ACTIVITY OF SULFUR COMPOUNDS OF PYRIDINE

1. Thiols and Sulfides

Ladd (*93*) investigated 2-pyridinethiol as a fungicide. Soo-hoo and Grunberg (*161*), Goodhue and Louthan (*312*), and Steiger (*165*) found that various metal salts of 3-pyridinethiol were active fungicides; the corresponding 2- and 4-pyridinethiol salts were less active. McGinty and Bywater (*103*) and Cheymoul *et al.* (*222,223*) investigated 2-pyridinethiol as an antithyroid agent, while Koch (*345*) tested it for protection against irradiation. Katz (*235*) screened a number of thiopyridinecarbohydrazides and found them to be less potent as fungicides and bactericides than their benzene prototypes. In addition, 3-thioisonicotinylhydrazide had considerably less activity than isonicotinylhydrazide as an antituberculous agent. 2-Pyridinethiol 1-oxide and its derivatives were reported to be highly active against a variety of bacteria and pathogenic fungi (*231,339–*

343,346,347). Räth (*136*) reported that the gold salt of 6-thionicotinic acid was bactericidal. Rothmann (*148*) found that the gold salt of 2,6-dithioisonicotinic acid was a spirocheticidal agent and the lead salt was useful in the treatment of cancer. Stein (*168*) reported that the bismuth salt of 2,6-dithioisonicotinic acid was effective in trypanosome infections. Freidheim (*59*) prepared (XV-70) for the treat-



(XV-70)

ment of trypanosomiasis. Kolmer *et al.* (*90*) found that bis(2-pyridyl) sulfide caused no bone-marrow depression or leukopenia in rats.

2. Sulfones

Nitti and Matti (*122*) found that 4-aminophenyl 5-amino-2-pyridyl sulfone was the most effective compound of a large series tested against streptococcal infections in mice. Roblin *et al.* (*146*) and Bambas (*11*) also reported that this compound was highly active against streptococcal and pneumococcal infections in mice. Filomeni (*52*) and DeCourcy (*281*) found that 5-nitro-2-pyridyl sulfone was effective against hemolytic streptococcal infections in mice. Forrest and Walker (*56*) examined the antibacterial activity of a number of pyridyl sulfones and concluded that they had considerably less activity than the corresponding compounds in the benzene series.

3. Sulfonic Acids and Sulfonamides

Adler *et al.* (*2*) found that 3-pyridinesulfonic acid was antagonistic to glucose dehydrogenase, while Carrara and Chiancone (*23*) studied its effect on catalase and oxidase. Cushing and Morgan (*39*) found that it had no significant effect on mumps or influenza virus. Dreizen (*45*), McIlwain (*104,105*), Meunier (*110*), and Moller and Birkofer (*115*) reported that it inhibited bacterial growth, presumably as a nicotinic acid antimetabolite. In contrast, Erlenmeyer (*48,49*) and Raoul (*135*) found that it supplemented the growth effects of nicotinic acid on bacteria. Gaebler and Beher (*62*) reported

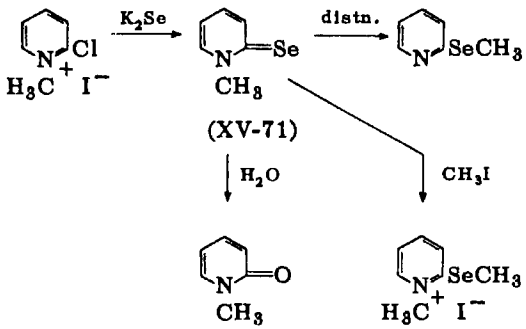
that normal or nicotinic acid-depleted dogs, if fed 3-pyridinesulfonic acid, showed no evidence of black tongue, nor was there any effect on their general health. Rudolph (*149*) reported that *N*-(2-pyridyl)-3-pyridinesulfonamide could replace nicotinic acid in certain instances as a growth substance, and regarded it as a pseudo vitamin. Steffenoni (*163,164*) found that 3-pyridinesulfonic acid increased resistance to histamine or adrenalin in isolated animal organs. α-Hydroxy-2-pyridinemethanesulfonic acid was a highly effective inhibitor of glycolic acid oxidase (*350*). 4-Pyridinesulfonamide was reported to be a highly selective cytotoxic agent for tumor tissue (*351*).

King and Ware (*80*) found that ammonium 4-pyridinesulfonate had no curative effect in streptococcal infections. Zienty (*218–221*) prepared a number of quaternary 3-pyridinesulfonamides and evaluated them as germicides. Vincke and Sucker (*199*) reported that the neodymium salt of 3-sulfoisonicotinic acid was an anticoagulant opposing the effects of prothrombin, and was well tolerated by humans.

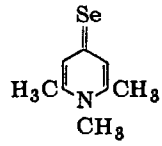
In spite of the considerable effort devoted to the synthesis and biological evaluation of pyridinesulfonic acids and pyridinesulfonamides, none of these compounds has been found to possess clinical utility.

O. SELENIUM COMPOUNDS OF PYRIDINE

Selenium compounds have been prepared by means of reactions described in the previous sections on sulfur compounds. Michaelis and Holken (*114*) reacted 2-chloropyridine methiodide with potassium selenide and obtained 1-methyl-2(1*H*)-pyridineselenone (XV-71); its reactions are shown. Similar reactions were carried out with

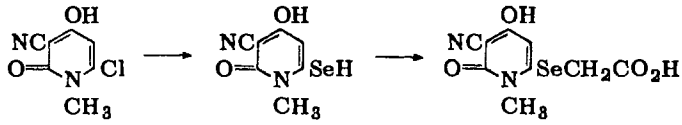


1,2,6-trimethyl-4(1*H*)-pyridineselenone (XV-72). Schroeter *et al.*



(XV-72)

(*155*) reacted chlororicinic acid with sodium selenide and obtained XV-73, which reacted with chloroacetic acid as shown.



(XV-73)

Keimatsu *et al.* (*76*) reacted 3-pyridinediazonium chloride with sodium benzeneselenide and obtained 3-(phenylseleno)pyridine.

Chierici and Passerini (*272*) reacted 2-chloro-5-nitropyridine with selenophenol as well as substituted selenophenols and obtained a series of 5-nitro-2-(arylseleno)pyridines; these, with tin and hydrochloric acid gave the corresponding 5-amino-2-(arylseleno)pyridines. Picolinaldehyde and selenium dioxide form a molecular compound, 2-PyCHO · SeO_2 · 1.5 H_2O, m.p. 117–119° (*363*).

Table XV-36 (pp. 425 ff.) lists the known selenium compounds of pyridine.

P. TABLES

TABLE XV-1. *S*-Pyridylthiuronium Halides

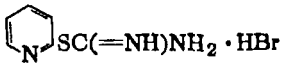
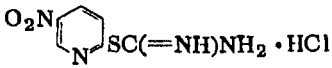
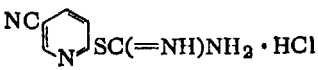
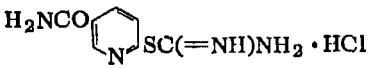
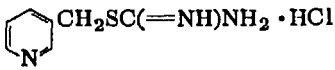
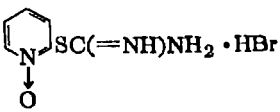
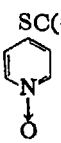
Compound	M.p., °C.	Ref.
	100	16,127,141
	191 (dec.)	21,127,171
	190–92	56
	195	56
	175–85	198
	160.0–60.5	156,211
	167	72

TABLE XV-2. 2-Pyridinethiols 

Substitutents	M.p., °C.	Ref.
None	125–28	16,108,127, 141,192
1-Oxide	65–67	156,306
5-Chloro	198	136
5-Bromo	203–4	136
5-Iodo	216	86,136
3-Nitro	174–75	150
5-Nitro	188–91	21,36,56,57, 98,127, 136,167, 175,365
5-Methyl-3-nitro	200 (dec.)	29
3,5-Dibromo	148	42
3,5-Diiodo	206.0–6.5	42,43,84,85
3-Chloro-5-nitro	193–94	136
3-Bromo-5-nitro	189 (dec.)	136
3-Iodo-5-nitro	195 (dec.)	136
3-Amino-6-methoxy	(picrate, m.p. 160, dec.)	283
3-Amino-6-ethoxy		261
5-Amino	245	86,127,136, 167
5-Acetamido	244–46	21
3-Amino-6-chloro	185–86	213
3-Acetamido-6-chloro	169 (*S*-acetate, m.p. 165–66)	215
5-Amino-3-nitro	192	188
5-Acetamido-3-nitro	184–85	188
3-Amino		213
3,4-Diamino	222	189
3-Carboxy	270	51,169
3-Carbomethoxy	204	51,245
3-($CONHNH_2$)	330	245
3-($2,4\text{-}Cl_2C_6H_3CH:NNHCO$)	265–67	245
5-Carboxy	272 (dec.)	86,136
5-Carbamyl	266–68	56
5-Thiocarbamyl	252 (dec.)	136
5-Cyano	255	56,86,137
5-Amidino	(hydrochloride, oil; benzoate, m.p. 248°; acetate, m.p. 224–26°)	56
3-Chloro-5-carboxy	235	136
3-Chloro-5-thiocarbamyl	193 (dec.)	136
3-Bromo-5-carboxy	230	136
3-Bromo-5-thiocarbamyl	195 (dec.)	136

(*continued*)

TABLE XV-2. (*continued*)

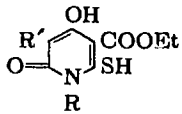
Substitutents	M.p., °C.	Ref.
3-Iodo-5-carboxy	232 (dec.)	136
3-Iodo-5-thiocarbamyl	194 (dec.)	136
6-Chloro-3-ureido	185–90 (dec.)	270
1-Oxide	68–70	156
4-Carbomethoxy 1-oxide	94–95	211
4-($CONHNH_2$) 1-oxide	(hydrazine salt, m.p. 184–85°)	211
2,4-Dimercaptonicotinic acid	235	148
2,6-Dimercaptoisonicotinic acid	230	15
Methyl 2,6-dimercaptoisonicotinate	156	15
2,4,6-Trimercaptonicotinic acid	>290	148
3-Cyano-4,6-dimethyl	264	307
3-Cyano-4-methyl-6-phenyl	223	307
3-Cyano-4-carboethoxy-3-cyano-6-methyl	200	307
3-Cyano-5-acetoxy-3-cyano-4,6-dimethyl	223–27 (dec.)	307
3-Cyano-5-acetamido-3-cyano-4,6-dimethyl	290	307
3-Cyano-6-hydroxy-4-methyl	251	307
3-Cyano-6-methyl	235	307
3-Carboxy-4,6-dimethyl	245 (dec.)	307
3-Cyano-4,6-dimethyl-5-benzodiazo	—	308
5-Amino-3-cyano-4,6-dimethyl	300	308
6-Chloro 1-oxide	—	354
4-Nitro 1-oxide	—	354

TABLE XV-3. 3-Pyridinethiols 

Substituents	M.p., °C.	Ref.
None		166,205
6-Hydroxy	(*S*-dimethyl carbamate, m.p. 78–80)	210
2,6-Diamino	63–82	86,187,270, 271
2-Carboxy	184	169
4-$CONHNH_2$	239–40	245
4-(2,4-$Cl_2C_6H_3CH$: NNHCO)	239–41	245
4-Ethyl	123–280	303

TABLE XV-4. 4-Pyridinethiols 

Substituents	M.p., °C.	Ref.
None	186 (dec.)	80,90,147
1-Oxide	200	72
3-Methyl	159–60°	279
2,6-Dimethyl	224	66,107, 267,353
2-(*o*,*p*-Dinitrophenyl)		200
3,5-Dichloro	188	43
3,5-Dibromo	222	43
3,5-Diiodo	206 (dec.)	5,43,84,85
3-Nitro	190 (dec.)	242
3-Carboxy	236–38	245
3-Carbomethoxy	170–71	245
3-$CONHNH_2$	304–5	245
3-(2,4-$Cl_2C_6H_3CH$: NNHCO)	254–55	245
2,6-Dimethyl-3-carboxy		89
2,6-Dicarboxy	243	90
2,6-Dicarbethoxy	176	90
2,6-Dimethyl-3,5-diiodo	247 (dec.)	267
3-Amino	213 (dec.)	262
3-Nitro-5-bromo	130–35	276
3-Amino-5-bromo	215 (*S*-*p*-nitro benzoate, m.p. 267, dec.)	276
1-Oxide	140°	306,311
3-Carboxy 1-oxide	201° (dec.)	318

TABLE XV-5. 1,5-Disubstituted 3-Carbethoxy-4-hydroxy-2-mercapto-6(1*H*)-pyridones 

R	R′	M.p., °C.	Ref.
Me	CN	280 (dec.)	155
Ph	*p*-MeC_6H_4NHCS	158–59 (dec.)	203
m-MeC_6H_4	*p*-MeC_6H_4NHCS	125–26	204
p-MeC_6H_4	H	174–75 (dec.)	203
p-MeC_6H_4	Br	238–39	203
p-BrC_6H_4	*p*-BrC_6H_4NHCS	179–81	204
p-$MeOC_6H_4$	*p*-$MeOC_6H_4NHCS$	162–63	204

TABLE XV-6. 1-Substituted Pyridinethiones

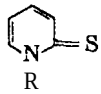
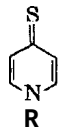
Substituents	R	M.p., °C.	B.p., °C.	Ref.
A. 1-Substituted 2(1*H*)-pyridinethiones 				
None	Me	89–90	188/21 mm.	114,141
	Et	46	189–90/21 mm.	60,141,142
	Pr		166.5/5 mm.	141,242
	Bu		173/5 mm.	141
	n-Decyl		198/1 mm.	252
	n-Dodecyl	31–33		252
	Myristyl	43–44		252
	Cetyl	43–45		252
	$PhCOCH_2$	180.5-81.5		251
	$PhCH_2$	183–85		319
3-CO_2Me	Me	59–60		245
3-$CONHNH_2$	hie	141–42		245
3-(2,4-$Cl_2C_6H_3$-CH :NNHCO.)	Me	204–5		245
3,5-Diethyl-6-propyl	Ph	127		38
B. I-Substituted 4(1*H*)-pyridinethiones 				
None	4-Py	200		7
2,6-Dimethyl	Me	267–68		114,305
2,6-Dimethyl	Et	248		114,305
2,6-Dicarbethoxy	Ph			8
2,6-Diphenyl	Me	248		305
2,6-Diphenyl	Et	210		305
2-Ph-6-(*p*-$MeOC_6H_4$)	Me	200		305
2-Ph-6-(*p*-$MeOC_6H_4$)	Et	162		305
2,6-(*p*-$MeOC_6H_4$)	Me	225		305
2,6-(*p*-$MeOC_6H_4$)	Et	220		305

TABLE XV-7. Pyridylalkylthiols and -thiolacetates

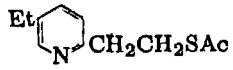
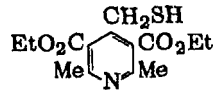
Compound	Physical properties, derivatives	Ref.
2-$PyCH_2CH_2SH$	b.p. 108–9°/20 mm., 94°/7 mm.	236,238
2-$PyCH_2CH_2SAc$	b.p. 95–97°/1 mm.	238
	b.p. 131–36°/9.5 mm.	238
2-P yCMePhSH	b.p. 118–24°/0.2 mm.; hydrochloride, m.p. 222–24°	233
2-PyCMePhSAc	m.p. 96–98°	233
3-$PyCH_2SH$	b.p. 118–25°/17–19 mm., 121°/13–15 mm.; picrate, m.p. 134°	238,256
	m.p. 86–87°	13

TABLE XV-8. Pyridine Thiolactones

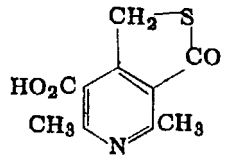
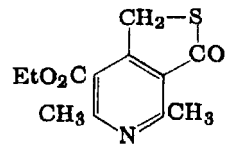
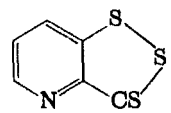
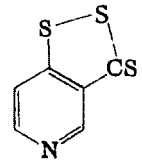
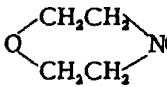
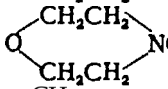
Compound	M.p., °C.	Ref.
	272 (dec.)	13
	115–16	13
	178	248
	206–8	245

TABLE XV-9. 2-Pyridyl Sulfides 

Substituents	R	Physical properties, derivatives	Ref.
None	Me	b.p. 98°/20 mm., 197°/760 mm.	37,114, 143,255
	Et	b.p. 108°/20 mm., 212°/760 mm.	37,60,255
	Pr	b.p. 53–55°/1 mm.	191
	Bu	b.p. 115°/13 mm., 235–38°/760 mm.	255
	$CH_2CH:CH_2$	b.p. 85–87°/3 mm.	191
	$MeCH:CH_2$	b.p. 88–93°/4 mm.	191
	CH_2CH_2OH	m.p. 113–14'	61
	CH_2COOH	m.p. 127°	107
	$PhCH_2$	b.p. 153–54°/4 mm.	255
	Ph	b.p. 154–58°/6 mm.	17,334
	2-MeC_6H_4	b.p. 165–75°/6	334
	3-MeC_6H_4	b.p. 174–80°/3	334
	4-MeC_6H_4	b.p. 175–80°/6	334
	4-ClC_6H_4	b.p. 185–90°/10, m.p. 36–8°; hydrochloride, m.p. 193–6 (dec.)	334,337
	2,4,5-$Cl_3C_6H_2$	m.p. 50.5–1.5; hydrochloride, m.p. 170–3° (dec.)	337
5-Cl	4-ClC_6H_4	m.p. 60–1°	337
	p-$NO_2C_6H_4$	m.p. 81.5–82.5°	10
	p-$NH_2C_6H_4$	m.p. 90–91°	10

	4-methyl-2-thiazolyl	b.p. 166–68°/0.05 mm.	123
	$Et_2NCH_2CH_2COCH_2$	dihydrobromide, m.p. 162.5–63.5°	251
	$Et_2NCH_2CH_2C(:NNHCONH_2)CH_2$	hydrobromide, m.p. 172.5–73.0°	251
	$Me_2NCH_2CH_2COCH_2$	dihydrobromide, m.p. 161.5–62.5°	251
	$Me_2NCH_2CH_2C(:NNHCONH_2)CH_2$	hydrobromide, m.p. 163.0–63.5°	251
		dihydrobromide, m.p. 205–207°	251
		hydrobromide, m.p. 183.5–84.0°	251
	$PhCOCH_2$	hydrobromide, m.p. 184.5–85.5°	251
	p-nitrobenzyl	m.p. 163.5–4.5°	285
3-Nitro	Ph	m.p. 103–4°	183
	p-chlorophenyl	m.p. 125–27°	183
	2,5-dichlorophenyl	m.p. 145–47°	183
	p-nitrophenyl	m.p. 158–59°	183
	o-aminophenyl	m.p. 124–26°	369
	o-acetamidophenyl	m.p. 141–42°	369
	2-amino-4-methylmercaptophenyl	m.p. 146–48°	357
	2-acetamido-4-methylmercaptophenyl	m.p. 132–34°	357
5-Nitro	Me	m.p. 115°	56,175, 188,365
	Et	m.p. 63'	56,175
	Pr	b.p. 116°/0.5 mm.	56
	i-Pr	b.p. 270–72°/760 mm.	175

(continued)

TABLE XV-9. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
	Bu	b.p. 140°/1 mm.	56,188, 216,265
	i-Bu		175
3-Cyano-6-hydroxy-4-methyl	*n*-hexyl	m.p. 84–85°	307
3-Cyano-6-methyl	Me	m.p. 100–101°	307
	CH_2COOH	m.p. 126°	35,171, 172
5-Amino-3-cyano-4,6-dimethyl	Me	m.p. 152°	308
	CH_2COOEt	m.p. 63°	172
3-Cyano-4,6-dimethyl-5-methoxy	Me	m.p. 73°	308
	C_6H_{13}	b.p. 133–34°/0.2 mm.	265
	$CH_2:CHCH_2$	m.p. 42–43°	265
	$PhCH_2$	m.p. 76–77°	265
	p-methoxybenzyl	m.p. 112–13°	265
	p-nitrobenzyl	m.p. 123–24°	265
	3-nitro-4-methoxybenzyl	m.p. 133–34°	265
	$Et_2NCH_2CH_2$	b.p. 146–47°/0.5 mm.	265
	HO_2CCH_2	m.p. 126–27°	265
	$HO_2CCH_2CH_2CH_2CH_2CH_2$	m.p. 102–3'	265
	$PhCOCH_2$	m.p. 101–2°	265
	$p\text{-}O_2NC_6H_4COCH_2$	m.p. 154–55°	265
	$p\text{-}MeOC_6H_4COCH_2$	m.p. 157–58°	265
	$3,4\text{-}(HO)_2C_6H_3COCH_2$	m.p. 183–84°	265
	2-furylmethyl	m.p. 114°	180
	5-nitro-2-furylmethyl	m.p. 145–46°	180
	Ph	m.p. 121°	133,177
	o-tolyl	m.p. 66°	126

	m-tolyl	m.p. 114–15°	126
	p-tolyl	m.p. 145–46°	126
	o-chlorophenyl	m.p. 77–78'	126
	m-chlorophenyl	m.p. 95–96°	126
	p-chlorophenyl	m.p. 136°	126,183
	2,5-dichlorophenyl	m.p. 123–25°	183
	m-bromophenyl	m.p. 98–99°	126
	p-bromophenyl	m.p. 123–25°	126
	m-iodophenyl	m.p. 121–22°	126
	p-iodophenyi	m.p. 123°	126
	p-nitrophenyl	m.p. 125–26°	11,44
	p-methoxyphenyl	m.p. 135–36°	126
	o-carboxyphenyl	m.p. 206–8°	36,137
	2-quinol yl	m.p. 127°	133
	6-nitro-2-benzothiazolyl	m.p. 208–10°	179
	Ph	m.p. 106–8°	183
	p-chlorophenyl	m.p. 140–41°	183
	2,5-dichlorophenyl	m.p. 142–44°	183
3-Amino-6-chloro	o-nitropheny1	m.p. 181°	284
3-(*o*-Nitrophenylamino)-6-chloro	Me	m.p. 182–83°	284
3-(*o*-Nitrophenylacetamido)-6-chloro	Me	m.p. 162–63°	284
3-[*N*-Methyl-*N*-(3-nitro-6-pyridyl)]-amino-6-chloro	Me	m.p. 119°	284
3-(3-Nitro-6-pyridyl)amino-6-chloro	Me	m.p. 184°	284
3-Amino-6-chloro	2,4-dichlorophenyl	m.p. 159°	284
3-Acetamido-6-chloro	2,4-dichlorophenyl	m.p. 147°	284
3-Amino-6-chloro	2,4-dinitrophenyl	m.p. 193–94°	284
3-Acetamidod-chloro	2,4-dinitropheny1	m.p. 204°	284
4-Et	Ph	b.p. 130° (0.01 mm.) hydrobromide, m.p. 127°	309
3,5-Dicyano-6-amino	Me	—	329

(*continued*)

TABLE XV-7. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
3-Cyano-5-carboxamido-6-amino	Me	m.p. 294–7.5°	327
3,5-Dicarboxy-6-amino	Me	m.p. 315–16°	329
1-Oxide	PhNHCO	m.p. 195–98°	356
	—CSNHCH$_2$CH$_2$NHCS—	m.p. 143.5–44.5°	356
	Et$_2$NCS—	dihydrochloride, m.p. 142–45°	356
	Et$_2$NCO—	dihydrochloride, 122–40°	356
	p-ClC$_6$H$_4$NHCO	m.p. 198–99.5°	356
3-Amino	Ph	m.p. 66–68°	183
	p-chlorophenyl	m.p. 149–51°	183
	2,5-dichlorophenyl	m.p. 110–12°	183
	p-aminophenyl	m.p. 131–32'	183
3-Amino-6-ethoxy	CH(COOEt)$_2$	m.p. 165°	261
3-Acetamido-6-chloro	Me	m.p. 54°	263
	Et	m.p. 134°	263
	Pr	m.p. 113°	263
	CH$_2$:CHCH$_2$	m.p. 104°	263
	CH$_2$COOH	m.p. 250–51°(dec.)	264
5-Amino	Me	m.p. 71–72°; b.p. 154–55°/5 mm.	56,151, 175,188
	Et	b.p. 126°/1 mm. dihydrochloride, m.p. 175–76°	56
	Pr	b.p. 142°/1 mm. hydrochloride, m.p. 154°	56

	Bu	b.p. 184°/10 mm.	265
		m.p. 127–28°	
		hydrochloride, m.p. 13P–41°	
		dihydrochloride, m.p. 128–29°	56,188, 265
	CH_2COOH		167
	C_6H_{13}	m.p. 125–27°	265
	$CH_2{:}CHCH_2$	m.p. **134–36°**	265
	$PhCH_2$	m.p. **201–2°**	265
	p-aminobenzyl	m.p. 165–70° (dec.)	265
	p-methoxybenzyl	m.p. 159–62° (dec.)	265
	3-amino-4-methoxybenzyl	m.p. 220–25° (dec.)	265
	Ph	m.p. 122–23°	133,177
	p-chlorophenyl	hydrochloride, m.p. 182–83° (dec.)	183
	2,5-dichlorophenyl	m.p. 106–7°	183
	p-aminophenyl		185
5-Acetamido	*p*-acetamidophenyl	m.p. 207–8°	185
5-Amino	o-carboxyphenyl	m.p. 204–6°	139
5-Acetamido	o-carboxyphenyl	m.p. 226–27° (dec.)	139
5-Amino	2-quinolyl	m.p. 144'	133
5-Sulfamyl	2-benzothiazolyl	m.p. 149'	179
5-Diethylsulfamyl	2-benzothiazolyl	m.p. **93–95°**	177
5-$Et_2NCH_2CH_2NH$	2-quinolyl	b.p. 275°/3 mm.	133
	Ph	b.p. 203°/1 mm.	133
5-$(Et_2NCH_2CH_2)_2N$	Ph	b.p. 224°/1 mm.	133
5-(5-Nitro-2-furfuralimino)	Et	m.p. 145.5–46.5°	182
5-(5-Nitro-2-furfuralethylideneimino)	Et	m.p. 118°	152
5-Acetylsulfanilamide	**Me**	m.p. 214'	185
5-(2-Carboxy-5-chloroanilino)	Me		173
3-Amino-6-chloro	**Me**		186

(continued)

TABLE XV-9. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
3-Acetarnido-6-chloro	Me	m.p. 166-67°	186,270
6-Chloro-3-ureido	Me	m.p. 286-95°	270
5-Amino-3-chloro	Ph	m.p. 78–79°	183
	p-chlorophenyl	m.p. 115-17°	183
	2,5-dichlorophenyl		183
5-Amino-3-nitro	Me	m.p. 94-95°	188
	Et	m.p. 141-42°	188
	Bu	m.p. 120-21°	59
3-Amino-Gethoxy	Me	b.p. 129-32°/9 mm.	186
3-Acetamido-6-ethoxy	Me	m.p. 124°	186
3-Amino-6-ethoxy	Et	b.p. 125-28°/4 mm.	186
3-Acetamido-6-ethoxy	Et	m.p. 83-85°	186
3-Carboxy	Ph	m.p. 171°	101
	o-carboxyphenyl	m.p. 192-93°	101
	o-carbomethoxyphenyl	m.p. 167-68°	101
3-Carbomethoxy	o-carbomethoxyphenyl	m.p. 77–78'	101
5-Carboxy	C_6H_{11}	m.p. 94-95°	140
6-Ethoxy-3-ureido	Me	m.p. 200-36°	270
	Et	m.p. 160-61°	270
5-Carboxy	p-nitrophenyl	m.p. 210°	140
	p-aminophenyl	m.p. 196-98°	140
5-Carbamyl	Me	m.p. 166–67'	56
5-Cyano	Me	m.p. 78°	56
	p-nitrophenyl	m.p. 133-35°	140
5-(*p*-Hydroxyphenylazo)	Et	m.p. 167–68'	151
5-(2,4-Dihydroxyphenylazo)	Et	m.p. 184-86°	151
5-(3-carboxy-4-hydroxyphenylazo)	Et	m.p. 249'	151

5-(2,4-Diaminophenylazo)	Et	m.p. 178°	151
5-(4-Sulfo-2-naphthylazo)	Et		151
5-(4-Amino-1-naphthylazo)	Et	m.p. 215–16°	151
5-(1-Amino-3-sulfo-2-naphthylazo)	Et		151
5-(1-Hydroxy-4-sulfo-2-naphthylazo)	Et		151
5-(2-Hydroxy-4,6-disulfo-1-naphthylazo)	Et		151
6-Chloro-3-(2-hydroxy-1-naphthylazo)	Me	189° (dec.)	263
5-(2,6-Diamino-3-pyridylazo)	Me	m.p. 130°	165
	Et	m.p. 143–44°	176
	i-Pr	m.p. 145°	176
	i-Bu	m.p. 146–47°	176
	Ph	m.p. 158–59°	177
5-(2-Acetamido-6-amino-3-pyridylazo)[a]	Et	m.p. 105–6°	174
5-(6-Acetamido-2-amino-3-pyridylazo)	Et	m.p. 115°	174
5-(2-Amino-6-hydroxy-3-pyridylhydrazino)	Et	m.p. 184°	174
5-(2-Amino-6-hydroxy-3-pyridylazo)	Et	m.p. 223–24°	174
1-Methiodide	Me	m.p. 156°	60
1-Ethiodide	Me	m.p. 161°	60
1-Ethiodide	Et	m.p. 110°	60
1-Oxide	$PhCH_2$	m.p. 167–69°	156
	$HOCH_2$	hydrochloride, m.p. 108–9°	342
	$MeOCH_2$	hydrochloride, m.p. 129.5–135°	336,342
	$EtOCH_2$	m.p. 69.5–72°	336,342
	EtOCHMe	oil	342
	n-$PrOCH_2$	m.p. 80.5–83.5°	336,342

(continued)

TABLE XV-9. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
	$Me(CH_2)_{11}OCH_2$	m.p. 78–79.5°	336,342
	$Me(CH_2)_{17}OCH_2$	m.p. 90–93°	336,342
	$MeSCH_2$	m.p. 105–107°	336
	n-$PrSCH_2$	hydrochloride, m.p. 98.5–100.5°	336
1-Oxide	2,4,5-$Cl_3C_6H_2$	m.p. 148.5–50.0	337
	PhP(S)OMe	oil	339
	PhP(S)OEt	oil	339
	2,4-$Cl_2C_6H_3OCH_2CO$	m.p. 90–91°	340
	p-$ClC_6H_4OCH_2CO$	m.p. 124–25°	340
	1-$C_{10}H_7CO$	oil	340
	2,4,5-$Cl_3C_6H_2OCH_2CO$	m.p. 121–26°	340
	$CH_2:CHCH_2$	m.p. 73–74°	341
	$CH_2:C(Me)CH_2$	oil	341
	$CH_2:CClCH_2$	oil	341

[a]Structure not certain

TABLE XV-10. 3-Pyridyl Sulfides 

Substitueats	R	MP., °C.	Ref.
None	CH_2COOH		166
	p-$NO_2C_6H_4$	115	253, 332
	$Me_2CHCH_2CH_2$	b.p. 138–40/12 mm.	286
	n-C_6H_{13}	b.p. 160–63/13 mm.	286
	n-$C_{12}H_{25}$	b.p. 211–15/8 mm.	286
	n-$C_{16}H_{33}$	m.p. 36–37	286
	p-$NO_2C_6H_4$	m.p. 93–95	332
	o-$H_2NC_6H_4$	m.p. 58–59	332
	p-$H_2NC_6H_4$	m.p. 88–90	332
	2,4-$(O_2N)_2C_6H_3$	m.p. 129–31	332
	2,4-$(H_2N)_2C_6H_3$	m.p. 129.5–30.5	332
	4,2-$Cl(O_2N)C_6H_3$	m.p. 95–96	332
	4,2-$Cl(H_2N)C_6H_3$	m.p. 115–17	332
	2,4-$Cl(O_2N)C_6H_3$	m.p. 111.5–12.0	332
	2,4-$Cl(H_2N)C_6H_3$	m.p. 94–94.5	332
	4,2-$Me(O_2N)C_6H_3$	m.p. 83–84	332
	4,2-$Me(H_2N)C_6H_3$	m.p. 102.5–103.5	332
	2-(p-$MeC_6H_4SO_2NH)C_6H_4$	m.p. 127–29	332
	2-$(Et_2NCH_2CH_2NH)C_6H_4$ hydrochloride	b.p. 170/0.06 mm. m.p. 137.5–38.5	332
6-Nitro	p-ClC_6H_4		183
	p-$NO_2C_6H_4$	112–13	11
	2,5-dichlorophenyl	93–95	183
2-carboxy	CH_2COOH		131, 157
6-Amino	p-ClC_6H_4	99–101	183
	2,5-dichlorophenyl	91–92	183
2-6-Diamino	Me		186
2,6-Diacetamido	Me	173–76	186
2-Carboxy	Ph	318 (dec.)	253
	p-$HO_2CC_6H_4$	215 (dec.)	253
	p-$NO_2C_6H_4$	190 (dec.)	253
	p-$NH_2C_6H_4$	195 (dec.)	253
4-Carboxy	Ph	227 (dec.)	253
4,6-Dihydroxy-5-carbethoxy-2-methyl	p-$NO_2C_6H_4$	276 (dec.)	20
4,6-Dihydroxy-2-methyl	p-$NO_2C_6H_4$	303 (dec.)	20
4,6-Diacetoxy-5-carbethoxy-2-methyl	p-NO,C_6H_4	123	20
4(6?)-Acetoxy-5-carbethoxy-6(4?)-hydroxy-2-methyl	p-$NO_2C_6H_4$	176	20
2,6-Diacetamido	Me	180–81	271

TABLE XV–11. 4-Pyridyl Sulfides 

Subsrituents	R	Physical properties, derivatives	Ref.
None	Me	—	80,310 335
	Et	—	20
	$CH_2:CHCH_2$	b.p. 86–87°/3mm. hydrochloride, m.p., 199–200°	279
	$C_{12}H_{25}$	m.p. 30–31° hydrochloride, m.p., 151–52°	279
	$C_{16}H_{33}$	m.p. 52°	279
	CH_2CO_2Me	m.p. 26–34'	240
	CH_2CO_2Et	b.p. 128–29°/1mm.	279
	CH_2CO_2H	b.p. 268–69°	279
2-Methyl	CH_2CO_2H	b.p. 236–38°	321
	Et	b.p. 120°/15mm.	321
	Pr	b.p. 131°/15mm.	321
	$CH_2CONHNH_2$	m.p. 105–7'	240,279
	$CH_2CONHN:CMe_2$	m.p. 140°	240
	$Me_2NCH_2CH_2$	m.p. 148–49°/13 mm.	266
	$Et_2NCH_2CH_2$	m.p. 141–42°/10 mm.	266
	CH_2CONEt_2	m.p. 47–51'	266
	CH_2COOH	m.p. 265°	266
	CH_2CONH_2	m.p. 181–83°	266
	Ph	b.p. 128–29°/2 mm.	162,279
	p-$NO_2C_6H_4$	m.p. 75–77'	240
	p-$NH_2C_6H_4$	m.p. 169–71°	240
1-Methiodide	Me	m.p. 183°	20,80, 117
1-Oxide	p-$NO_2C_6H_4$	m.p. 154–55°	73
	4-methyl-2-thiazolyl	m.p. 161–20°	73
	4,6-dimethyl-2-pyrimidyl	picrate, m.p. 191°	73
	4,5-dimethyl-2-imidazolyl	m.p. 190°	73
	Pr	m.p. 45°	321
1-Oxide-2-CO_2H	p-$NO_2C_6H_4$	m.p. 174–175°	327
	p-$NO_2C_6H_4CH_2$	m.p. 167'	327
	$PhCH_2$	m.p. 157°	327
3-Methyl	$C_{16}H_{33}$	m.p. 40–41° hydrochloride, m.p. 175°	279

TABLE XV-11. (continued)

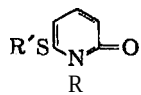
Substituents	R	Physical properties, derivatives	Ref.
2,6-Dimethyl	Me	m.p. 51°; b.p. 233°/76 mm.	107,114
	CH_2COMe	m.p. 83–84'	107
	CH_2COOH	m.p. 230'	267
3,5-Diiodo	Me	m.p. 120–21°	59
	CH_2CO_2H	m.p. 180–81'	59
	$CH_2CH_2CO_2H$	m.p. 212–13°	59
	$CHPrCO_2H$	m.p. 153°	5
	$CHBuCO_2H$	m.p. 153–56'	5
	$CH(i\text{-}C_5H_{11})CO_2H$	m.p. 134–36'	5
2-Nitro	$2,4\text{-}Br(Cl)C_6H_3$	m.p. 122.5–23.5'	366
2-Amino	$2,4\text{-}Br(Cl)C_6H_3$	m.p. 90–91.5°	366
2-Nitro	$o\text{-}BrC_6H_4$	m.p. 101.5–02.5'	336
2-Amino	$o\text{-}BrC_6H_4$	m.p. 96–97'	336
2-Nitro	$o\text{-}H_2NC_6H_4$	m.p. 146–47'	336
2-Nitro	$o\text{-}OCHNHC_6H_4$	m.p. 146–47.5°	336
3,6-Diiodo-2,6-dimethyl	CH_2COOH	m.p. 252–54° (dec.)	267
3-Carboxy	Ph	m.p. 236'	254
3-Cyano	Ph	m.p. 63.0–63.5°	254
3,5-Diiodo	o-carboxyphenyl	piperidine salt, m.p. 229–31°	5
3-Iodo	Ph	b.p. 149°/0.03 mm.	254
3-Nitro	Me	m.p. 133–34°	243
	Pr	m.p. 75°	243
	i-Pr	m.p. 64–65'	243
	$i\text{-}C_5H_{11}$	m.p. 57–58'	243
	$CH_2:CHCH_2$	m.p. 63°	243
	$ClCH_2CH_2$	hydrochloride, m.p. 198° (dec.)	262
	$MeCOCH_2$	m.p. 103–4'	264
	Ph	m.p. 86'	243
	$PhCOCH_2$	m.p. 184°	264
3-Amino	Me	hydrochloride, m.p. 165–66°	243
	Et	hydrochloride, m.p. 213° (dec.)	243
	$ClCH_2CH_2$	hydrochloride, m.p. 172° (dec.)	262
	Pr	m.p. 191° (dec.)	243
	i-Pr	hydrochloride, m.p. 182°	243
	$i\text{-}C_5H_{11}$	hydrochloride, m.p. 182–83°	243

(continued)

TABLE XV-11. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
	$CH_2:CHCH_2$	hydrochloride, m.p. 211' (dec.)	243
	Ph	m.p. 107.5–8.0 °	254
3-Acetamido	Me	m.p. 109 °	243
	Et	m.p. 101 °m	243
	Pr	m.p. 164 °	243
	i-Pr	m.p. 114 °	243
	i-C_5H_{11}	m.p. 128–30'	243
	$CH_2:CHCH_2$	m.p. 151–52 °	243
3-Carboxy-2,6-dimethyl	CH_2CO_2H		63
2,6-Dimethyl-3-(p-$NO_2C_6H_4SO_2NHCO$)	Me		64
2,6-Dimethyl-3-(p-$NH_2C_6H_4SO_2NHCO$)	Me		64
2-Methyl	$2,4$-$(O_2N)_2C_6H_3$	m.p. 163 °	321
1-Oxide	p-$Me_3SiC_6H_4$	picrate, m.p. 115–16'	352
	m-$Me_3SiC_6H_4$	m.p. 88–89' picrate, m.p. 107–8°	352

TABLE XV-12. 6-Alkylthio-2(1*H*)-pyridones



Substituents and positions			R	R'	M.p., °C.	Ref.
3	4	5				
CN	OH		Me	CH_2CO_2H	250 (dec.)	**155**
Ph	OH	CO_2Et	Ph	Me	148–49	204
m-MeC_6H_4NHCS	OH	CO_2Et	m-MeC_6H_4	Me	137–38	204
p-MeC_6H_4NHCS	MeO		p-MeC_6H_4	Me	153	203
	OH	CO_2Et	p-MeC_6H_4	Me	250 (dec.)	203
Br	OH	CO_2Et	p-MeC_6H_4	Me	166	203
CO_2H	OH	CO_2H	p-MeC_6H_4	Me	232–33 (dec.)	203
CO_2H	MeO	CO_2H	p-MeC_6H_4	Me	177–78	203
p-MeC_6H_4NHCS	OH	CO_2Et	p-MeC_6H_4	Me	151–52	203
p-BrC_6H_4NHCS	OH	CO_2Et	p-BrC_6H_4	Me	152	204
p-$MeOC_6H_4NHCS$	OH	CO_2Et	p-$MeOC_6H_4$	Me	152–53	204
p-$EtOC_6H_4NHCS$	OH	CO_2Et	p-$EtOC_6H_4$	Me	114–15	204

TABLE XV-13. Dipyridyl Sulfides PySPy′

Py	Py′	M.p., °C.	Ref.
2-Py	2-Py	b.p. 190°/6 mm.; hydrobromide, m.p. 274°	37,40,91, 255
4-Py	4-Py	69°	279
1-Oxido-4-pyridyl	1-oxido-4-pyridyl	228–30	72
2,6-Dimethyl-4-pyridyl	2,6-dimethyl-4-pyridyl	82–83	107
3-Nitro-2-pyridyl	3-amino-6-chloro-2-pyridyl	205 (dec.)	263
3-Nitro-5-bromo-2-pyridyl	3-amino-6-chloro-2-pyridyl	187–88 (dec.)	263
3-Nitro-5-bromo-4-pyridyl	3-nitro-5-bromo-4-pyridyl	185	276
3-Nitro-2-pyr idyl	4-Py	153–54	240
3-Nitro-4-pyridyl	4-Py	114.5–16.0	240
5-Nitro-2-pyridyl	2-Py	103	190
	4-Py	90–92	240
3-Nitro-4-pyridyl	3-nitro-4-pyridyl	133–34	242
5-Nitro-2-pyridyl	5-nitro-2-pyridyl	137	11,21,25, 35,170, 175
	3-amino-6-chloro-2-pyridyl	195	263
3,5-Dinitro-2-pyridyl	5-nitro-2-pyridyl	281	188
5-(2,6-Diamino-3-pyridylazo)-2-pyridyl	5-(2,6-diamino-3-pyridylazo)-2-pyridyl	145–47	177
3-Amino-2-pyridyl	4-Py	83–72	240
5-Amino-2-pyridyl	2-Py	165	170
	4-Py	153–55	240
3-Amino-4-pyridyl	4-Py	(hydrochloride, m.p. > 300")	240
5-Amino-2-pyridyl	5-amino-2-pyridy l	130.0–31.5[a]	25,170, 358
5-Acetamido-2-pyridy l	5-acetamido-2-pyridy l	265.0–66.5	170
2,6-di-*tert*-Butylpyridyl	2,6-di-*tert*-butyl	125–26	310
3-Methylamino-6-chloro-2-pyridyl	3-nitro-6-pyridyl	—	284
3Acetamido-6-chloro-2-pyridyl	3-nitro-6-pyridyl	170–71	284
6-Benzamido-6-chloro-2-pyridyl	3-nitro-6-pyridy l	147–48	284
3-p-Nitro benzamido-6-chloro-2-pyridy l	3-nitro-6-pyridyl	186–87	284
3-Amino-6-chloro-2-pyridyl	3-nitro-2-pyridyl	183	284
3-Amino-6-chloro-2-pyridyl	3-nitro-ri-pyridy l	219 (dec.)	284
3-Acetamido-6-chloro-2-pyridy l	3-nitro-4-pyridyl	230–31 (dec.)	284

[a] Unstable form m.p. 80–81°

TABLE XV-14. Pyridylalkyl Sulfides

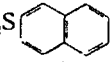
Compound	B.p., °C.	Ref.
3-$PyCH_2SCH_3$	118/15 mm.	256
3-$PyCH_2SC_2H_5$	128/15 mm.	256
3-$PyCH_2SC_3H_7$	128/15 mm.	256
3-$PyCH_2SCH(CH_3)_2$	127/15 mm.	256
3-$PyCH_2SC_4H_9$	142/15 mm.	256
3-$PyCH_2SCH_2CH(CH_3)_2$	138/15 mm.	256
3-$PyCH_2SC_6H_{13}$	148/15 mm.	256
3-$PyCH_2SC_6H_{11}$	145/15 mm.	256
3-$PyCH_2SCH_2C_6H_5$	175/15 mm.	256
3-$PyCH_2S(CH_2)_2N(CH_3)_2$	142/15 mm.	256
3-$PyCH_2S(CH_2)_2N(C_2H_5)_2$	153/15 mm.	256
3-$PyCH_2SCH_2CH(CH_3)N(CH_3)_2$	155/15 mm.	256
3-$PyCH_2SCH_2CH(CH_3)N(C_2H_5)_2$	168/15 mm.	256
2-$Py(CH_2)_2S(CH_2)_3CH_3$	110–12/2 mm.	132
p-$CH_3C_6H_4S(CH_2)_2$Py-2		132,237
2-$Py(CH_2)_2SPh$	178–80/12 mm.	280
2-$Py(CH_2)_2SC_6H_4$Me-*o*	193/16 mm.	280
2-$Py(CH_2)_2SC_6H_4$Me-*p*	193–95/12 mm.	280
2-$Py(CH_2)_2SCH_2Ph$	146/1 mm.	132,237
2-$Py(CH_2)_2S(CH_2)_7CH_3$	155–57/1 mm.	132
2-$Py(CH_2)_2SCH_3$	85/1.5 mm.	237
2-$Py(CH_2)_2SC(CH_3)_3$	108–22/3 mm.	237
2-$Py(CH_2)_2SC_{12}H_{25}$	182/0.13 mm.	237
2-$Py(CH_2)_2SC_2H_5$	129–30/20 mm.	236
2-$PyCCH_3C_6H_5SCH_2CH_2N(CH_3)_2$	162–66/0.1 mm. (hydrochloride, m.p. 123–25 °)	233
$(2\text{-}PyCH_2CH_2)_2S$	185–90/3 mm.	236
2-$Py(CH_2)_2S$ 	168–70/0.05 mm.	237
2-$Py(CH_2)_2S$ 	186–87/11 mm.	314
4-$Py(CH_2)_2S$ 	168-70/12 mm.	314
Me  $(CH_2)_2S$ 	177–80/16 mm.	314
Me  $(CH_2)_2S$  4-PyCHMeSPh	172/12 mm.	314

TABLE XV-15. Pyridyl Disulfides PySSR

Py	R	M.p., °C.	Ref.
2-Py	CH_3	—	81
2-Py	Ph	48–49, picrate m.p. 126	367
2-Py	*o*-MeC_6H_4	oil	367
2-Py	*p*-MeC_6H_4	40–41	367
2-Py	*p*-ClC_6H_4	oil	367
6-Methyl-2-pyridyl	*o*-MeC_6H_4	oil	367
6-Methyl-2-pyridyl	*p*-MeC_6H_4	38–39	367
6-Methyl-bpyridyl	*p*-ClC_6H_4	oil	367
4-Py	*o*-MeC_6H_4	oil	367
4-Py	*p*-MeC_6H_4	36	367
4-Py	*p*-ClC_6H_4	oil	367
4-Py	C_6H_{11}	—	81
4-Py	Ph	—	81
4-Py	2-Thenyl	—	81
2-Chloro-4-pyridyl	$CH_2{:}CHCH_2$	—	81
1-Oxido-2-pyridyl	CF_3CH_2	99, hydrochloride m.p. 85–119	343

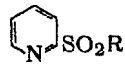
TABLE XV-16. Symmetrical[a] Dipyridyl Disulfides PySSPy

Py	M.p., °C	Ref.
2-Py	57–58	107,136
3-Py	hydrochloride, m.p. 183	65
4-Py	155	90,292
1-Oxido-4-pyridyl	136–37	72
3-Methyl-4-pyridyl	159–60	279
2-Methyl-4-pyridyl	47	321
2,6-Dimethyl-4-pyridyl	57	279
5-Chloro-2-pyridyl	80	321
5-Bromo-2-pyridyl	102	107
5-Iodo-2-pyridyl	155	136
3,5-Diido-4-pyridyl	23–31	136
3-Nitro-2-pyridyl	249–50 (dec.)	136
5-Nitro-2-pyridyl	156	83
3-Nitro-4-pyridyl	233 (dec.)	150,269
5-Methyl-3-nitro-2-pyridyl	246 (dec.)	56,86,136
3-Chloro-5-nitro-2-pyridyl	203–4	241,242
6-Amino-3-pyridyl	174–75	29
5-Acetamido-2-pyridyl	240–41	136
3-Amino-6-chloro-2-pyridyl	229–30	187
3-Acetamido-6-chloro-2-pyridyl	232	21
5-Amino-3-nitro-2-pyridyl		213,264
2-Carboxy-3-pyridyl	206	215
2-Carbomethoxy-3-pytidyl	210–12	188
2-$CONHNH_2$-3-pyridyl	hydrochloride, m.p. 310	169,245
4-Carboxy-3-pyridyl	307–8	245
4-Carbomethoxy-3-pyridyl	166–67 (dec.) (dihydrochloride)	245
3-Cyano-4,6-dimethyl-2-pyridyl	173	308,318

[a] All known dipyridyl disulfides are symmetrical except for 4-pyridyl 2-chloro-4-pyridyl disulfide (*82*), and 6-methyl-2-pyridyl pyridyl disulfide (367).

TABLE XV-17. Pyridyl Sulfoxides PySOR

Py	R	Physical properties	Ref.
2-Py	Me	b.p. 122°/5 mm.	37
2-Py	Et	b.p. 123°/4 mm.	37
2-Py	$PhCH_2$	m.p. 87–88'	156
2-Py	2-Py	b.p. 178°/6 mm.	37
3-Carbamyl-6-pyridyl	Me	m.P. 224–26°	56

TABLE XV-18. 2-Pyridyl Sulfones 

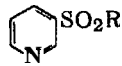
Substituents	R	Physical properties, derivatives	Ref.
None	Me	b.p. 157°/5 mm., 325°/760 mm.	37,107
	Et	b.p. 159°/4 mm.	37
	p-nitrophenyl	m.p. 170–71'	10
	p-aminophenyl	m.p. 160-61°	10,146
	4-amino-3-sulfamyl-phenyl	m.p. 261°	32,33
	4-acetamido-3-sulfamylphenyl	m.p. 208-10°	32
	4-methyl-2-thiazolyl	m.p. 121°	123
4-Chloro-6-methyl[a]	*p*-aminophenyl	m.p. 172'	20
	p-acetamidophenyl	m.p. 250-52°	20
5-Nitro	Me	m.p. 115'	56
	Et	m.p. 91°	178
	Bu	m.p. 58°; b.p. 182°/0.5 mm.	56,216, 265
	C_6H_{13}	m.p. 78-79°	265
	$PhCH_2$	m.p. 138-39°	265
	$p\text{-}NO_2C_6H_4CH_2$	m.p. 198-200°	265
	$PhCOCH_2$	m.p. 133–34'	265
	$p\text{-}NO_2C_6H_4COCH_2$	m.p. 208–10'	265
	Ph	m.p. 112–15'	178
	p-nitrophenyl	m.p. 253-54°	11,44, 178
	$p\text{-}MeC_6H_4$	m.p. 158-60°	333
	p-acetamidophenyl	m.p. 225-26°	44
	o-carboxyphenyl	m.p. 177–78'	36,139
5-Phenylazo	Et	m.p. 250-54°	151
5-Nitro	4-Py	m.p. 167-69°	240
5-Amino	Me	m.p. 171-73°	56
	Et	m.p. 104-5°	151,178
	Bu	m.p. 97°	56,216
	Ph	m.p. 222–23'	178
	p-aminophenyl	m.p. 178–200°	44,178
	p-acetamidophenyl	m.p. 271–72'	44
	o-carboxyphenyl	m.p. 237-39° (dec.)	139
5-Acetamido	o-carboxyphenyl	m.p. 226–27' (dec.)	137
5-Amino	4-Py	m.p. 196-98°	240
3-Amino-6-chloro	Me	m.p. 136-37°	187
3-Acetamido-6-chloro	Me	m.p. 148°	187

(continued)

TABLE XV-18. *(continued)*

Substituents	R	Physical properties, derivatives	Ref.
3-Acetamido-6-chloro	3-nitro-6-pyridyl	—	284
3-(3-Nitro-6-pyridylamino)-6-chloro	Me	212°	284
4-Et	Ph	89–90° picrate, m.p. 65–75°; perchlorate, m.p. 153–63; hydrobromide, m.p. 169–70°; no deriv. with $HgCl_2$	309
3-Amino-6-ethoxy	Me	m.p. 115°	187
3-Acetamido-6-ethoxy	Me	m.p. 129–31°	187
5-Carboxy	p-nitrophenyl	m.p. 226–28' (dec.)	140
	p-aminophenyl	m.p. 232–33° (dec.)	140
5-Carbamyl	Me	m.p. 210°	56
5-Amidino	Me	hydrochloride, m.p. 238°; benzoate, m.p. 210°; acetate, m.p. 196–98°	56
5-Cyano	Me	m.p. 133°	56

[a] May be the 6-chloro-2-methyl-4-pyridyl sulfone.

TABLE XV-19. 3-Pyridyl Sulfones 

Substituents	R	M.p., °C.	Ref.
None	p-nitrophenyl	172–74	273
	p-nitrobenzyl	204–5	273
	m-nitrobenzyl	158–60	273
	p-aminobenzyl	166–68	273
	p-acetamidobenzyl	181–83	273
	p-chlorobenzyl	163–64	273
6-Nitro	p-nitrophenyl	202–3	11
2,6-Diamino	Me	183	187
2,6-Diacetamido	Me	247–48	187,270
4,6-Dihydroxy	*p*-nitrophenyl	303	20
5-Carbethoxy-4,6-dihydroxy	*p*-nitrophenyl	276	20

TABLE XV-20. 4-Pyridyl Sulfones 

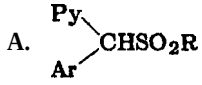
Substituents	R	M.p., °C.	Ref.
None	Me	165–66	80, 83
	Et	29	20
	CH_2COOH		80
	Ph	125	270
2-Methyl-1-oxide	Pr	87	321
2-Methyl	Pr	31	321
	ptolyl	137–38	20
	mnitrophenyl	169–71	146
	p-nitrophenyl	148–50	240
	m-aminophenyl	186–87	146
	paminophenyl	259(dec.); 269–71	240, 146, 290
	pacetamidophenyl	170–71	20
	p-cyanophenyl	182	20
1-Oxide	*p*-nitrophenyl	186–87	73
	p-aminophenyl	324–26	73
	4-methyl-2-thiazolyl	169–70	73
	4,5-dimethyl-2-thiazolyl	239	73
2,6-Dimethyl	Me	221 (picrate)	107
6-Chloro-2-methyl[a]	*p*-aminophenyl	172	20
	p-acetamidophenyl	250–52	20
3-Nitro	Me	123	243
	Et	91	243
	Pr	102	243
3-Amino	Me	109–10	243
	Et	206 (dec.)	243
	Pr	180(dec.)	243
3-Acetamido	Me	159–60	243
	Et	94–95	243
	Pr	101–3	243

[a] May be the 4-chloro-6-methyl-2-pyridyl sulfone.

TABLE XV-21. Dipyridyl Sulfones $PySO_2Py'$

Py	Py′	M.p., °C.	Ref.
2-Py	2-Py	216	37, 40
3-Py	4-Py	124–25	273
2,6-Dimethyl-4-pyridyl	2,6-dimethyl-4-pyridyl	114	107
5-Nitro-2-pyridyl	2-Py	188	190
	5-nitro-2-pyridyl	227–29	11, 25, 35, 52, 170, 171
	3-acetamido-6-chloro-2-pyridyl	178	263
5-Acetamido-2-pyridyl	2-Py	224	190
5-Amino-2-pyridyl	5-amino-2-pyridyl	238–39	170
5-Acetamido-2-pyridyl	5-acetamido-2-pyridyl	276–78	25, 170
2,6-di-*tert*-butylpyridyl	2,6-di-*tert*-butylpyridyl	250–51	310

TABLE XV-22. Pyridylalkyl Sulfones

A. 

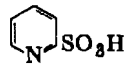
Py	Ar	R	M.p., °C.	Ref.
2-Py	Ph	Me	122.5–24.5	95
	Ph	Et	151.0–51.6	95
	Ph	Pr	121.6–22.8	95
	Ph	Bu	101.4–102.6	95
	p-tolyl	Et	195.6–98.0	95
	o-chlorophenyl	Et	196.5–98.5	95
	m-chlorophenyl	Me	116.2–17.0	95
	p-chlorophenyl	Et	121.6–22.9	95
	3,4-dichlorophenyl	Et	121.0–22.4	95
	p-methoxyphenyl	Et	138.8–40.8	95
4-Methyl-2-pyridyl	*p*-chlorophenyl	Me	209–10	95
	p-chlorophenyl	Et	208–10	95
	3,4-dichlorophenyl	Et	201–5	95
6-Methyl-2-pyridyl	*p*-chlorophenyl	Me	98.4–99.6	95

B. $Py(CH_2)_nSO_2C_6H_4R$

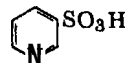
Py	n	R	M.p., °C.	Ref.
4-Py	1	Me	185–86 (dec.)	274
	2	H	178–80 (dec.)	274
	2	Me	95–96	274
	2	CH_3CONH	103–5	274
2-Py	2	Me	59–61	274
	2	CH_3CONH	169–71	274

C. 4-$PyCHRSO_2C_6H_4R'$

R	R′	m.p., °C.	Ref.
H	H	hydrochloride, m.p. 201.5°	309
Me	H	106–07 hydrochloride, m.p. 224–25°	309
Me	Me	143-43.5	309

TABLE XV-23. 2-Pyridinesulfonic Acids 

Substituents	M.p., °C.	Ref.
None	247–48	63,107,287, 300
3-Methyl		199
3,5-Dibromo	300	42
3,5-Diiodo	300	42
5-Nitro		98
3-Amino		128,129,130
3-Carboxy	282	169,199
3-Hydroxy		128,129
3-Amino-4-hydroxy	253	371
3-(3-Nitro-6-pyridylamino)-6-chloro	—	284

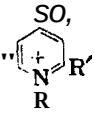
TABLE XV-24. 3-Pyridinesulfonic Acids 

Substituents	M.p., °C.	Ref.
None	352–56	46,63,71,79,97,102, 158,194,195,201, 205,287
1-Methyl (sulfobetaine)	130	68,111,112
2-Methyl[a]		79,113,197,206
4-Methyl	353–55	46,79,102,201,206, 208
5-Methyl	312–14	46,102,134
6-Methyl	338–41	46,102,108,125
2,6-Dimethyl	> 350	370
2,6-Dimethyl-4-hydroxy	290–95 (dec.)	370
5-Ethyl-2-methyl		206,208
2,6-Di-*tert*-butyl	310	18,277,297,310
2,6-Di-*tert*-butyl, Me ester	77–8	310
6-Chloro	265	136
5-Bromo-6-chloro	280	136
4-Amino	336	88
6-Amino	326–27 (dec.)	26,27,119,226
6-Acetamido	302–3 (dec.)	21,119
6-*p*-Aminoanilino	305	160
6-Sulfanilamido	326–28	121
2-Carboxy	206	169
4-Carboxy	318	46,169
5-Carboxy	335 (dec.)	46
6-Carboxy	287 (dec.)	46
4-Hydroxy	265	88
6-Hydroxy		26,27,119
6-Methoxy		1
6-Amino-5-bromo	300	136
6-Amino-5-nitro	265 (dec.)	136,226
1-Methyl-6(1*H*)-oxo	290–92	67,153
1-Carboxymethyl-6(1*H*)-oxo	80	153
5-Chloro-1-methyl-2(1*H*)-oxo[a]	325–27	67
5-Chloro-1-ethyl-2(1*H*)-oxo[a]	266–70	67
5-Bromo-1-methyl-2(1*H*)-oxo[a]	240–50	67
5-Iodo-1-methyl-2(1*H*)-oxo[a]		67
5-Nitro-1-methyl-2(1*H*)-oxo		153

[a] Structure not certain.

TABLE XV-25. 4-Pytidinesulfonic Acids 

Substituents	M.p., °C.	Ref.
None	134–35	80,90,194,244, 287,288, 292,298, 300
2-Methyl		244,288
2,6-Dimethyl	300,>350	107,244,288, 370
3,5-Dichloro	300	42,43
3,5-Dibromo	300(dec.)	42,43
3,5-Diiodo	300(dec.)	42,43
2,6-Di-*tert*-butyl	344–46(dec.)	294,297,310

TABLE XV-25a. 4-Pyridinesulfobetaines 

Substituents				
R	R'	R''	m.p., °C.	Ref.
Me	Me	Me	270	305
Et	Me	Me	248	305
Me	Ph	Ph	>360	305
Et	Ph	Ph	310	305

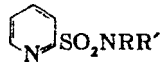
TABLE XV–26. Pyridinedisulfonic Acids

Compound	Ref.
3,5-Pyridinedisulfonic acid	97
2,6-Disulfoisonicotinic acid	15
1-Methyl-2(1*H*)-pyridone-3,5-disulfonic acid	153
3,5-Disulfoisonicotinic acid	330

TABLE XV-27. Pyridinesulfonyl Chlorides

Compound	Physical properties, derivatives	Ref.
2-Pytidinesulfonyl chloride		92,289
3-Pyridinesulfonyl chloride	hydrochloride, m.p. 141–44°	96,138,145
4-Pyridinesulfonyl chloride	unstable above 0°	289,293
6-Chloro-3-pyridinesulfonyl chloride	m.p. 51°, b.p. 132°/8 mm.	1,136,154
5-Bromo-6-chloro-3-pyridinesulfonyl chloride	m.p. 72°	136
5-Nitro-2-pyridinesulfonyl chloride	m.p. 212–13° (dec.)	22
6-Amino-3-pyridinesulfonyl chloride		50
6-Acetamido-3-pyridinesulfonyl chloride	m.p. 165–66° (dec.)	21
3,5-Pyridinedisulfonyl chlo	m.p. 129°	97

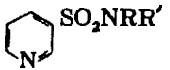
TABLE XV-28. 2-Pyridinesulfonamides and 2-Pyridinesulfohydrazides



Substituents	R	R'	M.p., °C.	Ref.
5-Nitro	3-carbamyl-2-pyridyl	H	253	22
	5-cyano-2-pyridyl	H	251	22
	5-carbamyl-2-pyridyl	H	260	22
5-Amino	H	H	184–85	21,50,57
	$NH_2C(:NH)$	H	220–21	21
	Ph	H	164–65	138
	2-Py		205–6	21
	5-chloro-2-pyridyl	H	221	22
	3,5-dichloro-2-pyridyl	H	201	22
	5-bromo-2-pyridyl	H	234	22
	3,5-dibromo-2-pyridyl	H	212	22
	5-iodo-2-pyridyl	H	219–20 (dec.)	21
	6-iodo-3-pyridyl	H	217	22
	3,5-diiodo-2-pyridyl	H	229	22
	3-carbamyl-2-pyridyl	H	239	22
	5-carboxy-2-pyridyl	H	281	22
	5-cyano-2-pyridyl	H	249	22
	5-carbamyl-2-pyridyl	H	248	22
	2-thiazolyl	H	226–27	21
	2-pyrimidyl	H	283–85 (dec.)	21
5-Acetamido	H	H	232–33	21,364
	$NH_2C(:NH)$	H	228–29	21
	Ph	H	213–14	21
	2-Py	H	231–32	21
	5-chloro-2-pyridyl	H	237	22
	3,5-dichloro-2-pyridyl	H	215	22
	5-bromo-2-pyridyl	H	240	22
	3,5-dibromo-2-pyridyl	H	232	22
	6-iodo-3-pyridyl	H	221	22
	5-iodo-2-pyridyl	H	225–26	21

TABLE XV-28. *(continued)*

Substituents	R	R'	M.p., °C.	Ref.
	3,5-diiodo-2-pyridyl	H	247	22
	5-carboxy-2-pyridyl	H	287	22
	2-pyrimidyl	H	231–32 (dec.)	21
5-*p*-Acetamido benzenesulfonamido	H	H		12
None	H	NH,	86–87 (dec.)	282
	H	N=CMe$_2$	172–74	282

TABLE XV-29. 3-Pyridinesulfonamides and 3-Pyridinesulfohydrazides 

Substituents	R	R'	M.p., °C.	Ref.
None	H	H	110–11	75
	Et	Et	49–50	91
	$C_{12}H_{25}$	H		218,221
	$C_{14}H_{29}$	H		218,221
	$C_{16}H_{33}$		78–79	218–221
	$BuEtCHCH_2$	$BuEtCHCH_2$		218–221
	Ph	H	145	138
	$PhCH_2CHMe$	H	117.0–17.5	91
	2-Py	H	185–86	49,105,138
	2-thiazolyl	H		145
	1,3,4-thiadiazol-2-yl	H		117,119,136
6-Chloro	H	H	158–59	245
	Me	H	111–12	118,120
	Me	Me	115–17	118,120
	Et	Et	86–87	118,120
	Bu	H	90–92	118,120
	cyclohexyl	H	116–18	118,120
	$CH_2:CHCH_2$	H	78	118,120
	$PhCH_2$	H		27
	CH_2CO_2H	H	193 (dec.)	121
	$Et_2N(CH_2)_3CHMe$	H	88	181
	$-(CH_2)_5-$		131–32	118,120
	$-(CH_2)_2O(CH_2)_2-$		143–44	117,119
	Ph	H	149–51	117,119
	3,5-dibromophenyl	H	193–94	181
	p-aminophenyl	H	197	118,120
	p-$NH_2SO_2C_6H_4$	H	200–2	117,119

	p-$Me_2NSO_2C_6H_4NHSO_2C_6H_4$-*p*	H	147–49	121
	2-$PyNHSO_2C_6H_4$-*p*	H	266	118,120
	o-carboxyphenyl	H	193–95	121
	2-Py	H	237–39	1,27
	3,5-dibromo-2-pyridyl	H	175	181
	5-sulfamyl-2-pyridyl	H	253–55	117,119
	6-ethylthio-3-pyridyl	H	159–61	181
	2-thiazolyl	H	224.5–26.5	235
	4-methyl-2-thiazolyl	H	179.0–80.5	235
	4,5-dimethyl-2-thiazolyl	H	227–38	235
	4-phenyl-2-thiazolyl	H	203–6	235
	2-benzothiazolyl	H	251–54	235
5-Bromo-6-chloro	H	H	150	136
6-Arnino	H	H	175–76	27,117,119
	Me	H	142	50,121
	Me	Me	157–59	121
	Et	H	149	50
	Et	Et	148.0–59.5	121
	Bu	H	114–16	121
	cyclohexyl	H	129–31	121
	CH_2 :$CHCH_2$	H	136–37	121
	CH_2CO_2H	H	226–27 (dec.)	121
	$-(CH_2)_5-$		160–62	121
	$-(CH_2)_2O(CH_2)_2-$		178–80	121
	$PyCH_2$	H	143	27,50
	Ph	H	176–78	50,117,119
	o-carboxyphenyl	H	250–52 (dec.)	121
	p-sulfamylpheny1	H	200–2	50,117,119
	p-$Me_2NSO_2C_6H_4NHSO_2C_6H_4$-*p*	H	171–72	121
	3-Py	H	205	27,50
	5-sulfamyl-2-pyridyl	H	260	117,119

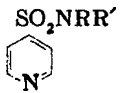
(continued)

TABLE XV-29. *(continued)*

Substituents	R	R′	M.p., °C.	Ref.
6-Acetamido	thiocarbamyl	H		78
6-Ethylamino	H	H	190–71	117,119
	Et	H	139–41	117,119
6-Diethylamino	H	H	116–17	117,117
6-Butylamino	H	H	121–22	117,119
6-Allylamino	H	H	195–201	117,119
6-Benzy lamino	H	H	199–201	117,119
6-Anilino	H	H	181–83	77,117,119
6-Sulfanilamido	H	H	227	106,121
	Me	Me	151–53	121
6-Acetylsulfanilamido	H	H	246–47	106
6-(6-Methoxy-8-quinolylamino)	$Et_2N(CH_2)_3CHMe$	H	223–25 (hydrochloride)	181
6-*p*-Aminobenzenesulfonyl	H	H	162	30
4-Carboxy	Ph	H	241	138
4-Carbethoxy	Ph	H	156	137
6-Hydroxy	H	H	269–71	118,120
	Me	H	188–90	118,120
	Me	Me	212–14	118,120
	Et	Et	163.5–65.8	118,120
	Bu	H	178–80	118,120
	cyclohexyl	H	169–72	118,120
	CH_2 :CHCH,	H	159–61	118,120
	$-(CH_2)_5-$		236–38	118,120
	$-(CH_2)_2O(CH_2)_2-$		262–64	118,120
	Ph	H	214–15	118,120
	3,5-dibromophenyl	H	> 240	181
	p-nitrophenyl	H	282	118,120
	p-aminopheny1	H	246	118,120

	o-carboxyphenyl	H	263 (dec.)	121
	p-sulfamylphenyl	H	250–52	118,120
	p-$Me_2NSO_2C_6H_4NHSO_2C_6H_4$-*p*	HO	188 (dec.)	121
	2-Py	H	268–69	121
	2-$PyNHSO_2C_6H_4$-*p*	H	301–2	118,120
	5-sulfamyl-2-pyridyl	H	295 (dec.)	118,120
	2-thiazolyl	H	292–95 (dec.)	235
	4-methyl-2-rhiazolyl	H	281.0–83.5	235
	4,5-dimethyl-2-thiazolyl	H	328–30	235
	4-phenyl-2-thiazolyl	H	323.5–25.5	235
	2-benzothiazolyl	H	303–5	235
2-Methoxy	H	H	149–50	1
6-Ethoxy	2-Py	H	180	118,120
6-Butoxy	$CH:CHCH_2$	H	67,68	118,120
6-(2-Benzothiazolyl)	H	H	149	179
6-(2-Benzothiazolyl)	Et	Et	93–95	179
None	H	NH_2	152–53 (dec.)	282
			monopicrate, m.p. 120–21 (dec.)	282
	H	$N{=}CMe_2$	152–53 (dec.)	282
			monopicrate, m.p. 126 (dec.)	282

TABLE XV-29a. 4-Pyridinesulfonamides and 4-Pyridinesul fohydrazides



Substituents	R	R′	M.p., °C.	Ref.
None	H	H	172–3 picrate 186–7 I-oxide 230 dec.	193,289,293
	Me	Me	67–9 picrate 168–9	289
	H	Ph	135–6	293
	H	NH_2	95–6 picrate 117–8	293
	H	N=CMe$_2$	148–9	282,326

TABLE XV-30. Pyridinedisulfonamides

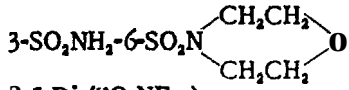
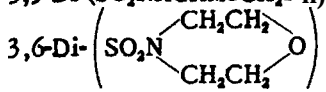
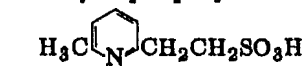
Substituents	M.p., °C.	Ref.
	182–83	117,119
3,5-Di-(SO_2NEt_2)	114.5–15.0	97
3,5-Di-($SO_2NHCHMeCH_2Ph$)	140–50	97
3,6-Di- 	183-91	117,119

TABLE XV-31. Pyridylalkylsulfonic Acids and Pyridylalkanolsulfonic Acids

Compound	M.p., °C.	Ref.
2-$PyCH_2CH_2SO_3H$	265–67	34,41,323
4-$PyCH_2CH_2SO_3H$	284–85	34,41,323
	282–83	34
2-$PyCH(OH)SO_3H$	205[a]	109
4-$PyCH(OH)SO_3H$	243"	109
	185[a]	109

[a]Sealed tube.

TABLE XV-32. Monocyclic Thiocyanatopyridines

Compound	Physical properties	Ref.
3-Thiocyanatopyridine	m.p. 32'; b.p. 124°/12 mm.	124
4-Thiocyana topyridine	m.p. 62–3°	355
3-Thiocyanatomethylpyridine	m.p. 110° hydrochloride, m.p. 166–67°	360
4-Thiocyanatomethylpyridine	m.p. 120' hydrochloride, m.p. 149–50°	360
2-Thiocyanatomethylpyridine	b.p. 139–40° (1 mm.) hydrochloride, m.p. 169–70°	360
6-Methyl-2-thiocyanotopyridine	HCNS salt, m.p. 136°	360
2-Thiocyanotoeth ylpyridine	HCNS salt, m.p. 208–12°	360
4-Thiocyanatoethylpyridine	HCNS salt, m.p. 149–50	360
2-(1,2-Dithiocyanatoethyl)-pyridine	HCNS salt, m.p. 181–82°	360
4-(1,2-Dithiocyanatoethyl)-pyridine	HCNS salt, m.p. 180–1	360
3-Nitro-2-thiocyanatopyridine	m.p. 119–20°	172, 189
5-Nitro-2-thiocyanatopyridine	m.p. 129–30°	172
3-Nitro-lbthioc yanatop ytidine	m.p. 139"	241
3,5-Dinitro-2-thiocyanatopyridine	m.p. 145–46°	188

TABLE XV-33. S-Pyridyl-O-Alkylthiocarbamates

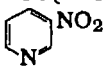
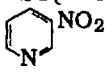
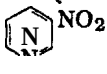
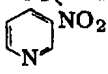
Compound	Physical properties, derivatives	Ref.
	m.p. 97–98'	242
	m.p. 67–68°	242
	hydrochloride, m.p. 176°	242
	hydrochloride, m.p. 148 (dec.)	242

TABLE XV-34. Condensed Thiocyanatopyridines and Aminopyridothiazoles

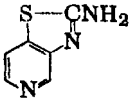
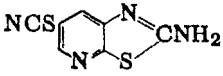
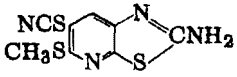
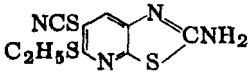
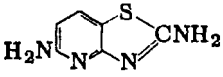
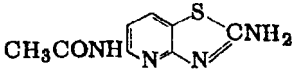
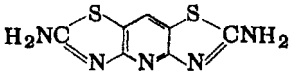
Compound	M.p., °C.	Ref.
	296	241
	193	212
	173	212
	194–95	212
	138–39	14
	184–85	14
	152–53 >300	228 14

TABLE XV-35. Pyridyldithiocarbamic Acid Derivatives

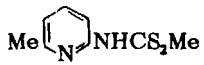
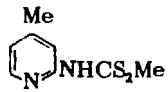
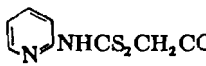
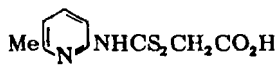
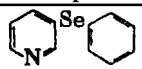
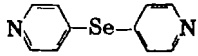
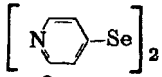
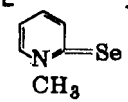
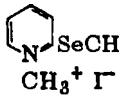
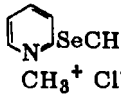
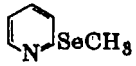
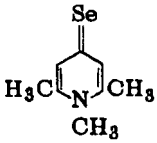
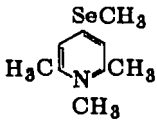
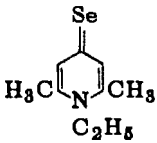
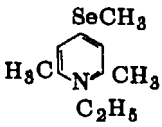
Compound	M.p. °C.	Ref.
	84–85	361
	76	361
	75–76	361
	141	361
	91	361
	89–90	361
	101–02	361
	142–44	361
	183	362
	125	362
	152–53	362

TABLE XV-36. Selenium Compounds of Pyridine

Compound	Physical properties	Ref.
	b.p. 128°/1.5 mm.	76
	m.p. 63–65° dihydrochloride, m.p. 225–230°	279
	m.p. 113–114°	279
	m.p. 79–80'	114
	m.p. 186°	114
	m.p. 86°	114
	b.p. 212'	114
	m.p. 268°	114
	m.p. 70'	114
	m.p. 254	114
	—	114

(continued)

TABLE XV-36. *(continued)*

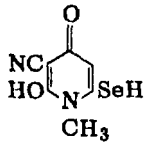
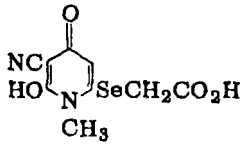
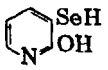
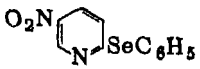
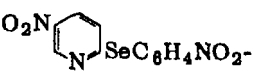
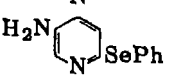
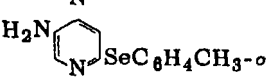
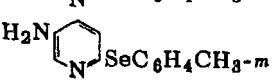
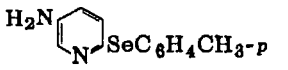
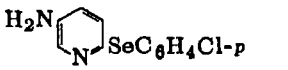
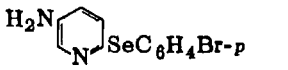
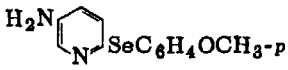
Compound	Physical properties	Ref.
	—	155
	—	155
	—	*9*
	m.p. 127–28'	272
	m.p. 63–64'	272
	m.p. 123°	272
	m.p. 156–57°	272
	m.p. 147–48'	272
	m.p. 137–38°	272
	m.p. 151–52°	272
	m.p. 118–19°	272
	m.p. 124–25'	272
	m.p. 59–61°	272
	m.p. 62°	272

TABLE XV-36. ***(continued)***

Compound	Physical properties	Ref.
	m.p. 100–5°	272
	m.p. 75–76°	272
	m.p. 90–92°	272
	m.p. 65–66°	272
	m.p. 161–62°	272

O. BIBLIOGRAPHY

1. Adams, Hine, and Campbell, *J. Am. Chem. Soc.*, 71, 385 (1949).
2. Adler, von Euler, and Skarzynski, *Arkiv Kemi, Mineral. Geol.*, A16, No. 9 (1943).
3. German patent 544,620, Allardt and von Schickh; *C.A.*, 26, 3519[6] (1932).
4. German patent 563,131, Allardt and von Schickh; *C.A.*, 27, 1002[7] (1933).
5. Archer, Hoppe, Lewis, and Haskell, *J. Am. Pharm. Assoc., Sci. Ed.*, 40, 143 (1951).
6. Armour Research Foundation, *Anal.* Chem., 20, $79, 897 (1948).
7. Arndt, *Ber.*, B65, 92 (1932).
8. Arndt and Kalischek, *Ber.*, B63, 587 (1930).
9. Australian patent 21,081.
10. Backer and Keverling Ruisman, Rec. *trav. chim.*, 64, 102 (194.5).
11. Bambas, *J. Am. Chem. Soc.*, 67, 668 (1945).
12. Belgian patent 445,915; *C.A.*, 39, 784[9] (1945).
13. Benary, *Ber.*, B51, 567 (1918).
14. Rernstein, Stearns, Shaw, and Lott, *J.* Am. *Chem. Soc.*, 69, 1157 (1947).
15. Bittner, Rer., B35, 2933 (1902).
16. Boarland and McOmie, *J.* Chem. *Soc.*, 1951, 1218.
17. Brooker, Keyes, Sprague, Van Dyke, Van Lare, Van Zandt. and White, *J.* Am. *Chem. Soc.*, 73, 5326 (1951).
18. Brown and Kanner, *ibid.*, 75, 3865 (1953).
19. German patent 208,638, Bucherer; *Friedl.*, 9, 1102.
20. Burton and Davy, *J. Chem. Soc.*, 1947, 52.
21. Caldwell and Kornfeld, *J.* Am. Chem. *Soc.*, 64, 1695 (1942).
22. Caldwell, Tyson, and Lauer, *ibid.*, 66, 1479 (1944).

23. Carrara and Chiancone, *Chim. e ind. (Milan).* **23,** 435, (1941); *C.A.*, **36,** 7033[5] (1942).
24. U.S. patent 2,508,745, Cavallito and Small; *C.A.*, **44,** 9975 (1950).
25. French patent 866,482, Chichibabin and Bertougelf; *C.A.*, **43,** 5050a (1949).
26. Chichibabin and Tyazhelova, *J. Russ. Phys. Chem. Soc.*, **50,** 495 (1918): *C.A.*, **18,** 1495[5] (1921).
27. Chichibabin antl Vialatout, *Bull. soc. chim. France,* **6,** 736 (1939).
28. Chichibabin and Vorozhtzov, *Ber.*, B66, 364 (1933).
29. Childress and McKee, *J. Am. Chem. Soc.*, **73,** 3504 (1951).
30. Swiss patent 240,728. Cilag, chemisches industrielles Laboratoriuni A.-G.; *C.A.*, **43,** 7063e (1949).
31. Swiss patent 235,881. Cilag, chemisches industrielles Laboratorium A.-G.; *C.A.*, **43,** 7042b (1949).
32. Swiss patent 240,720. Cilag, chemisches industrielles Laboratorium A.-G.: *C.A.*, **43,** 7961f (1949).
33. Swiss patent 240.721. Cilag, chemisches industrielles Laboratorium A.-G.; *C.A.*, **43,** 7961g (1949).
34. U.S. patent 2,508,904, Cislak.
35. Colonna. *Gazz. chim. ital.*, **70,** 154 (1940); *C.A.*, **34,** 4737[1] (1940).
36. Colonna, Boll. *sci. fac. chirn. ind. Univ. Bologna,* 1941, 145: C.A., **37,** 4399[3] (1943).
37. Courtot and Zwilling, *Congr. chim. ind. Nancy,* **18, II,** 796 (1938); *Chem. Zentr.*, **1939, II,** 3412.
38. Craig. Schaefgen, and Tyler, *J. Am. Chem. Soc.*, **70,** 1624 (1948).
39. Cushing antl Morgan, *Proc. Soc. Exptl. Biol. Med.*, **79,** 497 (1952).
40. Dewing, Gray, Platt, and Stephenson, *J. Chem. Soc.*, **1942,** 239.
41. Doering and Weil, *J. Am. Chem. Soc.*, **69,** 2461 (1947).
42. Dohrn and Diedrich, *Ann.*,, **494,** 281 (1932).
43. German patent 564,786, Dohrn and Diedrich; *Friedl.*, **19,** 1122.
44. U.S. patent 2,456,258, Dohrn and Laubereau.
45. Dreizen, Schloz, antl Spies. *Proc. Soc. Exptl. Biol. Med.*, **68,** 620 (1948).
46. Duesel and Scudi, *J. Am. Chem. Soc.*, **71,** 1866 (1949).
47. Duffin and Kendall, *J. Chem. Soc.*, **1951,** 734.
48. Erlenmeyer, Block, and Kiefer, *Helv. Chim. Acta,* **25,** 1066 (1942).
49. Erlenmeyer and Würgler, *ibid.*, **25,** 249 (1942).
50. British patent 216,288, Ewins, Phillips, and Newberry.
51. Fibel and Spoerri, *J. Am. Chem. Soc.*, 70, 3908 (1948).
52. Filomeni, *Boll. soc. ital. biol. sper.*, **16,** 15 (1941); *C.A.*, **40,** 6157[9] (1946).
53. Fisclier, *Ber.*, **B15,** 62 (1882).
54. Fisclier and Renouf, *Ber.*, **B17,** 755 (1884).
55. Fischer and Riemerschmid., *Ber.*, **B16,** 1183 (1883).
56. Forrest antl Walker. *J. Chem. Soc.*, **1948,** 1939.
57. U.S. patent 2,476,655, Fox. Diedrich, and Dohrn: *C.A.*, **43,** 8399i (1939).
58. Freytag, *J. prakt. Chem.*, **139,** 44 (1933).
59. British patent 587,015. Friedheim: *C.A.*, **42,** 218a (1948).

60. Fry and Kendall, J. *Chem. Soc.*, **1951**, 1716.
61. Fullhart, Jr., *Iowa State Coll. J. Sci.*, **22**, 27 (1947); *C.A.*, **42**, 1907d (1948).
62. Gaebler and Beher, *J. Biol. Chem.*, **188**, 343 (1951).
63. Van Gastel and Wibaut, *Rec. trav. chim.*, **53**, 1031 (1934).
64. British patent 598,472, J. R. Geigy, A.-G.; C.A., **42**, 6851h (1948).
65. British patent 582,638, Gibbs and Penny, Glaxo Laboratories, Ltd.; *C.A.*, **41**, 2755d (1947).
66. Cuthzeit and Epstein, *Ber.*, **B20**, 2113 (1887).
67. German patent 597,452, Haack; *Fried.*, **21**, 518.
68. Hantzsch, *Ber.*, **B19, 31** (1886).
69. Den Hertog and Wibaut, *Rec. trav. chim.*, **51**, 944 (1032).
70. Hoffmann and Königs, *Ber.*, **B16**, 727 (1883).
71. Hope and de Leon, *Ciencia (Mex.)*, 8, 263 (1948); C.A., **44**, 7320c (1950).
72. Itai, *J. Pharm. Soc. Japan*, **69**, 542 (1949); C.A., **44**, 4473h (1950).
73. Itai, *ibid.*, **69**, 545 (1949); C.A., **44**, 4474c (1950).
74. Kao, *J. Chem. Eng. (China)*, **15**, 80 (1948); *C.A.*, **44**, 3993e (1950).
75. Karrer and Manz, *Helv. Chim. Acta*, **29**, 1152 (1946).
76. Keimatsu, Yokota, and Satoda, *J. Pharm. Soc. Japan*, **53**, 994 (1933); *C.A.*, **29**, 7800^9 (1935).
77. Hungarian patent 124,130, Kereszty and Wolf; C.A., **34**, 72979 (1940).
78. Hungarian patent 135,689, Kereszty and Wolf; *C.A.*, **44**, 4041h (1950).
79. French patent 685,062, I. G. Farbenindustrie **A.-G.**; C.A., **24**, 5307^8 (1930).
80. King and Ware, *J. Chem. Soc.*, **1939**, 873.
81. U.S. patent 2,510,893, Kleiman.
82. U.S. patent 2,510,894, Kleiman.
83. Klingsberg and Papa, J. Am. *Chem. Soc.*, **71**, 2373 (1949).
84. Klingsberg and Papa, ibid., **73**, 4988 (1951).
85. U.S. patent 2,676,969, Klingsberg and Papa.
86. U.S. patent 1,753,658, Kochendoerfer.
87. Koenigs and Geisler, *Ber.*, **B57**, 2076 (1924).
88. Koenigs and Jungfer, *Ber.*, **B57**, 2080 (1924).
89. Koenigs and Kantrowitz, *Ber.*, **B60**, 2097 **(1927)**.
90. Koenigs and Kinne. *Ber.*, **B54**, 1357 (1921).
91. Kolmer, Brown, and Raiziss, J. *Pharmacol. Exptl. Therap.*, **61**, 253 (1937).
92. German patent 574,836, Kranzlein and Hopff; *Fried.*, **19**, 627.
93. **U.S.** patent 2,429,096, Ladd.
94. Leone and Oliveri, *Gazz. chim. ital.*, **15**, 274 (1885).
95. Lewis and Archer, *J. Am. Chem. Soc.*, **73**, 2109 (1951).
96. Macheck, *Monntsh.*, **72**, 77 (1938).
97. Macheck, *ibid.*, **73**, 180 (1940).
98. Mangini and Colonna, *Gazz. chim. ital.*, **73**, **313** (1943); *C.A.*, **41**, 1224f (1947).
99. Mangini and Passerini, *Boll. sci. fac. chim. ind. univ. Bologna*, **7, 63**, 64 (1940); *C.A.*, **44**, 8771a (1950).
100. Mangini and Passerini, *ibid.*, 8, 4 pp. (1950); C.A., **45**, 3241d (1951).

101. Mann and Reid, *J. Chem. Soc.*, **1952,** 2057.
102. McElvain and Goese, *J. Am. Chem. Soc.*, **65,** 2233 (1943).
103. McGinty and Bywater, *J. Pharmacol. Exptl. Therap.*, **84,** 342 (1945).
104. McIlwain, *Lancet,* **1942,** I, 412.
105. McIlwain, *Nature,* **146,** 653 (1940).
106. French patent 966,769, Manufactures produits chimiques nord, Établissements Kuhlmann; *C.A.*, **46,** 7589b (1952).
107. Marckwald, Klemm, and Trabert, *Ber.*, **B33,** 1156 (1900).
108. Marion and Cockburn, *J. Am. Chem. Soc.*, **71,** 3402 (1949).
109. Mathes and Sauermilch, *Chem. Ber.*, **84,** 648 (1951).
110. Meunier, *Bull. soc. chim.*, **12,** 517 (1945).
111. Meyer, *Ber.*, **B36, 616** (1903).
112. Meyer, *Monatsh.*, **24,** 195 (1903).
113. Meyer and Ritter, *ibid.*, **35,** 765 (1914).
114. Michaelis and Holken, *Ann.*, **331,** 245 (1904).
115. Moller and Hirkofer. *Ber.*, **B75,** 1118 (1942); *C.A.*, **37,** 5105 (1943).
116. Morel and Stoll, *Helv. Chim. Acta,* **33,** 516 (1950).
117. U.S. patent 2,170,209, Naegeli.
118. U.S. patent 2,211.702, Nacgeli.
119. Naegeli, Kündig, and Brandenburger, *Helv. Chim. Acta,* **21,** 1746 **(1938).**
120. Naegeli, Kiintlig, and Brandenburger, *ibid.,* **22,** 912 (1939).
121. Naegeli, Kiintlig. and Suter, ibid., **25,** 912 (1939).
122. Nitti and Matti. *Compt. rend. soc. biol.,* **136,** 401 (1942).
123. Ochiai and Takubo, *J. Pharm. Soc. Japan,* **61,** 1 (1941); *C.A.*, **35,** 36339 (1941).
124. Panouse, *Compt. rend.*, 230, 846 (1930).
125. Parker and Shive, *J. Am. Chem. Soc.,* **69, 63** (1945).
126. Passerini, *Boll. sci. fac. chim. ind. univ. Bologna,* **9, 31 (1951); *C.A.*, 45,** 10210h (1951).
127. Phillips and Shapiro, *J. Chem. Soc.,* **1942,** 584.
128. **Plazek,** *Roczniki Chem.*, **16,** 403 (1936); *C.A.*, **31,** 1808[5] (1937).
129. Plazek. ibid., **17,** 97 (1937); *C.A.*, **31,** 4669[2] (1937).
130. Plazek and Marcinkow, ibid., **14,** 326 **(1934): *C.A.*, 29,** 2535[3] (1935).
131. Plazek and Sucharda, *Ber.,* **B59,** 2282 (1926).
132. Prill, Hartzell, and Arthur, *Contrib. Boyce Thompson Inst.*, **14,** 127 (1946).
133. German patent 550,327, Putzer and Schönhofer; *Friedl.*, **19,** 1414.
134. British patent 602,882, Pyridium Corp.; *C.A.*, **43,** 696h (1949).
135. Raoul, *Compt. rend. soc. biol.*, **139, 649** (1945).
136. Räth, *Ann.*, **487,** 105 (1931).
137. Räth, *Ann.*, **487,** 127 (1931).
138. Reinhart, *J. Franklin Inst.*, **236, 316** (1943).
139. Reinhart, ibid., **249,** 248 **(1950).**
140. Reinhart, *ibid.*, **249,** 427 (1950).
141. Renault, *Bull. soc. chim. France,* **20,** 1001 (1953).

142. Renault, *Compt. rend.*, **232,** 77 (1951).
143. Kenault, *ibid.*, **232,** 1228 (1951); *C.A.*, **46,** 7101e (1952).
144. Kenault. *ibid.*, **233,** 182 (1951): **C.A., 46,** 7101d (1952).
145. U.S. patent 2,367,058, Rohlin and Clapp.
146. Koblin, Williams, and Anderson. *J.* Am. Chem. *Soc.*, **63,** 1930 (1941).
147. Ross, J. *Chem. Soc.*, **1951,** 1374.
148. British patent 380,083, Kotlimann; **C.A., 27,** 4031[1] (1933): *Chem. Zentr.*, **1932 II,** 3917.
149. Rudolph, *Ärztl. Forsch.* **1,** 215 (1947); **C.A., 44,** 3107g (1950).
150. Saikachi, *J. Pharm.* **Soc.** Japan, **64,** 201 (1944); *C.A.*, **45,** 4717b (19.51).
151. Saikachi, *J. Pharm. Soc. Japan,* **64,** 328 (1944); *C.A.*, **45,** 4717g (1951).
152. Saikachi antl Hoshida, *J.* Phnrm. Sor. *Japan,* **71,** 982 (1951); C.A., **46,** 8082e (1952).
153. German patent 601,896, von Schickh; *Friedl.*, **21,** 517.
154. German patent 678,148, von Schickh: **C.A., 33,** 7818[8] (1939).
155. Schroeter, Seidler, Sulzbacher, and Kanitz, *Ber.*, **B65,** 432 (1932).
156. Shaw, Herstein, Losee, and Lott, *J. Am. Chem. Soc.*, **72,** 4362 (1950).
157. Sheehan and Lcitner, *ibid.*, **74,** 5501 **(1952).**
158. U.S. patent 2,409,806, Shive and Glenn: **C.A., 41,** 2087i (1947).
159. Smith and Hurnett, *J. Econ. Entomol.*, **42,** 439 (1949); *C.A.*, **44,** 6567a (1950).
160. French patent 846,191, Société usines chimiques Rhône-Poulenc; *C.A.*, **35,** 1184[6] (1941).
161. Soo-hoo and Grunberg, *J. Invest. Dermatol.*, **14,** 169 (19.50); *C.A.*, **45,** 9726f (1951).
162. Sprague antl Hrooker, *J. Am. Chem. Soc.*, **59,** 2697 (1937).
163. Steffenoni, *Arch. farmacol. sper.*, **72,** 44 (1941); *C.A.*, **36,** 1087[8] **(1941).**
164. Steffenoni. *Roll. soc. ital. biol. sper.*, **16,** 224 (1941): *C.A.*, 39, 1926[4] (1945).
165. British patent 637,130, Steiger; **C.A., 44,** 8380c (1950).
166. U.S. patent 2,544,904, Steiger; C.A., **45,** 5370d (1951).
167. U.S. patent 2,584,639, Steiger antl Keller; *C.A.*, **46,** 11238f **(1952).**
168. Stein, *Z. Immunitätsforsh.*, **78,** 489 (1933); **C.A., 27,** 5411[3] (1933).
169. Sucharda and Troszkiewicz, *Roczniki* Chem., **12,** 493 (1932); *C.A.*, **27,** 5076[2] (1933); *Chem. Zentr.*, **1932 II,** 3400.
170. Surrey and Lindwall, *J. Am.* Chem. *Soc.*, **62,** 173 (1940).
171. Surrey antl Lindwall, *ibid.*, **62,** 1697 (1940).
172. Takahashi and Goto, *J. Pharm. Soc. Japan,* **63,** 425 (1943); *C.A.*, **45,** 4716i (1951).
173. Takahashi and Hayase, *ibid.*, **64, No. 7/8A, 9** (1944); *C.A.*, **46,** 110h **(1952).**
174. Takahashi and Morita, *ibid.*, **64, No. 7A,** 11 (1944); *C.A.*, **45,** 8014d (1951).
175. Takahashi and Saikachi, *ibid.*, **62,** 140 (1942): C.A., **45,** 1592h (1951).
176. Takahashi and Saikachi, *ibid.*, **62,** 143 (1942); **C.A., 45,** 1593a (1951).
177. Takahashi, Saikachi, and Akai, *ibid.*, **63,** 153 (1943); *C.A.*, **45,** 4716g (1951).
178. Takahashi, Saikiichi, and Itoh, *ibid.*, **62,** 486 (1942); C.A., **45,** 4716d (1951).

179. Takahashi, Saikachi, and Sasaki, *ibid.*, *64*, 221 (1944); *C.A.*, **46**, 112h (1952).
180. Takahashi. Saikachi, Sasaki, and Kimura, *ibid.*, **69**, 289 (1949); *C.A.*, **44**, 5373f (1950).
181. Takahashi, Saikachi, and Satake, *ibid.*, **64**, No. 8A, 23 (1944); *C.A.*, **46**, 110b (1952).
182. Takahashi, Saikachi, Yoshina, and Mizuno, *ibid.*, **69**, 284 (1949); *C.A.*, **44**, 5372f (1950).
183. Takahashi, Shibasaki. *ibid.*, **72**, 1141 (1952); *C.A.*, **47**, 7498e (1953).
184. Takahashi, Shirmamura, Uyeda, and Hashimoto, *ibid.*, *64*, No. 2A, **14** (1945).
185. Takahashi and Taniyama, *ibid.*, **64**, No. 10A, 49 (1944); *C.A.*, **46** 110e (1952).
186. Takahashi, Tsubaki, and Yajima, *ibid.*, **62**, 488 (1942); *C.A.*, **45**, 4716e (1951).
187. Takahashi and Ueda. *ibid.*. **73**, 442 (1953); *C.A.*, **48**, 5187h (1954).
188. Takahashi and Yamamoto, *ibid.*, **70**, 187 (1950); *C.A.*, **44**, 7320d (1950).
189. Takahashi and Yamamoto, *ibid.*, **72**, 1491 (1952); *C.A.*, **47**, 8069h (1953).
190. Takahashi. Yatsuka, and Onuma, *ibid.*, 63, 235 (1944); *C.A.*, **45**, 4717d (1951).
191. Tarbell and McCall, *J.* Am. *Chem. Soc.*, **74**, 48 (1952).
192. Thirtle, *ibid.*, **68**, 342 (1946).
193. **U.S.** patent 2,349,060, Tiesler; *C.A.*, **39**, 8205 (1945).
194. **U.S.** patent 2,330,641, Tiesler; C.A., **38**, 12499 (1944).
195. **U.S.** patent 2,406,972, Tisza and Duesel: *C.A.*, **41**, 489 (1947).
196. British patent 572,835, Tisza and Duesel; *C.A.*, **43**, 7514b (1949).
197. Urbansky, *J. Chem. Soc.*, **1947**, 132.
198. Vejdelek and Protiva, *Cham. Listy*, **45**, 451 (1951); *C.A.*, **47**, 8068f (1953).
199. Vinckc and Sucker, *Z. Vitamin-, Hormon- it. Fermentforsch.*, **3**, 69 (1949); *C.A.*, **44**, 6027f (1950).
200. Vompe, Turitsyna and Levkoev, *Doklady Akati. Nauk. S.S.S.R.*, **65**, 839 (1949); *C.A.*, **43**, 6626g (1949).
201. Webb and Corwin, *J. Am.* Chem. *Soc.*, **66**, 1456 (1944).
202. Weidel and Murmann, *Monatsh.*, **16**, 750 (1875).
203. Worrall, *J. Am. Chem. Soc.*, **61**, 2966 (1939).
204. **Worrall.** ibid., **62**, 578 (1940).
205. Wuest and Sakal, *ibid.*, **73**, 1210 (1951).
206. German patent 541,036, Wulff; *Friedl.*, **17**, 2443.
207. German patent 541,681, Wulff; *Friedl.*, **17**, 2437.
208. German patent 563,373, Wulff; *Fried.*, **18**, 2777.
209. U.S. patent 1,880,645, Wulff.
210. U.S. patent 1,880,646 Wulff.
211. Yale, Losee, Martins. Holsing, Perry, and Bernstein, *J. Am.* Chem. *Soc.*, **75**, 1933 (1953).
212. Yamamoto, *J. Pharm. Soc. Japan*, **71**, 662 (1951); *C.A.*, **46**, 8109a (1952).
213. Yamamoto, *ibid.*, **71**, 916 (1951); *C.A.*, **46**, 8109g (1952).

214. Yamamoto, *ibid.*, **71,** 920 (1951); *C.A.*, **46,** 8110a (1952).
215. Yamamoto, ibid., **71,** 1436 (1951); *C.A.*, **46,** 8110c (1952).
216. Yamamoto, *ibid.*, **71,** 1017 (1951); *C.A.*, **46,** 10285h (1952).
217. Yamamoto and Oya, *ibid.*, **72,** 1022 (1952); *C.A.*, 46, 10286f (1952).
218. Zienty, *J. Am. Pharm. Assoc., Sci. Ed.*, **37,** 97 (1948).
219. Zienty, *ibid.*, 97.
220. U.S. patent 2,473,121, Zienty; *C.A.*, **43,** 6671e (1949).
221. U.S. patent 2,541,902, Zientv; *C.A.*, **45,** 7154f (1951).
222. Cheymol, Renault, and Pazin, *Arch. intern. pharmacodynamie,* **93,** 143 (1953); C.A., **47,** 10697a (1953).
223. Cheymol, Chabrier, Renault. and Pazin, *Thérapie,* **7,** 514 (1952): *C.A.*, **47,** 8908a (1953).
224. Gautier and Renault, *Compt. rend.*, **234,** 2081 (1952).
225. Kahn and Petrow, *J. Chem. Soc.*, **1945,** 858.
226. Korte, *Chem.* Ber., 85, 1012 (1952).
227. Linctskay and Sapozhnikova, *Doklady Akad. Nauk. S.S.S.R.*, 86, 763 (1952); *C.A.*, **47,** 955h (1953).
228. Maggiolo. *J. Am.* Chem. *Soc.*, **73,** 5815 (1951).
229. U.S. patent 2,620,342, Mathes and Sauermilch.
230. Mizuno and Nojima, *Japan. J. Med. Sci. & Biol.*, **5,** 397 (1952): *C.A.*, **47,** 8816h (1953).
231. Panzy, Stander, Koerber, and Donovick, *Proc. Soc. Exptl. Biol. Med.*, 82, 122 (1953).
232. Petrow and Rewald, *J. Chem. Soc.*, **1945,** 591.
233. U.S. patent 2,606,190, Shelton and Tilford.
234. Sieburth and McLaren, Ann. *Entomol.* Sor. Am., **46,** 13 (1953); C.A., **47,** 11579b (1953).
235. U.S. patent 2,611,770, Smith.
236. Thompson, Chenicek, and Symon, *Ind., Eng. Chem., 44,* 1659 (1952).
237. U.S. patent 2,607,775, Vinton.
238. U.S. patent 2,607,776, Vinton.
239. Craig, *J. Am.* Chem. *Soc.*, **55,** 2855 (1933).
240. Takahashi, Shibasacki, and Uchibayashi, *Phnrm. Bull. (Tokyo),* **2, 30** (1954).
241. Takahashi and Ueda, *ibid.*, **2,** 34 (1954).
242. Takahashi and Ueda, ibid., **2,** 78 (1954).
243. Takahashi, Ueda, and Ichimoto, *ibid.*, **2, 196** (1954).
244. Ochiai and Suzuki, *ibid.*, **2,** 247 (1954).
245. Katz, Schroeder, and Cohen, *J. Org. Chem.*, **19,** 711 (1954).
246. Evans and Smiles, *J. Chem. Sor.*, **181,** 1263 (1935).
247. Penfold, *Acta Cryst.*, **6,** 707 (1953).
248. Liittringhaus, Cordes, and Schmidt, *Angew. Chetn.*, **67,** 275 (1955).
249. Hurd and Morrissey, *J. Am. Chem. Sor.*, **77,** 4658 (1955).
250. Gautier. Lambin, Renault, and Desvignes, *Ann. pharm. franç.*, **12,** 17 (1954).

251. Djerassi antl Pettit, *J. Atn. Chem. Soc.*, **76,** 4470 (1954).
252. Gautier and Renault, *Bull. soc. chim. France*, **1954,** 1463.
253. Kruger and Mann, *J. Chem. Soc.*, **1954,** 3905.
254. Kruger antl Mann, *ibid.*, **1955,** 27.55.
255. Renault. Thesis. University of Paris, 1955.
256. Vedjelek, Trcka, Hejny, and Vysatova, Collection *Czechoslov. Chem. Communs.*, **19,** 1274 (1954).
257. Vejdelek, Trcka, and Vysatova, *Chem. Listy*, **48,** 1221 (1954).
258. Mosher and Welch, *J. Am. Chem. Soc.*, 77, 2902 (1955).
259. Gautier antl Renault, *Compt.* rend., 234, 2081 (1952).
260. Legrand antl Lozach, *Bull. soc. chim. France,* **1955,** 79.
261. Takahashi and Yoshii, *Pharm. Bull.* (Tokyo). **2, 382** (1954).
262. Takahashi. Ueda, and Ichimoto, *ibid.,* **3,** 356 (1955).
263. Takahashi and Maki, *ibid.*, 3, 361 (1955).
264. Takahashi and Maki, *ibid.*, **3,** 92 (1955).
265. Senionsky and Cerny, *Collection Czechoslov. Chem. Communs.*, 20, 1221 (1955).
266. Musante and Fabrini. *Gazz. chim. ital.*, **84, 584** (1954).
267. Ochiai and Fujimoto, *Pharm. Bull.* (Tokyo). **2, 131 (1954):** *C.A.*, **50,** 990a (1956).
268. Tenenbaum, private communication.
269. Fridman, *J. Gen. Chem. U.S.S.R.*, **26,** 864 (1956); *C.A.*, **50,** 14753a (19.56).
270. Ueda. *Pharm. Bull. (Tokyo)* **4,** 396 (1956).
271. Ueda, *ibid.*, **4,** 402 (1956).
272. Chierici and Passerini, *La Ricerca Scientifica (Rome)*, **25,** No. 8. 2316 (1955).
273. U.S. patent 2,761,866, Goldberg and Teitel; *C.A.*, **51,** 3671a **(1956).**
274. U.S. patent 2,761,865, Goldberg and Teitel: *C.A.*
275. Larivé, Collect, and Dennilauler, *Bull. soc. chim. France*, **1956,** 1443.
276. Takahashi and Yamashita, *Pharm. Bull.* (Tokyo). **4,** 20 (1956).
277. Van der Plas and den Hertog, *Chem. Week.*, **53,** 560 (1957).
278. French patent 1,004,350, Société anom. Chimico-technic and Duperray; *C.A.*, **51,** 7044a (1957).
279. Jerchel, Fischer. antl Thomas, *Chem. Ber.*, **89,** 2921 (1956).
280. Profft, *Chem. Tech.* (Berlin), **7,** 577 (1955).
281. DeCourcy, Jr., Reinhart, and Batt, *J. Franklin Inst.*, **263,** 557 (1957); C.A., **51,** 16729a (1957).
282. Talik antl Plażek, *Acta Polon. Pharm.*, **12,** 179 **(1955):** *C.A.*, **51,** 17911e (1957).
283. Takahashi and Maki, *Yakugaku Zasshi,* **77,** 481 (1957); *C.A.*, **51,** 14738a (1957).
284. Takahashi and Maki, *ibid.*, **77,** 485 (1957); *C.A.*, **51,** 14738f (1957).
285. U.S. patent 2.758,658: *C.A.*, **51,** 11394 (1957).
286. Fürst anti Dietz, *J. prakt. chem.* [4], **4,** 147 (1956).

287. den Hertog, Van der Plas, and Buurman, *Rec. trav. chim.*, **77**, 963 (1958).
288. Ochai and Suzuki, *Pharm.* Bull. *(Tokyo)*, **2**, 109 (1954).
289. Talik and Plafek, *Acta Polon. Pharm.*, **12**, 5 (1955); *C.A.*, **51**, 17911c (1957).
290. Hansen and Hammer, *Ada chem. Scand.*, **7**, 1331 (1953).
291. Adams and Ferreti, J. *Am. Chem. Soc.*, **81**, 4927 (1959).
292. Angulo and Municio, *Anales real soc. expan. fis. y quim. (Madrid)*, **54B**, 383 (1958); *C.A.*, **53**, 6225d (1959). *Chem. & Ind. (London)*, **1958**, 1175.
293. Cornrie and Stenlake, J. *Chem. Soc.*, **1958**, 3514.
294. Muller and Wallace, *J. Org. Chem.*, **24**, 1151 (1959).
295. Profft, *Wiss. Z. Tech. Hochsch. Chem. Leuna-Merseburg*, **2**, 101 (1959–1960); *C.A.*, **54**, 11018e (1960).
296. Spinner, J. *Chem. Soc.*, **1960**, 1237; J. *Org. Chem.*, **23**, 2037 (1958).
297. Van der Plas and den Hertog, *TefrahedronLefters*, **1**, 13 (1960).
298. Evans and Brown, *Chem. & Ind. (London)*, **1958**, 1559.
299. Takahashi and Maki, Pharm. *Bull. (Tokyo)*, **6**, 369 (1958); C.A., **53**, 9228a (1959).
300. den Hertog, Van der Plas, and Buurman, *Rec. trav. chim.*, **77**, 963 (1958).
301. Jones and Katritzky, J. *Chem. Soc.*, **1958**, 3610.
302. Kreisky, *Monatsh.*, **89**, 685 (1958).
303. Hansch, Carpenter, and Todd, J. *Org. Chem.*, **23**, 1924 (1958).
304. Schmidt and Giesselmann, *Angew. Chem.*, **72**, 709 (1960).
305. Elkaschef and Nosseir, J. *Am. Chem. Soc.*, **82**, 4344 (1960).
306. Jones and Katritzky, J. *Chem. Soc.*, **1960**, 2937.
307. Schmidt and Kubitzek, *Chem. Ber.* **93**, 1559 (1960).
308. Schmidt and Giesselmann, *ibid.*, **93**, 1590 (1960).
309. Foldi, *Acta Chim. Acad. Sci. Hung.*, **19**, 205 (1959); *C.A.*, *54*, 2325c (1960).
310. Van der Plas, doctoral dissertation, University of Amsterdam, July 6, 1960.
311. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
312. U.S. patent 2,842,549; *C.A.*, **54**, 21140a (1960).
313. U.S. patent 2,940,978: *C.A.*, **54**, 21140c (1960).
314. Profft, *Monatsber. deut. Acad. Wiss. Berlin*, **1**, 694 (1959); *C.A.*. **54**, 21084a (1960).
315. Wendt and Bernhart, *Arch. Biochem. Biophys.*, **88**, 270 (1960); *C.A.*, **54**, 22621 (1960).
316. Rernhart, D'Amato, and Tornarelli, *ibid.*, 267 (1960); *C.A.*, 54, 19993 (1960).
317. Klemm and Reed, J. *Org. Chem.*, **25**, 1816 (1960).
318. Taylor and Driscoll, J. *Am. Chem. Soc.*, **82**, 3141 (1960).
319. Katritzky and Jones, *J.* Chem. *Soc.*, **1960**, 2947.
320. Fairfull and Peak, *ibid.*, **1955**, 796.
321. Profft and Rolle, J. *prakt. Chem.* [4], **11**, 22 (1960); see also *Wiss.* Z. *Tech. Hochsch. Chem. Leuna-Merseburg*, **2**, 187 (1959–1960); *C.A.*, **55**, 1609g (1961).
322. Howard and Michels, *J. Org. Chem.*, **25**, 829 (1960).
323. Rauer and Gardella, *ibid.*, **26**, 82 (1961).

324. Kröhnke, Ahrenholz, and Gross, *J. prakt. Chem.* [4], **11,** 256 (1960).
325. Czuba, *Roczniki Chem.,* **34,** 1149 (1960); C.A., **55,** 14448g (1960).
326. Comrie and Stenlake. *J. Pharm. & Pharmacol.,* **13,** 26 (1961).
327. Prolft and Steinke, *J. prakt. Chem.* [4], **13,** 58 (1961).
328. Zccher and Kriihnke, *Chem. Ber.,* **94,** 707 (1961).
329. Cottis and Tieckelmann, *J. Org. Chem.,* **26,** 79 (1961).
330. Ostroshchenko, Sadykov, and Ziyaer, *J. Gen. Chem. (U.S.S.R.)* **31,** 678 (1961); *C.A.,* **55,** 23527b (1961).
331. Albert and Barlin, *J. Chcm. Soc.,* **1959,** 2384.
332. U.S. patent 2,977,368; C.A., **55,** 16572e (1961).
333. Deavin and Rees, *J. Chem. Soc.,* **1961,** 4970.
334. Bradsher, Quin, LeBleu, and McDonald, *J. Org. Chem., 28,* 4944 (1961).
335. Martin, *Dissertation Abstr., 20,* 3533 (1960); *C.A.,* **54,** 11665g (1960).
336. McClure and Koss, *J. Org. Chetn.,* **27,** 304 (1962).
337. van Zweiten, van Velthuijsen, and Huisman, *Hec. trav. chim.,* **80,** 1066 (1961).
338. **Suzuki,** *Yakugaku Zasshi,* **81,** 1146 (1961).
339. U.S. patent 2,922,791.
340. U.S. patent 2,922,792.
341. U.S. patent 2,922,793.
342. U.S. patent 2,932,647.
343. U.S. patent 2,932,780.
344. Kametani, Fukumoto, and Umezawa, Yakugaku *Kenkyu,* **31,** 132 (1959); *C.A.,* **54,** 11019a (1960).
345. Koch, Arch. *exptl. Pathol. Pharmakol.,* **238,** 116 (1960); *C.A.,* **54,** 11283b (1960); see also *Acta* Chem. *Scand.,* **12,** 1873 (1958).
346. Moe, Kirpan, and Linegar, *Toxicol. Appl. Pharmacol.,* **2, 156** (1960).
347. Cation, *Mich. State Univ. Agr. Expt. Sta.* Bull., **41,** 685 (1959); C.A., **54,** 8829b (1960).
348. Mason, *J.* Chem. *Soc.,* **1960,** 219.
349. van Ammers and den Hertog, Rec. *trav. chim.,* **78, 586 (1959).**
350. Zelitch, *J. Biol. Chem.,* **234,** 3077 (1959).
351. Manski and Sawisza, null. *Acad. Polon. Sci., Ser. Sci. Biol.,* **5,** 231 (1957); C.A., **54,** 6955 (1960).
352. Sakata and Hashimoto, *Yakugaku Zasshi,* **79,** 827 (1959); *C.A.,* **54,** 3571 (1960).
353. Woods, Texas *J. Sci.,* **11,** 28 (1959); C.A., **54,** 521c (1960).
354. German patent 1,013,113; C.A., **54,** 16732f (1960).
355. Talik and Plażek, *Roczniki Chem.,* **33,** 1343 (1959): *C.A.,* **54,** 13123e (1960).
356. U.S. patent 2,940,978; *C.A.,* **54,** 21140c (1960).
357. Bourquin, Schwarb, Gamboni, Fischer, Kuesch. Gultimann, Theus, and Schenker, *Helv. Chim. Acta,* **42,** 2541 (1959).
358. British patent 822,871: C.A., **54,** 6763h (1960).
359. Katritzky and Lagowski. *J. Chem. Soc.,* **1958,** 4155.

360. U.S. patent 2,848,457; C.A., **53,** 13841 (1959).
361. U.S. patent 2,839,403; ***C.A.,*** **53,** 944g (1959).
362. U.S. patent 2,839,404; C.A., **53,** 946e (1959).
363. Jerchel, Heidcr, and Wagner, ***Ann.,*** **613,** 180 (1958).
364. Pala, Ed. ***sci.,*** **13,** 461 (1958); C.A., 53, 5267i (1959).
365. Takahashi, Ueda, and Iwai, *Yakigaku Zasshi,* **78,** 1447 (1958); C.A., **53,** 8133a (1959).
366. Saggiomo, Craig, and Gordon, ***J. Org.*** Chem., **23,** 1906 (1958).
367. Runge, Jumar, and Held, *J. prakt.* Chem., 8, 441 (1959).
368. Kennard and Burness, *J.* Org. Chem., 24, 464 (1959).
369. Yale and Sowinski, ***J.*** Am. ***Chetn. Soc., 80,*** 1651 (1958).
370. Evans and Brown, *J. Org.* Chem., **27,** 1329 (1962).
371. Fischer, Eilingsfeld, and Neurnann, ***Ann.,*** **651,** 49 (1962).

CHAPTER XVI

Arsenic, Antimony, and Phosphorus Compounds of Pyridine

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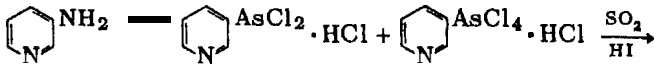
A. ARSENIC COMPOUNDS

1. Pyridinearsonic Acids

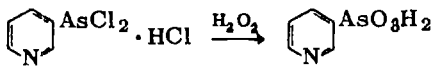
a. Preparation

(a) From Diazonium Compounds. The preparation of pyridinearsonic acids via the reaction of a diazonium compound with arsenic trichloride or sodium arsenite was a natural development once the

Bart reaction was established as the most useful method for the synthesis of aromatic arsonic acids. The first report was that of Scheller (*81,82*), who treated a mixture of 5-amino-2-pyridinol hydrochloride, arsenic trichloride, cuprous chloride, and acetic acid with an aqueous solution of sodium nitrite, heated to 55° until the diazonium compound had reacted completely. reduced tlie crude reaction product with sodium hydrosulfite, and reoxidized with hydrogen peroxide to obtain 6-hydroxy-3-pyridinearsonic acid. Several years later, Binz and von Schickh (*51*) reported a more detailed account of the Scheller reaction and showed that with 3-aminopyridine, for example, tlie first product was a mixture of dichloro-3-pyridylarsine hydrochloride (XVI-1) and tetrachloro-3-pyridylarsine hydrochloride (XVJ-?); reduction with sulfur dioxide converted XVI-2 to XVI-I; and reoxidation, followed by hydrolysis, gave 3-pyridinearsonic acid (XVI-3).

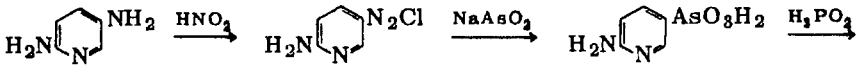


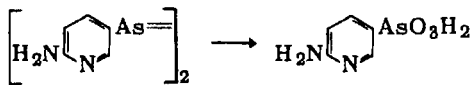
(XVI-1) (XVI-2)



(XVI-3)

In exploring tlie diazonium reaction more fully, Binz, Räth, and their co-workers (*6,12,28,42,50*) showed that it can be used to prepare nuclear substituted 3-pyridinearsonic acids. As before, the crude product, consisting of a mixture of tri- and pentavalent arsenic: compounds, was purified by the reduction-reoxidation technique first employed by Scheller (XVI-4). Further purification of the arsonic:

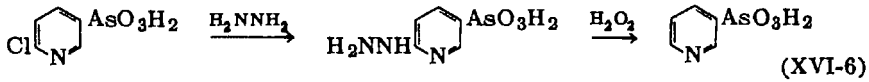




(XVI-4)

acids could be effected by solution in aqueous sodium bicarbonate and reprecipitation with hydrochloric acid; for example, 6-hydroxy-3-pyridinearsonic acid was obtained by this procedure as a snow-white crystalline solid in about 50% yield. Subsequently, it was found that many substituted 3-pyridinearsonic acids could be crystallized from water or ethanol.

In their early efforts, Rinz *et al.* **(43)** found that 3-pyriclinearsonic acid (XVI-5) could not be ohtainetl from diazotized 3-aminopyridine and sodium arsenite. They resorted *to* the indirect method shown in equation XVI-6, which gave a 10–12% yield of a sirup that gradu-



(XVI-6)

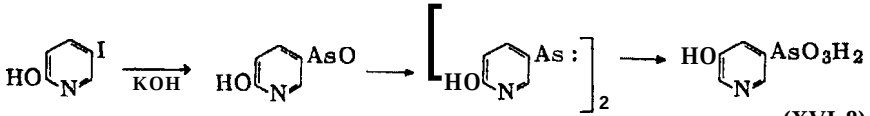
(XVI-5)

ally solidified to a hygroscopic solid, m.p. 112–113°, soluble in aqueous sodium carbonate but insoluble in ethanol. Subsequently, McCleland and Wilson (*76*) reported that XVI-5 could be prepared in 6% yield by the Bart reaction with 3-aminopyridine; the product formed non-hygroscopic white prisms, m.p. 158–159°, after recrystallization from ethanol, and gave a crystalline monohydrochloride, m.p. 196–198°. As a consequence, Binz and von Schickh (*51*) reinvestigated the reaction and, employing the Scheller method described above, obtained 73–85% yields of product having the properties reported by McCleland and Wilson.

The diazonium reaction has been used to convert 3-aminopicolinic acid to 3-arsonopicolinic acid (78).

2-Aminopyridine did not undergo the Scheller or Bart reactions (*61*).

(b) From Halopyridines. 6-Hydroxy-3-pyridinearsonic acids (XVI-7) was prepared by Binz and Räth (*32,46*) by refluxing for two hours an aqueous mixture of 5-iodo-2-pyridinol, arsenious oxide, potassium hydroxide, and a trace of copper bronze (or a copper salt). Presumably. the first product was 5-arsenoso-2-pyridinol, which was then reduced and reoxidized in the usual manner (XVI-8). With the same reactants. 5-bromo-2-pyridinol required a twenty-hour reflux



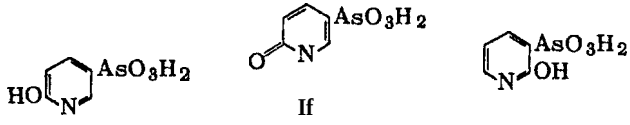
(not isolated)

(XVI-8)

(XVI-7)

period to give XVI-7; 3-bromo-5-iodo-2-pyridinol gave 5-bromo-6-hydroxy-3-pyritiinearsonic acid.

(c) Nuclear Arsonation of Aminopyridines and Pyridinols. Binz and Räth (*33*) fused 2-aminopyridine and arsenic acid at 200° for ten hours, allowed the melt to cool, treated the product first with hypophosphorous acid in aqueous hydrochloric acid and then with hydrogen peroxide, and obtained 6-amino-3-pyridinearsonic acid. A similar fusion of 2-pyridinol and arsenic acid was first reported by Binz, Kath, and Maier-Bode (*45,46*) to give the tautomers, XVI-9 and XVI-10. Several years later, however, Binz and Maier-Rode (*6*) found, in fact, that the fusion reaction gave the isomeric arsonic acids, XVI-9 and XVI-11. The former product, which is identical



If

(XVI-9) (XVI-10) (XVI-11)

with that obtained from the diazotization of 5-amino-2-pyridinol, predominates when the reaction period is three hours; a twelve- to twenty-four-hour reaction period gives predominantly XVI-11, which is identical with the product obtained by the diazonium reaction from 3-amino-2-pyridinol.

2-Pyridinol has also been arsonated with ClAsO (prepared from arsenious oxide and arsenic trichloride); the product, presumably 5-arsenoso-2-pyridinol, was oxidized to XVI-7 (27).

Plazek (78) reacted 2-dimethylaminopyridine with arsenic trichloride, introducing the dicliloroarsine group in the 5 position; hydrolysis followed by the usual reduction-reoxidation gave 6-dimethylamino-3-pyridinearsonic acid. 2-Methylaminopyridine and arsenic acid were fused at 190–200° for ten hours to give a 6-methylamino-x-pyridinearsonic acid of undetermined structure (*34*).

(d) From Other Arsenic Compounds of Pyridine. Pyridinearsonic acids are formed by hydrolysis, oxidation, or a combination of both, from dichloropyridylarsines, tetrachloropyridylarsines, arsenosopyridines, or arsenopyridines. Some of these reactions have already been cited and others are mentioned in later sections of this chapter.

b. Properties

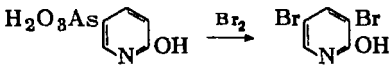
Only 3-(or 5-)pyridinearsonic acids are known. They are high melting, generally crystalline solids, insoluble in water, but soluble in aqueous sodium bicarbonate. These compounds are remarkably stable: the carbon-arsenic linkage is unaffected by (*a*) hydrochloric, nitric, and sulfuric acid, even at 100°; (*b*) reducing agents such as sodium amalgam, sulfur dioxide, ferrous sulfate, sodium hydrosulfite, or hypophosphorous acid; or (c) aqueous sodium hydroxide. An aqueous solution of the disodium salt of 6-hydroxy-3-pyridinearsonic acid was kept for one year without evidence of decomposition; even brief heating at 170° was without effect. The pyridinearsonic acids and their salts are more stable than the corresponding benzenearsonic acids.

Pyridinearsonic acids form insoluble barium, magnesium, mercury, copper, and silver salts.

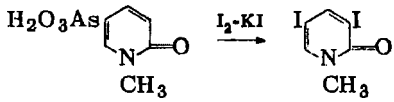
The known pyridinearsonic acids are listed in Table XVI-1 (p. 454) and the *N*-substituted pyridinearsonic acids in Tables XVI-2–XVI-4 (pp. 455 f.).

c. *Reactions*

Despite the stability of the carbon-arsenic bond, the arsonic acid group can be displaced by halogen, as shown in equations XVI-12 (*46*) and XVI-13 (*45*) (cf. ref. *48*). Nuclear halogenation is also possible without displacing the arsonic acid group (*9,12,19,37–40*).

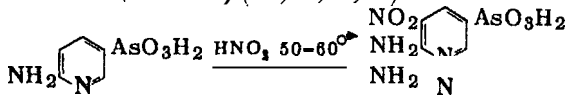


(XVI-12)

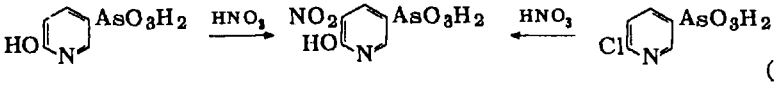


(XVI-13)

Normal nitration is also possible, as shown in equation XVI-14 (8). Similarly, 6-hydroxy-3-pyridinearsonic acid nitrates in tlie **5** position (*8,17,18,29*); the same product is obtained by nitrating the 6-halo-3-pyridinearsonic acid (XVI-1**5**) (*24,25,48,83*).

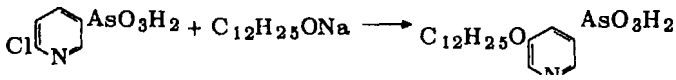


(XVI-14)

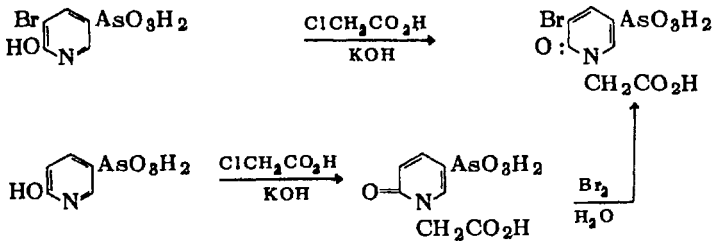


(XVI-15)

Other normal reactions of substituted pyridinearsonic acids include metathetical replacement of chlorine (XVI-16) (*18*) and *N*-alkylation of 2-pyridones (XVI-17) (*9,13*).



(XVI-16)



(XVI-17)

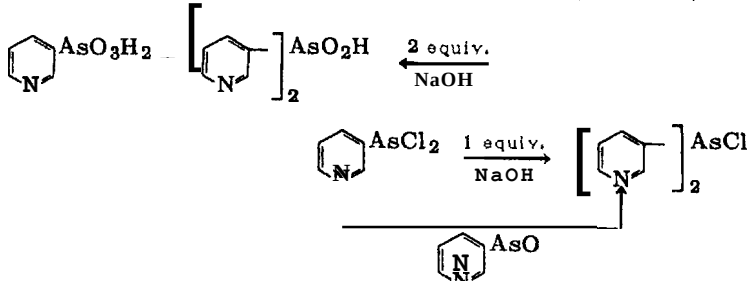
Reduction of pyridinearsonic acids in hydrochloric acid with sulfur dioxide gives the dichloropyridylarsine (*43*); zinc reduction in mineral acid gives the pyridylarsine (*12,21,43*) or tlie arsenopyridine (*50*), although arsenopyridines are more generally prepared by hypophosphorous acid reduction (see p. 449).

2. Chloropyridylarsines

As reported by Binz and von Schickh (*51*), the Scheller reaction of 3-aminopyridine, arsenic trichloride, and copper bronze in acetic acid with aqueous sodium nitrite gave a mixture of dichloro-3-pyridylarsine and tetracliloro-3-pyridylarsine: tlie latter compound is reduced to the former with sulfur dioxide in the presence of a trace

of hydrogen iodide. Dichloro-3-pyridylarsine is also obtained by the reduction of 3-pyridinearsonic acid in concentrated hydrochloric acid with sulfur dioxide (*43*), and from 3-pyridylmercuric chloride and arsenic triciiloride (76). 2-Dimethylaminopyridine and arsenic trichloride gave dichloro(2-dimethylamino-5-pyridyl)arsine (*78*).

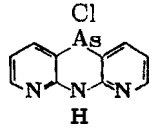
Dichloro-3-pyridylarsine reacts with one equivalent of *N* sodium hydroxide or with 3-arscnosopyridine to give chlorobis(3-pyridyl)-arsine; two equivalents of sodium hydroxide gives 3-pyridinearsonic acid and bis(3-pyridyl)arsinic acid (XVI-18) (*70–73,76*).



(XVI-18)

Attempts to prepare the azaphenarsazine compounds XVI-19 and XVI-20 by the cyclization of 2-anilinopyridine and bis(2-pyridyl)-amine, respectively, with arsenic tricliloride, were unsuccessful ***(64)***.

(XVI-19)



(XVI-20)

The chloropyridylarsine hydrochlorides are stable crystalline compounds only slightly affected by water. With aqueous sodium hydroxide, as noted above, the hydrolysis proceeds stepwise. The properties of these compounds demonstrate again the remarkable stability of arsenic compounds of pyridine.

The known chloropyridylarsines are listed in Table XVI-5 (p. 457).

3. Arsenosopyridines

Arsenosopyridines are obtained by sulfur dioxide reduction of the corresponding pyridinearsonic acids (*9,12,78*). 5-Arsenoso-2-

pyridinol has been obtained from 2-pyridinol and ClAsO at 130–180° (*27*), by the hydrolysis of dichloro(2-hydroxy-5-pyridyl)arsine (*45*), and by the dehydration of 6-hydroxy-3-pyridinearsonous acid (*9,12*).

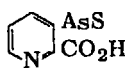
The arsenosopyridines are usually obtained as high melting amorphous solids. soluble in water and insoluble in methanol, etlianol, acetone, ether, and benzene. 5-Arsenoso-2-oxo-1(2*H*)-pyridineacetic acid forms a crystalline disodium salt ***(9)***.

Xrsenosopyridines arc oxidized by hydrogen peroxide to the corresponding pyridinearsonic acids (*9,51*). With thiophenol, 3-arsenosopyridine gave dithio-3-pyridinearsonous acid diphenyl ester, 3-PyAs(SPh)$_2$. McCleland and Wilson (*76*) reported that the distillation of 3-arsenosopyridine followed by oxidation of the distillate with hydrogen peroxide gave tris(3-pyridyl)arsine oxide. Dichloro(3-pyridyl)arsine and 3-arsenosopyridine gave chlorobis(3-pyridyl)arsine.

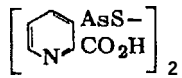
The known arsenosopyridines are listed in Table XVI-6 (p. 458). Only 3-(or 5-)arsenosopyridines are known.

4. Pyridylarsine Sulfides

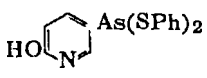
Plazek (78) dissolved 3-arsenosopicolinic acid in concentrated aqueous ammonia, treated the solution with hydrogen sulfide and obtained 3-thioarsenosopicolinic acid (XVI-21); 3-arsonopicolinic acid in water with hydrogen sulfide gave XVI-22. 5-Arsenoso-2-pyridinol and thiophenol gave XVI-23. Cragoe and Hamilton ***(59)***



(XVI-21)

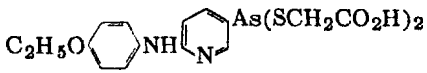


(XVI-22)



(XVI-23)

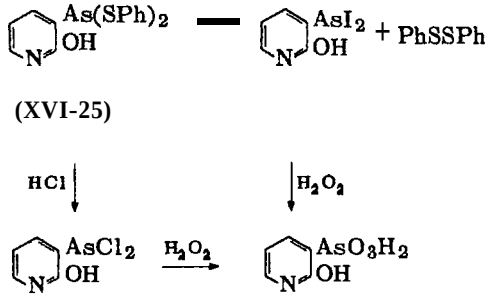
treated 6-(*p*-ethoxyanilino)-3-pyridinearsonic acid with thioglycolic acid in aqueous alkali and obtained XVI-24. Derivatives with 2-mercaptobenzothiazoles and ethylenebisdithiocarbamic acids have been reported (*95,96*).



(XVI-24)

Compounds of the structure XVI-23, XVI-24, and XVI-25 are stable crystalline solids. Binz and Maier-Bode, by the fusion of 2-pyridinol and arsenic acid, obtained a mixture of 2-hydroxy-3-pyridinearsonic acid and **6-hydroxy-3-pyridinearsonic** acid, which could not be separated. Reduction with sulfur dioxide gave the arsenoso derivatives, which reacted with thiophenol to give **XVI-23** and XVI-25; these were separated by fractional crystallization from methanol (*45,46*).

Compounds **XVI-23** and **XVI-25,** treated with methanolic iodine or hydrochloric acid followed by hydrogen peroxide, gave the corresponding hydroxypyridinearsonic acids **(XVI-26)** (*45*).



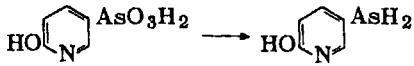
(XVI-26)

The known pyridylarsine sulfides are listed in Table XVI-7 **(p. 459).**

5. Pyridylarsines

a. Compounds of the Type PyAsH₂

The reduction of pyridinearsonic acids with zinc and dilute hydrochloric or sulfuric acid gives 3-pyridylarsines (XVI-26a) (12.21, *43*).



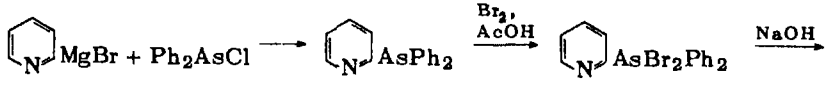
(XVI-26a)

These compounds are water-soluble unstable solids which oxidize readily to the corresponding arsenopyridines.

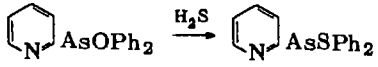
The **known** compounds of this type will be found in Table **XVI-8** (p. **460).**

b. Compounds of the Type PyR_2As, Py_2RAs, Py_3As, and Their Pentavalent Derivatives

2-Pyridylmagnesium bromide reacted with chlorodiphenylarsine to give diphenyl-2-pyridylarsine (XVI-26b) and with dichlorophenylarsine to give bis(2-pyridyl)phenylarsine (75). Gilman and Avakian (65) obtained dimethyl-3-pyridylarsine from 3-pyridyllithium and iododimethylarsine. Tris(2-pyridyl)arsine was prepared from 2-pyridylmagnesium bromide and arsenic trichloride. Some of the reactions of diphenyl-2-pyridylarsine are shown in equation XVI-26c.

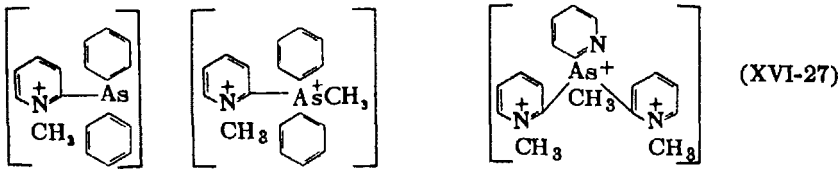


(XVI-26b)



(XVI-26c)

Diphenyl-2-pyridylarsine forms a monopicrate; with methyl iodide in benzene, it gives a monomethiodide, and with methyl iodide alone, a dimethiodide. Even under the most vigorous conditions, phenylbis(2-pyridyl)arsine formed only a dimethiodide, while tris(2-pyridyl)arsine formed a trimethiodide. Since pyridine reacted more vigorously than triphenylarsine with methyl iodide, Mann and Watson (75) reasoned that the methyl iodide attacked the pyridyl nitrogen atom first and the tertiary arsenic atom only under more vigorous conditions. There was evidence, therefore, for the existence of the cations XVI-27.



(XVI-27)

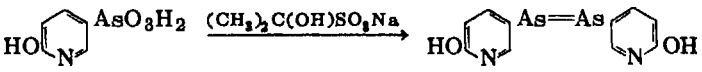
α-Picolyldimethylarsine has recently been prepared; it forms chelates with the heavy metals (93).

Compounds of the general formulas PyR_2As, Py_2RAs, and Py_3As are obtained as high-boiling distillable oils or crystalline solids.

The known compounds of these types are listed in Table XVI-9 (p. 460).

6. Arsenopyridines

During the preparation of pyridinearsonic acid by the Scheller method or its modifications, the crude arsonic acids were converted to arsenopyridines by means of hypophosphorous acid in dilute hydrochloric acid; the crude arsenopyridines were then reoxidized to the arsonic acids with hydrogen peroxide. This remains the most general method for the synthesis of arsenopyridines. Another procedure, applicable only with 6-hydroxy-3-pyridinearsonic acid, is reduction in aqueous sodium carbonate by means of sodium acetone sulfoxylate or sodium formaldehyde sulfoxylate (XVI-29) (*1,8,9,11, 15,30*). The 2,2′-dihydoxy-5,5′-arsenopyridine (XVI-28), obtained in

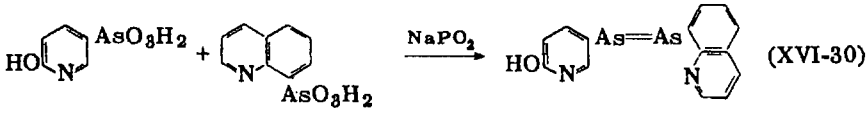


(XVI-29)

(XVI-28)

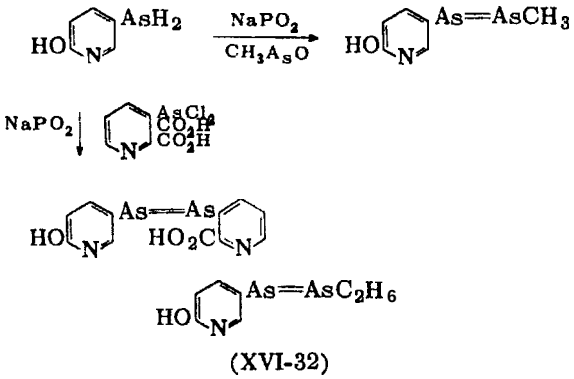
this procedure by precipitation from the aqueous sodium carbonate solution with hydrochloric acid, could be redissolved in aqueous sodium hydroxide but not in aqueous sodium carbonate. When, however, reduction was effected with sodium hyophosphite, the product, apparently the same compound, was insoluble in aqueous sodium hydroxide. There was no satisfactory explanation for this anomaly.

6-Chloro-3-pyridinearsonic acid and (*a*) zinc dust in dilute sulfuric acid or (*b*) electrolytic reduction in 5% sulfuric acid with a lead cathode, gave the same product, 3,3′-arsenopyridine (50). The reduction of a mixture of 6-hydroxy-3-pyridinearsonic acid and 8-quinolinearsonic acid by means of sodium hypophosphite gave the unsymmetrical arseno compound (XVI-30) (*12,22,30,36*). The re-



(XVI-30)

action of an arsenosopyridine or a dichloropyridylarsine with a pyridylarsine also led to unsymmetrical arsenopyridines (XVI-31) (*14,21,76*). A mixture **ot** magnesium ethylarsinate, 6-hydroxy-3-pyridinearsonic acid, and hypophosphorous acid in dilute hydrochloric acid gave (XVI-32) (*60*).



(XVI-31)

(XVI-32)

While most arsenopyridines are water-insoluble high melting amorphous solids, several have been obtained crystalline. These compounds are often inadequately described, since they have usually been isolated only as intermediates in the reduction-reoxidation method of purifying pyridinearsonic acids.

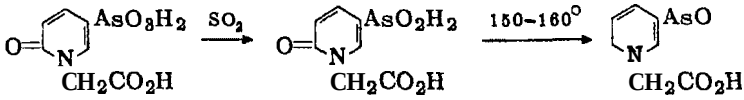
The arsenopyridines are oxidized by hydrogen peroxide to the corresponding pyridinearsonic acids. On stirring, until solution occurred, a mixture of 2,2′-dihydroxy-3,3′-diamino-5,5′-arsenopyridine and sodium formaldehyde sulfoxylate in water, and then adding methanol, a yellow solid separated which redissolved readily in water and gave a neutral solution; the structure of this compound was not disclosed.

The known symmetrical arsenopyridines are listed in Table XI-10, symmetrical *N,N′*-disubstituted arsenopyridones in Table XI-11, and unsymmetrical arsenopyridines in Table XI-12 (pp. 461 ff.). Only 3-(or 5-)arsenopyridines are known.

7. Pyridinearsonous and Pyridinearsinic Acids

Comparatively little effort has been devoted to the synthesis of pyridinearsonous and pyridinearsinic acids, and, in general, the few compounds synthesized have been described inadequately.

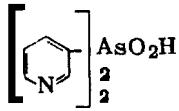
Binz and Räth *(9)* reported that the reduction of 5-arsono-2-oxo-1(2*H*)-pyridineacetic acid with sulfur dioxide gave the arsonous acid (XVI-33); this gave the arsenoso derivative at 150–160° **(XVI-34).**



(XVI-34)

(XVI-33)

McCleland and Wilson (76) obtained 3-pyridinearsonous acid by the hydrolysis **of** dichloro-3-pyridylarsine. Ishikawa (*72,73*) reported **the** preparation **of** XVI-35 by the reaction of chlorobis(3-pyridyl)-



(XVI-35)

arsine with one equivalent of *N* sodium hydroxide solution, or with aqueous potassium cyanide or silver cyanide. The known pyridinearsonous and pyridinearsiriic acids are listed **in** Table XVI-13 (p.462).

8. Chemotherapy and Pharmacology of Arsenic Compounds of Pyridine

The important contributions **of** Binz. Räth, and their co-workers were divided between the synthesis and chemotherapeutic evaluation of their compounds. **It** seemed likely that these compounds should find utility as trypanosomicidal and spirocheticidal agents. In spite of the considerable effort to demonstrate the activity in experimental typanosomiasis and syphilis *(2,4,5,8,19,20,23,?7–40,44,47, 49,58,63,66,67,74,85)*, there is no report of their clinical use. The reason for this, in part at least, was that the pyridine arsenic compounds showed greater toxicity than their benzene analogs.

B. ANTIMONY COMPOUNDS

6-Hydroxy-8-pyridinestibonic acid has been prepared in about 20% yield by the Bart reaction From 5-amino-2-pyridinol *(31)*. **Tetrachloro-3-pyridylstibine** was prepared **by** the Scheller reaction

from 3-aminopyridine (*51*). The Bart reaction was used to prepare 6-(carboxymethylthio)-3-pyridinestibonic acid (*86*).

The pyridinestibonic acids have been inadequately described. The carbon-antimony bond is considerably weaker than the carbon-arsenic bond and was cleaved by an attempt to reduce 6-hydroxy-3-pyridinestibonic acid with hypophosphorous acid.

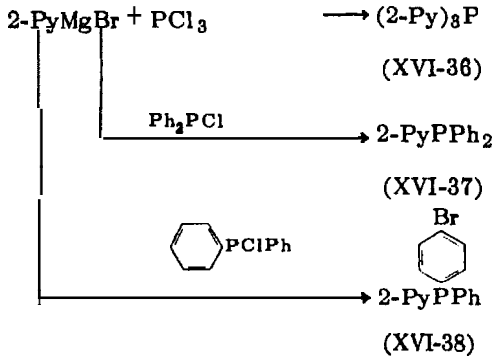
The known antimony compounds of pyridine are listed in Table XVI-14 (p. 462).

No bismuth compounds of pyridine have been described.

C. PHOSPHORUS COMPOUNDS

By heating 2-dimethylaminopyridine and phosphorus trichloride for eight hours at 100°, Plazek (*78*) apparently obtained dichloro-(2-dimethylamino-5-pyridyl)phosphine, although he did not isolate the compound. With aqueous sodium hydroxide, this gave 6-dimethylamino-3-pyridinephosphonous acid, a weak monobasic acid, neutral to litmus and acid to phenolphthalein, which formed soluble alkali metal salts and insoluble heavy metal salts, and was oxidized with mercuric chloride to 6-dimethylamino-3-pyridinephosphonic acid. The decomposition of 3-pyridyldiazonium fluoroborate by phosphorus trichloride gave 3-pyridylphosphonic acid ***(91)***. The addition of dialkylphosphites to 2- and 4-vinylpyridines gave the corresponding pyridylethylphosphonic acid esters, which were hydrolyzed to the phosphonic acids (*94*).

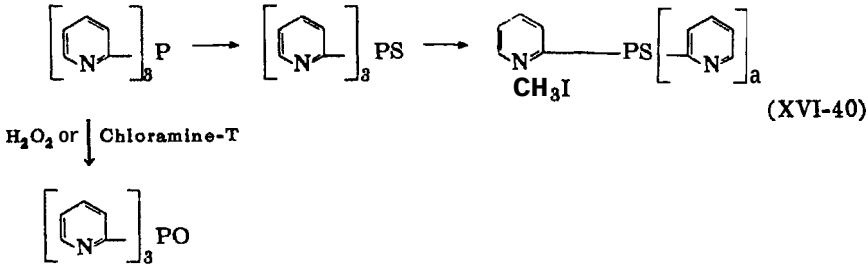
Davies and Mann (*89*) and Mann and Watson (*75*) prepared a number of tertiary phosphines by the reactions shown (XVI-39).



(XVI-39)

These compounds were obtained as distillable viscous oils or crystalline solids. Attempts to resolve XVI-38 or the corresponding 3-pyridyl isomer by means of camphor- or bromocamphorsulfonic acid were unsuccessful. With methyl iodide, XVI-36, **XVI-57,** and diphenyl-2-pyridylphosphine formed only monomethiodides, apparently phosphonium compounds. Tlie phosphonium ion evidently deactivated the pyridine nitrogen atom toward addition of methyl iodide.

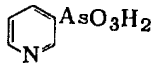
By heating with sulfur in benzene solution, the tertiary phosphines formed phosphine sulfides. These also add a molecule of methyl iodide, but only under more vigorous conditions than required for the tertiary phosphines themselves. Here of course phosphonium salt formation is no longer possible; addition presumably occurs at one of the pyridine nitrogen atoms. The tertiary phosphines react with hydrogen peroxide in acetone or Chloramine-T in ethanol, to give phosphine oxides (XVI-40) (75). The known



(XVI-40)

phosphorus compounds of pyridiiie are listed in Table XVI-15 (p. **465).**

D. TABLES

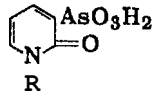
TABLE XVI-1. 3-Pyridinearsonic Acids 

Substituents	M.p., °C.	Ref.
None	158–59 (hydrochloride, m.p. 195–97)	4,43,50,51,72,73,76
6-Chloro	178–79	12,28,32,43,50,51,72,77
6-Bromo	175	12
6-Iodo	173	12
5-Chloro-6-hydroxy	237	12,28
5-Bromo-6-hydroxy	>300	4,9,12,19,37,38,39,40,46
5-Bromo-6-acetoxy		23
5-Iodo-6-hydroxy	289	6,12,23
5-Iodo-2-hydroxy	270–72	20,48
5-Nitro		26,35
6-Amino-5-nitro		24,25
6-Hydroxy-5-nitro	250	17,18,24,25,29,46,48
2-Hydroxy-5-nitro		26,35
5-Amino		26,35
6-Amino	135–37 200 (dec.)	4,12,28,33,56
6-Dimethylamino		78
6-Ethylamino		4,7
6-Diethylamino		4
5-Amino-6-hydroxy		4,23,26,35,48
5-NH_2COCH_2NH-6-OH		48
5,6-(—$NHCO_2$—)		48
5-Amino-2-hydroxy		26,35
5-Acetamido-6-hydroxy		4,23,48
6-*p*-Carboxyanilino	247–48	59
6-p-Arsonoanilino	>250	59
6-(*p*-$NH_2SO_2C_6H_4NH$)	>250	59
6-p-Phenetidino	216–18	59
6-(2-Morpholino-5-pyridylamino)	128–29	57
6-(2-Thiomorpholino-5-pyridylamino)	174–75	59
6-Hydrazino	>240	43
6-P-Nitrobenzalhydrazino		43
6-p-Aminobenzalhydrazino		43
6-(5-Keto-3-Methyl-1-pyrazolyl)		43
6-Hydroxy	215, >350	5,6,12,27,28,32,33,45,46,51

TABLE XVI-1 ***(continued)***

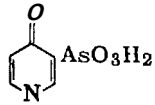
Substituents	M.p., °C.	Ref.
2-Hydroxy	219–20	6
4-Hydroxy		4,9
6-Methoxy	>260	8,45
6-Ethoxy	>260	8
6-Propoxy	>260	8
6-Butoxy	>260	8
6-*i*-Pentyloxy	115	8
6-(2-Octyloxy)	>260	8
6-Dodecyloxy	>275	8
6-Ethylthio	145	87
2-Carboxy	280–300	78

TABLE XVI-2. 1-Substituted 1,2,-Dihydro-2-oxo-3-pyridinearsonic acids



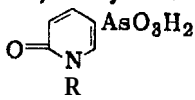
R	M.p., °C.	Ref.
CH_3	255–57	6
C_4H_9	188–89	9
$CH_2CH{:}CH_2$	178–79	9
$CH_2C_6H_5$	237–38	9
CH_2COOH	231 (dec.)	9
CH_2CONH_2	262–63 (dec.)	3,9

TABLE XVI-3. 1-Substituted 1,4-Dihydro-4-oxo-3-pyridinearsonic acids



R	M.p., °C.	Ref.
CH_3	285 (dec.)	9
C_4H_9	107–108	9
$CH_2C_6H_5$	221–22	9
CH_2CONH_2	232 (dec.)	3,9

TABLE XVI-4. 1-Substituted **1,6-Dihydro-6-oxo-3-pyridinearsonic** Acids



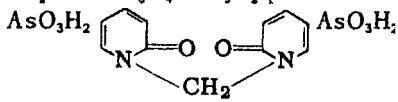
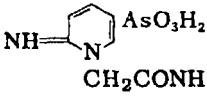
Substituents	R	M.p., °C.	Ref.
5-Iodo	CH_3	254–57	8,9,45
5-Nitro		250	9
5-CH_3CONH		270	9
	C_2H_5	183 (dec.)	45
	C_3H_7	197	45
	C_4H_9	146–47	45
	$CH_2CH(CH_3)_2$	213	9,34
	$CH_2CH_2CH(CH_3)_2$	154–55	9
	$CH_2CH:CH_2$	154–55	9
	$CH_2C_6H_5$	227–28	9,34
	CH_2CO_2H	270	9
5-Bromo	CH_2CO_2H	240–41	9
	CH_2CONH_2	220 (dec.)	3,9
	$CH_2CONHC_6H_5$	240 (dec.)	9
	$CH_2CONHC_6H_4AsO_3H_2$-*p*	262	3,4
			72
			3

TABLE XVI-5. Chloropyridylarsines, $PyAsCl_2$, $PyAsCl_4$, and Py_2AsCl

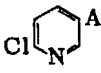
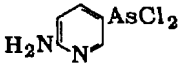
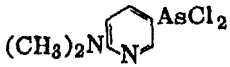
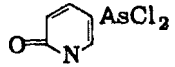
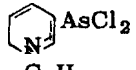
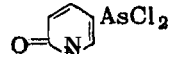
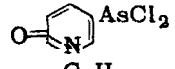
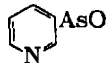
Compound	Physical properties, derivatives	Ref.
3-$PyAsCl_2$	m.p. 137°; hydrochloride, m.p. 226–27°	43,51,71,76
$(3\text{-}Py)_2AsCl$	dihydrochloride, m.p. 283–85°	71,76
3-$PyAsCl_4$		51
		71
		71
	forms a hydrochloride, m.p. unreported	78
	hydrochloride, m.p. 154°	45,51
		45
	forms a hydrochloride, m.p. unreported	78
	m.p. 167"	45
	hydrochloride, m.p. 132°	45
	hydrochloride, m.p. 124°	45
	hydrochloride, m.p. 113–15	45

TABLE XVI-6. 3-Arsenosopyridines 

Substituents	Mp., °C.	Ref.
None	187 (dec.)	43,51,71
6-Chloro	138 (dec.)	12
6-Brorno	159 (dec.)	12
6-Iodo	145 (dec.)	12
2-Hydroxy	244–47	6
6-Hydroxy	251 (dec.)	12,27
6-Butoxy	186	8
5-Chloro-6-hydroxy	195 (dec.)	12
5-Bromo-6-hydroxy	232 (dec.)	12
5-Iodo-6-hydroxy	200 (dec.)	12
6-Amino	90 (dec.)	12
6-Dimethylamino		78
5-Amino-6-hydroxy		48
2-Carboxy	316 (dec.)	78
1(2*H*)-Carboxymethyl-2-0x0	231 (dec.)	9
1(6*H*)-Methyl-6-oxo	102–17	45
I(6*H*)-Ethyl-6-oxo	92–93	45
1(6*H*)-Propyl-6-oxo	74–75	45
1(6*H*)-Butyl-6-oxo	83 (dec.)	45
1(6*H*)-Carboxymethyl-6-oxo	230–34 (dec.)	9

TABLE XVI-7. Pyridylarsine Sulfides

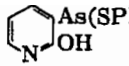
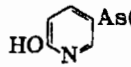
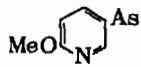
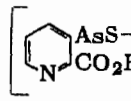
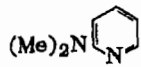
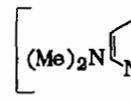
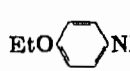
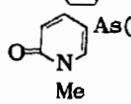
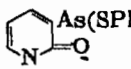
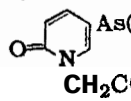
Compound	M.p., °C.	Ref.
	122	6
	153	45
	91	45
	250 (dec.)	78
		78
	205–6	78
	118–20	78
	200–1	59
	122	45
	132	6
	176	9

TABLE XVI-8. Pyridylarsines $PyAsH_2$

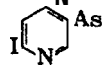
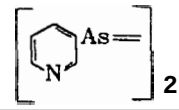
Compound	M.p., °C.	Ref.
	102 (dec.)	43
	135 (dec.)	12
		12
	140 (dec.)	12
		12,21

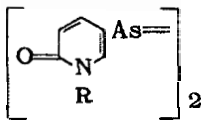
TABLE XVI-9. Unsymmetrical Arsines, $PyAsR_2$ and Py_2AsR, and Pentavalent Derivatives

Compound	Physical properties, derivatives	Ref.
3-$PyAs(Me)_2$	b.p. 90–91°/14 mm.	65
2-$PyAs(Me)_2$	b.p. 146–48°/16 mm.	65
$(2\text{-}Py)_3As$	m.p. 85.0–85.5°; dipicrate, m.p. 152–53° (dec.); trihydrochloride, m.p. 152° (dec.); dimethiodide, m.p. 213–15° (dec.); dimethopicrate, m.p. 180–82°	75,89,91
2-PyAsPh,	m.p. 62°; b.p. 192–250°/0.2 mm.; monopicrate, m.p. 171.5–72.5°; monomethiodide, m.p. 160–62°; dimethopicrate-H_2O, m.p. 152.5–53.0°	75
$(2\text{-}Py)_2AsPh$	m.p. 88°; dipicrate, m.p. 142–43°; dihydrochloride, m.p. 146–47°; dimethiodide, m.p. 193–95° (dec.); dimethopicrate, m.p. 190–91°	75
2-$PyAsBr_2Ph_2$		75
$(3\text{-}Py)_3AsO$	m.p. 226°; trihydrochloride, m.p. 221° (dec.)	76
2-$PyAsOPh_2$	monopicrate, m.p. 144–45°	75

TABLE XVI-10. Symmetrical Arsenopyridines 

Substituents	Ref.
	43,50,51,76
6-Chloro	12
6-Bromo	12
6-Iodo	12
2-Hydroxy	6
4-Hydroxy	7
6-Hydroxy	1,12,21,36,42
2-Hydroxy-5-iodo	28
5-Chloro-6-hydroxy	12
5-Bromo-6-hydroxy	12
5-Iodo-6-hydroxy	12
6-Amino	12
6-dimethylamino	12
5-Amino-6-hydroxy	4,48
2-Carboxy[a]	78

[a] M.p. 230–45° (dec.) No m.p.'s are reported for the other compounds in this table.

TABLE XVI-11. Symmetrical 1,1′-Disubstituted 6(1*H*)-Dioxo-3,3′-arsenopyridines 

R	M.p., °C.	Ref.
Me	215–40 (dec.)	45
Et	162–64 (dec.)	45
Pr	121–132	45
Bu	250–51	9,45
CH_2CO_2H	210–15	9
CH_2CONH_2	267	9

TABLE XVI-12. Unsymmetrical Arsenopyridines

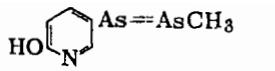
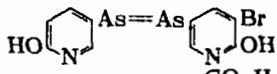
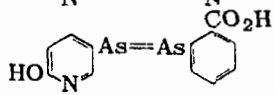
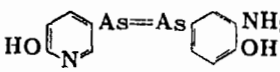
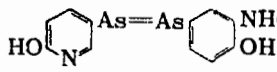
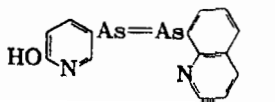
Compound	Ref.
	21
	1,30
	21,22,55
	22
	22,55
	

TABLE XVI-13. Pyridinearsonous and Pyridinearsinic Acids

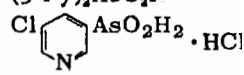
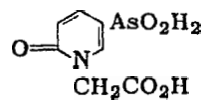
Compound	M.p., °C.	Ref.
$(3\text{-Py})_2AsO_2H$	203–4	72,73,76
		72
	191 (dec.)	9

TABLE XVI-14. Antimony Compounds of Pyridine

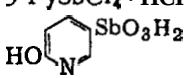
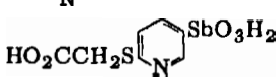
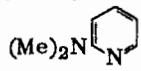
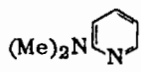
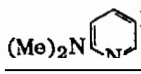
Compound	M.p., °C.	Ref.
$3\text{-PySbCl}_4 \cdot HCl$	240 (dec.)	4,51
		4,31
		86

TABLE XVI-15. Phosphorus Compounds of Pyridine

Compound	Physical properties, derivatives	Ref.
$(2\text{-Py})_3P$	m.p. 115°; dipicrate, m.p. 142–43°; trihydrochloride, m.p. 207.5–209.5 °; monomethopicrate · H_2O, m.p. 157–58°.	75,89
$(2\text{-Py})_2PMe$	dimethiodide · H_2O, m.p. 190°	75
$(2\text{-Py})_2PPh$	m.p. 96°; b.p. 196–210°/0.4 mm.	75
2-PyPPh_2	m.p. 84–85°; b.p. 132–55°/0.05 mm.; dipicrate · $2H_2O$, m.p. 128–30°; dihydrochloride, m.p. 185–87°; monomethiodide, m.p. 134–35°.	75
$p\text{-BrC}_6H_4PPhPy\text{-}3$	b.p. 202–10°/0.15 mm.; picrate, m.p. 143–44° (dec.)	89
$p\text{-BrC}_6H_4PPhPy\text{-}2$	m.p. 90–91°; b.p. 180–230°/0.01 mm.; picrate, m.p. 132°	89
$(2\text{-Py})_3PO$	m.p. 209°; monopicrate, m.p. 144–48°	75
$(2\text{-Py})_3PS$	m.p. 161°; monopicrate, m.p. 158–59°; monomethiodide, m.p. 156–57° (dec.); monomethopicrate, m.p. 208–11°(dec.)	75
2-PyPSMe_2	monomethopicrate, m.p. 145–47°	75
2-PyPSPh_2	m.p. 119°	75
$(2\text{-Py})_2PSPh$	monopicrate, m.p. 141.5–42.5 °; dihydrochloride, m.p. 165–71° (dec.); monomethopicrate · H_2O, m.p. 200–202° (dec.)	
$p\text{-BrC}_6H_4PSPhPy\text{-}3$	m.p. 115–16°	89
$p\text{-BrC}_6H_4PSPhPy\text{-}2$	m.p. 109°; methiodide, m.p. 132–34°(dec.)	89
		90
	m.p. 250–52° (dec.)	90
	m.p. > 300°	90

BIBLIOGRAPHY

1. U.S. patent 1,667,238, Binz; *C.A.*, **22**, 1981[3] (1928).
2. Hinz. *Angew. Chem.*, **43**, 452 (1930).
3. German patent 556,738, Binz; *C.A.*, **27**, 3741 (1933).
4. Hinz. *Angew. Chem.*, **28**, 425 (1935).
5. German patent 671,563, Hinz; *C.A.*, **33**, 6531[8] (1939).
6. Binz and Maier-Bode, *Ann.*, **487**. 119 (1931).
7. Hinz and Maier-Bode, *Angew. Chem.*, **49**, 486 (1936).
8. Hinz, Maier-Bode, and Morisawa, *ibid.*, **46**, 349 (1933); *C.A.*, **27**, 4233[8] (1933).

9. Hiriz. Maier-Bode, and Rost, *ibid.*, **44,** 835 (1931).
10. British patent 255.861. Binz and Kith: *C.A.*, **21,** 29078 (1927).
11. Hritish patent 255,892, Hinz and Kiith; *C.A.*, **21,** 29079 (1927).
12. Binz and Riith, *Ann.*, **455,** 127 (1927).
13. Canadian patent 267,560, Binz and Kiitli: *C.A.*, **21,** 16607 (1927).
14. Canadian patent 267,561, Hinz and Riith; *C.A.*, **21,** 16607 (1927).
15. Canadian patent 267,562, Hinz and Kiitli; *C.A.*, **21,** 16608 (1927).
16. U.S. patent 1,678,760, Hinz and Kith: *C.A.*, **22,** 36687 (1928).
17. British patent 275,590, Binz and Kiith; *C.A.*, **22,** 22443 (1928).
18. U.S. patent 1,675,402, Binz and Kith; *C.A.*, **22,** 31709 (1928).
19. U.S. patent 1,680,587, Binz and Kiitli; *C.A.*, **22,** 37371 (1928).
20. Hinz and Räth, *Biochem. Z.*, **203,** 218 (1928); *Chem. Zentr.*, **1929 I,** 1125.
21. German patent 475,937, Hinz and Riith; *C.A.*, **23,** 37136 (1929).
22. German patent 488,574, Hinz and Kiitli: *C.A.*, **24,** 21385 (1930).
23. Binz and Kiitli, *Klin. Wochschr.*, **9, 2297** (1930); *C.A.*, **25,** 21929 (1931).
24. German patent 504,829, Binz and Riith; *C.A.*, **25,** 5243 (1931).
25. Austrian patent 112,133, Binz and Riith; *Chem. Zentr.*, **1929 II,** 489.
26. U.S. patent 1,802,073, Binz and Kith: *C.A.*, **25,** 33617 (1931).
27. German patent 525,090, Binz and Kiith; *C.A.*, **25,** 40122 (1931).
28. German patent 528,1IS. Hint and Kiith; *C.A.*, **25,** 45589 (1931).
29. Swiss patent 130,148, Binz and Räth; *Chem. Zentr.*, **1929 II,** 489.
30. German patent 528.114, Binz and Kiith. *C.A.*, **25,** 45584 (1931).
31. German patent 530,495, Binz and Kiitli; *C.A.*, **25,** 51785 (1931).
32. German patent 536,424, Binz and Kiitli. *C.A.*, **26,** 9989 (1932).
33. German patent 537.896, Binz and Kiitli: *C.A.*, **26,** 13018 (1932).
34. German patent 544,361, Hinz and Kiith: *C.A.*, **26,** 35198 (1932).
35. German patent 544,667, Hinz and Kiith: *C.A.*, **26,** 36238 (1932).
36. German patent 544,779, Hinz and Räth; *C.A.*, **26,** 35169 (1932).
37. German patent 544,960, Hinr and Räth; *C.A.*, **26,** 36237 (1932).
38. British patent 263,142, Binz and Räth; *C.A.*, **22,** 1409 (1928).
39. French patent 625,784, Hinz and Kiith.
40. Swiss patent 124,525, Hinz and Räth.
41. German patent 546,144, Binz and Kiith: *C.A.*, **26,** 33357 (1932).
42. U.S. patent 1,902,756. Binz and Kiith: *C.A.*, **27,** 32237 (1933).
43. Hinr, Kith. and Gante, *Ann.*, **467,** 11 (1928).
44. Hinz, Räth, and Junkmann, *Biochem Z.*, **227,** 200 (1930); *Chem. Zentr.*, **1931 I, 963.**
45. Binz, Räth, and Maier-Bode, *Ann.*, **478,** 22 (1930).
46. Hinz, Kiith, and Maier-Bode, *Ann.*, **480,** 172 (1930).
47. Hinz, Kith, and Rost, *Biochem. Z.*, **223,** 249 (1930).
48. Hinz, Räth, and Urbschat, *Ann.*, **475, 136** (1929).
49. Hinz. Kiitli. and Wilke, *Biochem.* %, **223,** 176 (1930).
50. Hinz and von Schickh, *Ber.*, **68B,** 319 (1935).
51. Hinz and von Schickh, *Ber.*, **69B,** 1527 **(1936).**
52. German patent 633,867, Hiriz and von Schickh: *C.A.*, **31,** 8179 **(1937).**

53. Binz, Räth, and Wilke, *Biochem. Z.*, **223**, 176 (1930).
54. Binz and Wilke, *ibid.*, **241**, 256 (1931).
55. British patent 255,839, Binz and Räth; *C.A.*, **21**, 2907[8] (1927).
56. Chichibabin and Kirsanov, *J. Russ. Phys.-Chem. Soc.*, **59**, 405 (1927); *C.A.*, **22**, 2563[4] (1928).
57. Chichibabin and Kirsanov, *Ber.*, **60**, 766 (1927).
58. Christison, *Zentr. Bakteriol. Parasitenk, Abt. I Ref.*, **132**, 228 (1934); *C.A.*, **28**, 6851[7] (1934).
59. Cragoe and Hamilton, *J. Am. Chem. Soc.*, **67**, 536 (1945).
60. Austrian patent 117,478, Deutsche Gold and Silber-Scheideanstalt vorm Roessler; *Chem. Zentr.*, **1930 II**, 813.
61. Doak, Steinman, and Eagle, *J. Am. Chem. Soc.*, **62**, 3012 (1940).
62. German patent 554,950, Dohrn and Diedrich; *C.A.*, **26**, 5970[8] (1932).
63. Eagle, Hogan, Doak, and Steinman, *J. Am. Chem. Soc.*, **65**, 1236 (1943).
64. Gibson, Johnson, and Vining, *Rec. trav. chim.*, **49**, 1006 (1930).
65. Gilman and Avakian, *J. Am. Chem. Soc.*, **76**, 4031 (1954).
66. U.S. patent 2,435,392, Hamilton; *C.A.*, **42**, 4614g (1948).
67. Hasskó, *Zentr. Bakteriol. Parasitenk, Abt. I Ref.*, **127**, 299 (1933); *C.A.*, **27**, 2498[9] (1933).
68. Hatelid, Ph.D. Thesis, Univ. of Nebraska, 1942; mentioned in Reference (59).
69. Ishikawa, *J. Chem. Soc. Japan*, **62**, 1178 (1941); *C.A.*, **41**, 5512a (1947).
70. Ishikawa, *ibid.*, **63**, 801 (1942); *C.A.*, **41**, 3463a (1947).
71. Ishikawa, *ibid.*, **63**, 804 (1942); *C.A.*, **41**, 3463c (1947).
72. Ishikawa, *ibid.*, **63**, 811 (1942); *C.A.*, **41**, 3463d (1947).
73. Ishikawa, *ibid.*, **63**, 1262 (1942); *C.A.*, **41**, 3463d (1947).
74. Leiter, Downing, Hartwell, and Shear, *J. Natl. Cancer Inst.*, **13**, 365 (1952).
75. Mann and Watson, *J. Org. Chem.*, **13**, 502 (1948).
76. McCleland and Wilson, *J. Chem. Soc.*, **1932**, 1497.
77. Pieroni, *Atti accad. Lincei*, [6] **5**, 303 (1927); *C.A.*, **21**, 1814[5] (1927).
78. Plazek, *Roczniki Chem.*, **10**, 751 (1930); *Chem. Zentr.*, **1931 I**, 1453.
79. Austrian patent 107,595, Räth.
80. U.S. patent 1,753,658, Räth; *C.A.*, **24**, 2471[5] (1930).
81. U.S. patent 1,704,106, Scheller; *C.A.*, **23**, 1907[8] (1929).
82. German patent 522,892, Scheller; *C.A.*, **25**, 3664[8] (1931).
83. Austrian patent 112,133, Schering-Kahlbaum; *Chem. Zentr.*, **1929 II**, 489.
84. Von Schickh, *Angew. Chem.*, **51**, 779 (1938).
85. Schlossberger and Schüffner, *ibid.*, **47**, 768 (1934); *C.A.*, **29**, 5075 (1935).
86. U.S. patent 2,584,639, Steiger and Keller; *C.A.*, **46**, 11238f (1952).
87. Takahashi and Morita, *J. Pharm. Soc. Japan*, **64**, No. **7A**, 11 (1944); *C.A.*, **45**, 8014d (1951).
88. U.S. patent 1,827,680, Tisza and Joos; *C.A.*, **26**, 496[1] (1932).
89. Davies and Mann, *J. Chem. Soc.*, **1944**, 279.
90. Plazek, *Roczniki Chem.*, **14**, 1198 (1934); *Chem. Zentr.*, **1935 I**, 2177.
91. Gilman, Gregory, and Spatz, *J. Org. Chem.*, **16**, 1788 (1951).

92. Bennett, Burger, and Volk, *ibid.*, 23, 940 (1958).
93. Goodwin and Lions, *J. Am. Chem. Soc.*, 81, 311 (1959).
94. Maruszewska-Wieczorkowska and Michalski, J. Org. *Chem.*, 23, 1886 (1958).
95. Japan patent 8147–8 (1959); *C.A.*, 54, 2652a (1960).
96. Japan patent 7750 (1959); *C.A.*, 54, 21625f (1960).

CUMULATIVE SUBJECT INDEX

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