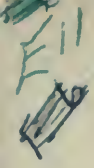

MONOGRAPHS ON INDUSTRIAL CHEMISTRY

EDITED BY SIR EDWARD THORPE C.B., LL.D., F.R.S.

SYNTHETIC COLOURING MATTERS

DYESTUFFS DERIVED FROM PYRIDINE, QUINOLINE, ACRIDINE AND XANTHENE

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DYESTUFFS DERIVED FROM PYRIDINE, QUINOLINE, ACRIDINE AND XANTHENE

BY

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TO MY OLD STUDENTS AND CO-WORKERS

PREFACE.

Nearly four years ago, Sir Edward Thorpe asked me to write a monograph on dyestuffs of the Acridine, Xanthene, Azine and Oxazine Groups for the Series on Industrial Chemistry which he is editing. The amount of material to be dealt with appeared large for one volume and it was decided to write two books, one dealing with acridine and xanthene compounds, the other with azines and oxazines.

In the course of the work it was found necessary to refer so frequently to pyridine and quinoline that the scope of the present monograph was enlarged. This seemed the more desirable on account of the interest recently taken in sensitising dyes derived from quinoline.

Patent literature has necessarily been used for much of the information. It is scarcely requisite to point out to the reader that a specification does not always contain the whole truth and nothing but the truth.

Much use has been made of the works of Schultz and Friedländer. With regard to the latter work my task has been very greatly facilitated by the gift of a copy of "Fortschritte der Theerfabrikation" from my old students at East London College, to whom my warmest thanks are due.

J. T. Hewitt.

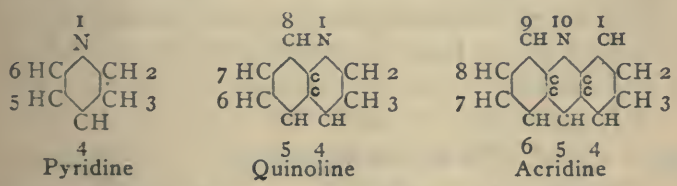
Manor House, Sutton,
Heston, Middlesex.

CONTENTS.

CHAPTER I.

PYRIDINE AND ITS HOMOLOGUES

The three bases, pyridine (C_5H_5N), quinoline (C_9H_7N), and acridine ($C_{13}H_9N$), although colourless, exhibit selective absorption in the ultra violet, and furnish compounds by substitution which are often coloured and sometimes behave as dyestuffs; this is more especially true of the derivatives of acridine. The constitution of the three bases may be represented as follows:-



and it is at once apparent that their relationships to one another resemble in a way those of benzene, naphthalene and anthracene.

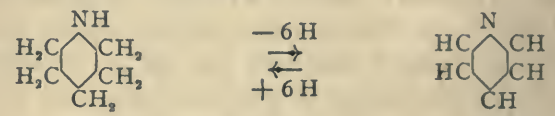
The constitution of pyridine is definitely settled by its relationship to piperidine, $C_5H_{11}N$, a secondary base obtainable from piperine, the alkaloid of pepper *(Piper nigrum)*, by heating with soda-lime (Cahours, *Ann. Chim. Phys.*, 1853, III, *38*, 76; Anderson, *Annalen*, 1861, *84*, 345). Piperidine has a six-membered ring; this is clear from its synthesis, for it may be prepared by adding 4 parts of sodium to a solution of one part of trimethylene cyanide in 8 parts of absolute alcohol (Ladenburg, *Annalen*, 1888, *247*, 53),

$$CH_2\langle\begin{matrix}CH_2\cdot CN\\CH_2\cdot CN\end{matrix} + 8\,H = CH_2\langle\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}\rangle NH + NH_3$$

and also by the dry distillation of the hydrochloride of pentamethylenediamine (Ladenburg, *Ber.*, 1885, *18*, 3101).

$$CH_2\langle \begin{matrix} CH_2\cdot CH_2\cdot NH_2 \\ CH_2\cdot CH_2\cdot NH_2 \end{matrix} = CH_2\langle \begin{matrix} CH_2\cdot CH_2 \\ CH_2\cdot CH_2 \end{matrix}\rangle NH + NH_3$$

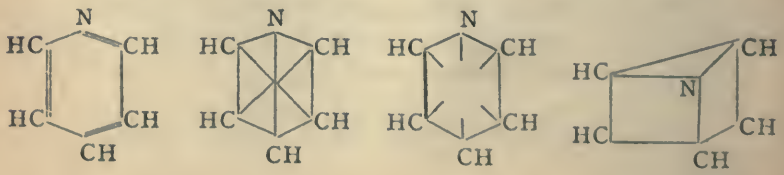
Since piperidine is also obtainable from pyridine by reducing its hot alcoholic solution with sodium (Ladenburg and Roth, *Ber.*, 1884, *17*, 388, 773; *Annalen*, 1888, *247*, 51), it follows that the carbon and nitrogen atoms of pyridine must also form a six-membered ring; this is confirmed by the fact that piperidine is oxidised to pyridine when heated with concentrated sulphuric acid to 300° (Koenigs, *Ber.*, 1879, *12*, 2344). The two bases are consequently related to one another in the following way,



The constitution of quinoline is fixed by its synthesis from aniline and its degradation to pyridine, and that of acridine by its synthesis from formyldiphenylamine and degradation to quinoline.

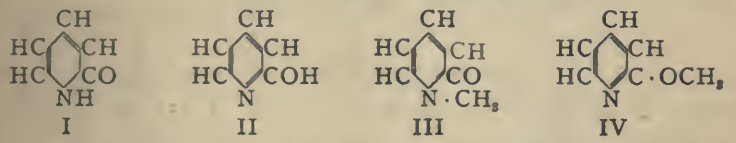
Dewar (*Zeitschr. f. Chem.*, 1871, 117), was the first to suggest a ring constitution for pyridine; he arranged the extra valencies of the nitrogen and carbon atoms in the following manner:

This is, however, only one way of representing the carbon atoms as tetravalent and the nitrogen as tervalent; just as several formulae have been proposed for benzene, so we may represent pyridine as constituted in various ways; e. g.-

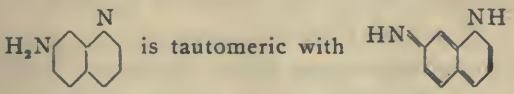


we may go even further and suppose that the molecule at one instant possesses one structure, at another instant, a different one. Corresponding formulae may be assigned to quinoline and acridine: these will be discussed later.

Many derivatives of these bases, especially those in which hydrogen in certain positions is replaced by the amino- or hydroxyl-group, exhibit tautomerism. For example, 2- and 4-N-methylpyridones exist, as well as the isomeric 2- and 4-methoxypyridines, but in each case only one corresponding hydrogen compound is known. Thus 2-pyridone corresponds to either formula I or II, but 2-methylpyridone (III) and 2-methoxypyridine (IV) are distinct compounds.



In the case of quinoline and acridine, tautomerism may be caused not only by substitution in the ring of which the nitrogen atom is a member, but also by substitution in a ring, all of whose members are carbon atoms, thus:



A somewhat different type of tautomerism is also possible in the case of the amino- and hydroxy-phenylpyridines.

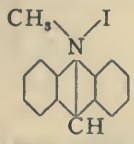
These various types of tautomerism should be kept in mind, for it is generally only such compounds as may be represented by tautomeric formulae, i. e. can possess a quinonoid configuration, which form real dyestuffs.[1])

Whilst acridine gives rise to a large number of dyestuffs,

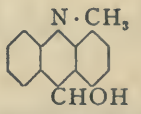
1) The author is not making a confession of quinonoid faith, but simply pointing out a fact. Thus in the azo-series, the dyestuffs are possibly (probably) not quinonoid, nevertheless they may be written with a tautomeric quinonoid structure.

quinoline to comparatively few and pyridine hardly any, a short account of the two simpler bases is desirable for a better understanding of the synthesis, reactions and properties of the acridine compounds; especially since the dyes used as photographic sensitisers are mostly derived from quinoline.

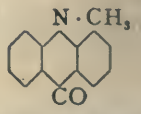
As tertiary bases, pyridine, quinoline and acridine each unite with one molecular proportion of an alkyl halide. The corresponding quaternary ammonium hydroxides are unstable, they usually undergo isomerisation to pseudo-bases which are then readily oxidised. The relationships in the case of acridine methiodide, methylacridol and methylacridone may be represented in the following way.



Acridine-methiodide



Methylacridol



Methylacridone

Occurence and Synthesis of Pyridine and its Derivatives

The pyridine bases are found in bone-oil (Anderson, *Annalen*, 1848, *70*, 38; 1851, *80*, 44) and amongst the products of distillation of bituminous shales (Williams, *Jahresb.*, 1854, 492) and of coal (Williams, *Jahresb.*, 1855, 552; Thenius, *ibid.*, 1861, 501). They are also produced when cinchonine is distilled with caustic potash (Williams, *ibid.*).

Many syntheses of the pyridine ring have been effected.

1. Ramsay obtained pyridine by passing a mixture of acetylene and hydrocyanic acid through a red-hot tube (*Ber.*, 1877, *10*, 736).

$$2\,C_2H_2 + HCN = C_5H_5N.$$

Liubawin was unable to confirm this reaction (*J. Russ. Phys.-Chem. Soc.*, 1885, *17*, 250).

2. Pyridine is formed when ethylallylamine is passed over litharge at 400—500° (Koenigs, *Ber.*, 1879, *12*, 2344).

$$NH(C_2H_5)(C_3H_5) + 3\,O = C_5H_5N + 3\,H_2O.$$

3. Piperidine is oxidised to pyridine not only by heating with concentrated sulphuric acid (v. s.), but also by nitrobenzene at 250—260° (Lellman and Geller, *Ber.*, 1888, *21*, 1921).

A peculiar oxidation of the piperidine to the pyridine nucleus occurs on heating benzoylpiperidine with benzaldehyde, when a dibenzylpyridine is formed (Rügheimer, *Annalen*, 1894, *280*, 36).

4. Aldehydes of the aliphatic series yield pyridine bases when heated with ammonia, e. g. —

$$4\,CH_3\cdot CHO + NH_3 = C_5H_2(CH_3)_3N + 4\,H_2O$$

$$2\,CH_2:CH\cdot CHO + NH_3 = C_5H_4(CH_3)N + 2\,H_2O$$

(Baeyer, *Annalen*, 1870, *155*, 283; Claus, *Annalen*, 1871, *158*, 222).

Pyridine and β-picoline are formed when glycerine is heated with ammonium sulphate and sulphuric acid. Pyridine is formed when "oxytrialdin" and "oxytetraldin" are heated with soda-lime (Schiff, *Annalen*, 1874, Suppl. Bd. *6*, 21).

Tschitschibabin (*J. Russ. Phys.-Chem. Soc.*, 1905, *37*, 1239) found in all the cases he investigated, that the action of ammonia on aldehydes proceeds according to the equation

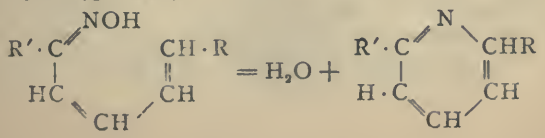
$$3\,R\cdot CH_2\cdot CHO + NH_3 = CH\begin{cases} CR:C(CH_2R) \\ CR \text{———} CH \end{cases}N + H_2 + 3\,H_2O$$

5. Some ketones give pyridine derivatives on heating with ammonia. Collidine is obtained from acetone and ammonium chloride at 265° (Riehm, *Annalen*, 1887, *238*, 17),

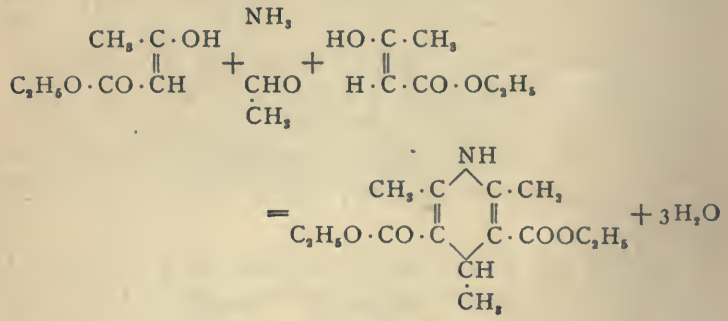
$$3\,C_3H_6O + NH_4Cl = C_5H_2(CH_3)_3N\cdot HCl + 3\,H_2O + CH_4$$

or from acetone and urea at 110—140° (Riehm), or from acetone and aldehyde-ammonia at 200° (Dürkopf, *Ber.*, 1888, *21*, 2713).

6. Substituted pyridines are formed by distilling oximes of ketones of the general formula $R\cdot CH:CH\cdot CH:CH\cdot CO\cdot R'$ (Scholtz, *Ber.*, 1895, *28*, 1726; 1899, *32*, 1935; 1903, *36*, 845; 1910, *43*, 1861).



7. Aldehyde-ammonia condenses with ethyl acetoacetate to give the di-ethyl ester of dihydrocollidinedicarboxylic acid: the two extra hydrogen atoms may be removed by oxidation with nitrous acid, and, after hydrolysis, carbon dioxide is removable by heating with lime with the result that collidine (trimethylpyridine) is obtained (Hantzsch, *Annalen*, 1882, *215*, 32).

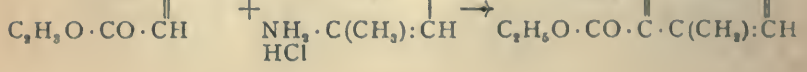


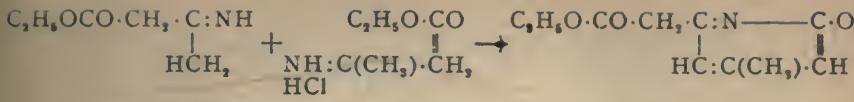
From aldehyde-ammonia, acetoacetic ester and aldehyde, dimethylpyridinecarboxylic acid may be obtained by an analogous series of reactions (Michael, *Ber.*, 1885, *18*, 2022). In the following papers, the mechanism of the reaction is discussed and a number of syntheses described (C. Beyer, *Ber.*, 1891, *24*, 1662; E. Knoevenagel, *Ber.*, 1898, *31*, 738, 761, 767, 1025; 1902, *35*, 2172, 2390; 1903, *36*, 2180).

8. Collie obtained various pyridine derivatives by distilling ethyl aminocrotonate, chiefly ethyl lutidonemonocarboxylate, m. p. 164—164 (*Annalen*, 1884, *226*, 297; *Trans. Chem. Soc.*, 1891, *59*, 172; 1895, *67*, 215

$$2\,C_6H_{11}O_2N = C_{10}H_{13}O_3N + NH_3 + C_2H_5OH$$

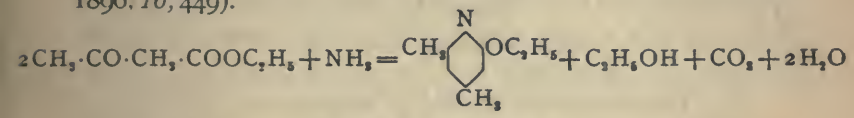
By heating the hydrochloride of ethyl β-aminocrotonate, two isomerides, viz. ethyl pseudolutidostyrilcarboxylate, m. p. 138—139°, and ethyl 2-hydroxy-4-methylpyridine-6-acetate, m. p. 166—167°, were obtained (Collie, *Ber.*, 1887, *20*, 445; *Trans. Chem. Soc.*, 1897, *71*, 299).



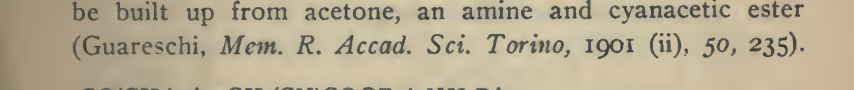


Numerous derivatives were prepared.

9. The ethyl ether of hydroxylutidine is formed by heating ethyl acetoacetate with excess of zinc chloride-ammonia for five hours at 100° (Canzoneri and Spica, *Gazzetta*, 1896, *16*, 449).

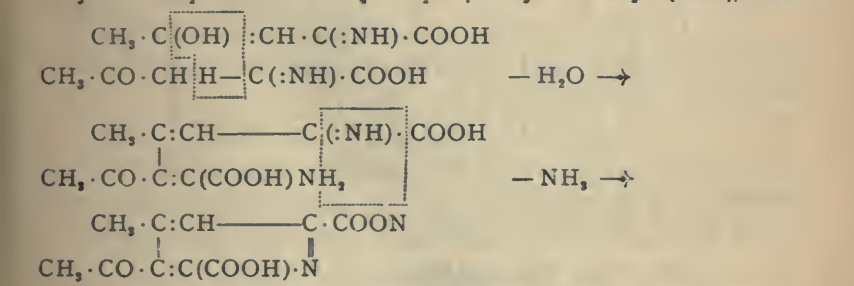


10. A six-membered ring with one nitrogen atom may be built up from acetone, an amine and cyanacetic ester (Guareschi, *Mem. R. Accad. Sci. Torino*, 1901 (ii), *50*, 235).

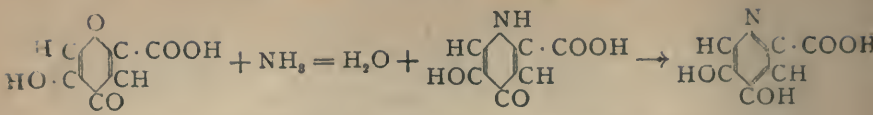


There are many other papers by Guareschi and his co-workers from 1895 onwards.

11. The ammonium salt of acetylpyruvic acid loses water giving *α*-imino-*γ*-ketopentoic acid as an intermediate product, and then 3-acetopicoline-2:6-dicarboxylic acid (Mumm and Bergell, *Ber.*, 1912, *45*, 3044; see also Mumm and Hüneke, *Ber.*, 1917, *50*, 1568; 1918, *51*, 150).

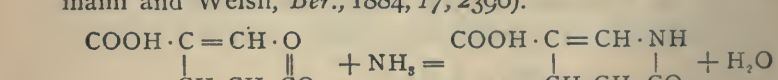


12. Comenic acid (derived from meconic acid) boiled with an excess of ammonia gives comenamic acid (Dihydroxypicolinic acid) (How, *Annalen*, 1851, *80*, 91).



The conversion of derivatives of γ-pyrone into corresponding pyridine compounds has engaged the attention of many chemists (Reibstein, *J. pr. Chem.* 1881, II, *24*, 285; Ost, *ibid.*, 1883, II, *27*, 275, 278, & c.; Bellmann, *ibid.*, 1884, II, *29*, 14; Krippendorf, *ibid.*, 1885, II, *32*, 162; Haitinger and Lieben, *Monatsh.*, 1885, *6*, 300; Lerch, *ibid.*, 1884, *5*, 402; Peratoner, *Gazzetta*, 1911, *41*, II, 619).

13. Hydroxynicotinic acid is obtained by the action of ammonia on coumalic acid or its methyl ester (Von Pechmann and Welsh, *Ber.*, 1884, *17*, 2390).



Glutazine, $NH{:}C\langle\begin{matrix}CH_2CO\\CH_2CO\end{matrix}\rangle NH$, is tautomeric with aminodihydroxypyridine; when it is boiled with concentrated hydrochloric acid, ammonia is eliminated and trihydroxypyridine formed (Stokes and von Pechman, *Ber.*, 1886, *19*, 2701).

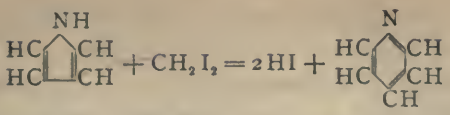
A number of syntheses from esters of α-pyrone-carboxylic acids and related compounds are due to Gutzeit and co-workers (*Annalen*, 1891, *262*, 89; *Ber.*, 1893, *26*, 2795; *Annalen*, 1895, *285*, 36; Haussmann, *ibid.*, 61; Band *ibid.*, 108).

14. Citramide, treated with sulphuric acid of 70—75 %, yields citrazinic acid (dihydroxypyridinecarboxylic acid) (Behrmann and Hofmann, *Ber.*, 1884, *17*, 2687).

$$C_6H_{11}O_4N_3 = C_6H_5O_4N + 2NH_3$$

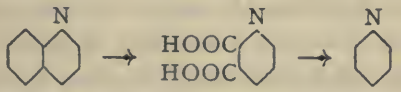
Ruhemann (*Trans. Chem. Soc.*, 1893, *63*, 259) obtained 2:6-dihydroxy-3-benzylpyridine by the action of ammonia on ethyl benzylglutaconate (See also, Ruhemann and Morrell, *Trans. Chem. Soc.*, 1891, *59*, 743).

15. A small amount of pyridine is formed when pyrrole is heated with methylene iodide and sodium methoxide above 200° (Dennstedt and Zimmermann, *Ber.*, 1885, *18*, 3317).



The potassium derivative of pyrrole gives 2-chloropyridine on treatment with chloroform (Ciamician and Dennstedt, *Ber.*, 1881, *14*, 1153; Compare, *Ber.*, 1882, *15*, 1172).

16. Quinolinic acid obtained by the oxidation of quinoline is a pyridine-dicarboxylic acid, and by loss of carbon dioxide is converted into pyridine (Hoogewerf and van Dorp, *Rec. trav. chim.*, 1882, *1*, 107; Compare Riedel, *Ber.*, 1883, *16*, 1615).



Phenylpyridines can be oxidised to pyridine-carboxylic acids which yield pyridine on distillation with lime (Skraup and Cobenzl, *Monatsh.*, 1883, *4*, 453).

Pyridine and Picoline

The chief commercial source of pyridine and its homologues is the light oil obtained on distilling coal-tar. The light-oil consists in greater part of benzene and its homologues; to obtain these in a marketable condition "tar acids" (phenol etc.) and basic substances must be removed; this also extends to the unsaturated hydrocarbons, which would resinify on exposure to the air.

To remove phenolic compounds, the oil is agitated with caustic soda solution, the layers separated, and the hydrocarbon mixture stirred with strong sulphuric acid, The latter treatment dissolves basic compounds, polymerises indene and other unsaturated hydrocarbons and sulphonates to a greater or less extent the thiophene and its homologues contained in the light oil.

After agitation with the light oil the sulphuric acid layer is very viscous, and when it is diluted with water, a resinous mass separates, whilst the bases remain in the aqueous solution as sulphates. By addition of oxidising agents (e. g. chro-

mates) to the acid layer, aniline etc. may be destroyed; on rendering alkaline and distilling, pyridine and other bases pass over together with water.

On the face of it, a more rational method would be to extract the bases from the light oil by washing with dilute acid before removing the tar acids by alkaline treatment but in practice the method does not work well since phenol added to a solution of pyridine in benzene hinders its extraction by dilute acids, whereas the pyridine does not hinder the removal of the phenol by alkalies to anything like the same extent. W. H. Hatcher and F. W. Skirrow (*J. Amer. Chem. Soc.*, 1917, *39*, 1939) show that although a quadrimolecular proportion of phenol added to a solution of pyridine in benzene greatly reduces the extraction of the base by dilute sulphuric acid, the extraction of phenol from its solution in benzene by means of caustic soda is very slightly reduced by the addition of a quadrimolecular proportion of pyridine. (Phenol and pyridine form two compounds, (C_6H_6O) (C_5H_5N) and $(C_6H_6O)_2$ (C_5H_5N). Bramley, *Trans. Chem. Soc.*, 1916, *109*, 475).

Pyridine mixes with water in all proportions at the ordinary temperature; it may be partially separated from the water accompanying it on distillation by the addition of caustic soda, pyridine and other bases rising as an oil. This upper layer contains a certain amount of water, and on rectifying the product, a considerable fraction is always obtained about 92—93°. This constant boiling point mixture has been erroneously described as a definite hydrate, C_5H_5N, $3\,H_2O$ (Goldschmidt and Constam, *Ber.*, 1883, *16*, 2077); it may however be dehydrated with caustic soda, and on destillation gives a smaller amount of „hydrate".

Even with good rectifying plant, the separation of pyridine from its homologues is a matter of considerable difficulty. After purifying as far as possible by distillation, which furnishes a pyridine sufficiently pure for solvent purposes or for denaturing alcohol, it is necessary to convert the base into a crystalline substance if it is required chemically pure. For this purpose, some well crystallised, not too soluble salt

is chosen, from which the base is regenerated by treatment with alkali. On a small scale, Ladenburg *(Annalen*, 1888, *247*, 4) dissolved 20 grams of pyridine in 100 grams of 10 per cent hydrochloric acid and precipitated with 135 grams of mercuric chloride in one litre of hot water. The precipitate (C_5H_5N, HCl, $HgCl_2$, m. p. 177—178°) was recrystallised from boiling water and distilled with caustic soda. To prepare pure pyridine on a larger scale, it would be advisable to use a double compound with a salt of a metal of lower atomic weight and less expensive than mercury. For the removal of ammonia from commercially pure pyridine, Barthe *(Bull. soc. chim.*, 1905, III, *33*, 459) recomends shaking with water and magnesium hydrogen phosphate; this combines with ammonia and amines to form salts of the type of magnesium ammonium phosphate.

For a description of the separation of pyridine from coal-tar, the reader is referred to Lunge's "Coal Tar and Ammonia". The separation of pyridine and quinoline bases from Dorsetshire (Kimmeridge) shale oils is described by Greville Williams *(Q. J. Chem. Soc.*, 1855, *7*, 97), and from Scottish Shale oils by G. C. Robinson *(Trans. R. S. Edin.*, 1879. *28*, 561; 1880, *29*, 265, 273), G. Beilby *(J. Soc. Chem. Ind.*, 1889, *16*, 886) and F. C. Garrett and J. A. Smythe (*Trans. Chem. Soc.*, 1902, *81*, 449). The recovery of pyridine bases from light wood tar oils is dealt with by Thenius *(Allg. Oesterr. Chem. u. Tcch. Zeitsch., 18* (9), 7), the same author also describes *(ibid., 18* (10), 5) their recovery from crude peat tar oils (Abstracts in *J. Soc. Chem. Ind.*, 1900, *19*, 652).

Pyridine is a colourles liquid having a sharp smell; the pure base is not so unpleasant as a mixture with higher homologues. Specific gravity, 1.0033 (0°/4°, Ladenburg); 0.88245 (110°/4°, Schiff); 0.989305 (15°/4°, Constam and White). Specific Heat: 0.4313 (Kahlenberg) or 0.3848 + 0.000774 t, Constam and White); Latent heat of vaporisation, 104.0 (Kahlenberg); 107.33 (Constam and White). Boiling point, 114.5° (Kahlbaum, see *Siedetemp. und Druck.*, 95; data given as to boiling points at various pressures); 114.8°

(Ladenburg); 116—116.2°/759.5 mm. (Schiff); 115.2° (Constam and White).

Head of combustion, 675.070 (Thomsen); for liquid, v = c, 664.68, for liquid, p = c, 665.1, for gas, p = c, 673.7 (Delepine).

Molecular Refraction, Brühl and Constam and White. The latter authors have determined several physical constants (*Amer. Chem. J.*, 1903, *29*, 1).

The absorption spectra of pyridine and its homologues and derivatives have been measured by Hartley (*Trans. Chem. Soc.*, 1885, *47*, 685), Baker and Baly (*ibid.*, 1907, *91*, 1122) and Purvis (*ibid.*, 1909, *95*, 294). There is a marked band in the ultra-violet with head at oscillation frequency 3950, addition of acid increases the persistency of the band and causes a slight shift towards the red. The absorption spectra of pyridine and some derivatives have been described by Pauer (*Wied. Ann.*, 1897, *61*, 363) and Purvis (*Trans. Chem. Soc.*, 1910, *97*, 692).

Pyridine is a weak base, introduction of methyl groups in place of hydrogen increases the value of the affinity constant. Constam and White (*Amer. Chem. J.*, 1903, *29*, 1) give the following values,

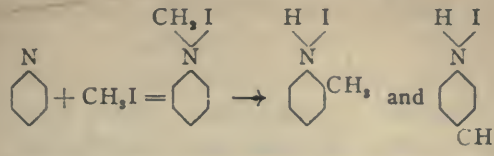
Pyridine	3.0×10^{-9}
α–Picoline	3.2×10^{-8}
β–Picoline	1.1×10^{-8}
γ–Picoline	1.1×10^{-8}

The salts of pyridine with mineral acids are generally very easily soluble: those with complex acids, less so. Thus the ferrocyanide has been recommended for the isolation of pyridine (Mohler, *Ber.*, 1888, *21*, 1015), but found to be of little use by Garrett and Smythe.

Pyridinium Compounds.

Pyridine methiodide (Methylpyridinium iodide) is formed when pyridine is added to methyl iodide at the ordinary temperature, the reaction being very energetic (Lange, *Ber.*, 1885, *18*, 3438). When the methioidide is heated to 290°, iso-

merisation takes place and the hydriodides of 2- and 4-methylpyridines (α and- γ-picolines) are produced.



Several methylpyridinium salts were described by Bally (*Ber.*, 1888, *21*, 1773); the hydroxides of alkylpyridinium bases are readily oxidised to N-alkylpyridones.

Pyridine ethiodide. Anderson (*Annalen*, 1855, *94*, 364) heated pyridine with ethyl iodide to 100°. The resulting salt forms shining leaflets, easily soluble in water, alcohol and ether. By heating it to 290°, Ladenburg (*Ber.*, 1883, *16*, 2059; 1885, *18*, 2961) obtained ammonia, free pyridine, α- and γ-ethylpyridines and $\alpha\gamma$-diethylpyridine.

Pyridine combines similarly with benzyl chloride, ethylene dibromide, chloracetic acid (betaine formation) etc.; furthermore, addition compounds, presumably pyridinium salts, are obtained by the action of 1-chloro-2:4-dinitrobenzene (Zincke, *Annalen*, 1904, *330*, 361) and cyanogen bromide (König, *J. pr. Chem.*, 1904, ii, *69*, 105).

α-Picoline

This base accompanies pyridine obtained from coal tar, bone oil or shale oil and is contained in the mixture of pyridine bases as separated by the method sketched out previously. It may be purified to a considerable extent by fractional distillation; from a fraction boiling between 128° and 134°, Ladenburg and Lange (*Annalen*, 1888, *247*, 7) isolated α-picoline by means of the compound with mercuric chloride and decomposition of this with caustic potash.

Picoline has been synthesised by several methods, the action of aldehyde on aldehyde-ammonia may be mentioned specially (Dürkopf and Schlaugk, *Ber.*, 1888, *21*, 297).

$$CH_3CH(OH)(NH_2) + 2CH_3CHO = C_5H_4(CH_3)N + 3H_2O$$

Specific gravity, 0.9652 (0°/4°, Ladenburg and Lange);

0.96161 (0°/4°, Thorpe, coefficient of expansion also given, *Trans. Chem. Soc.*, 1880, *37*, 223).

Boiling point, 129° (Ladenburg and Lange); 133.5° (Thorpe); 129.5° (Garrett and Smyth).

Most of the salts are easily soluble (*picrate*, needles, moderately soluble in water, m. p. 165°, Ladenburg and Lange) and the base combines with alkyl halides.

The reactivity of the methyl group in 2-picoline is important. By heating picoline with methylal and some zinc chloride to 280°—290°, Ladenburg obtained dipicolylmethane (*Ber.*, 1888, *21*, 3100).

$$2\,C_5H_4(CH_3)N + CH_2(OCH_3)_2 = 2\,CH_3OH + CH_2(C_5H_4N)_2$$

With 2-picoline and paraldehyde at 250—260°, the reaction followed a different course resulting in the formation of 2-allylpyridine (Ladenburg, *Annalen*, 1888, *247*, 26).

$$CH_3CHO + CH_3 \cdot C_5H_4N = H_2O + CH_3 \cdot CH : CH \cdot C_5H_4N$$

The simplest explanation is to suppose that an aldehyde first condenses to form an alcohol base (alkine),

$$R \cdot CHO + CH_3 \cdot C_5H_4N = R \cdot CHOH \cdot CH_2 \cdot C_5H_4N$$

and that the hydroxyl group then reacts either with a second molecule of 2-picoline or else is eliminated as water with formation of an ethylenic linkage. In this case one might expect that picoline under suitable conditions would react with formaldehyde to give 2-hydroxyethylpyridine (Monomethylol-picoline).

$$H \cdot CHO + C_5H_4(CH_3)N = C_5H_4(CH_2 \cdot CH_2OH)$$

Ladenburg obtained this and other alkine bases (*loc. cit.*, and *Ber.*, 1889, *22*, 2584; Alexander, *Ber.*, 1890, *23*, 2715; Ladenburg and Adam, *Ber.*, 1891, *24*, 1671; Ladenburg, *Annalen*, 1898, *301*, 124); the reaction was also examined by Königs and Happe (*Ber.*, 1902, *35*, 1344) who found that when 2-picoline was heated with 40 per cent formaldehyde solution, a small amount of dimethylolpicoline, $C_5H_4[CH(CH_2OH)_2]N$, was formed in addition to the monomethylol compound.

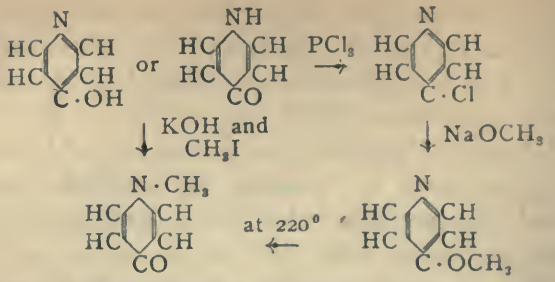
(Methyl in position 4 also reacts with formaldehyde, Königs proved this in the case of 4-methyl–2-ethylpyridine. *Ber.*, 1902, *35*, 1349.) Further results were obtained by A. Lipp and J. Richard *Ber.*, 1904, *37*, 737).

Although this behaviour of 2-picoline has not been utilised for the production of dyestuffs, the substanc has been condensed with phthalic anhydride to give pyrophthalone, a product possessing weak tinctorial properties. It will be seen later that 2-methylquinoline derivatives react in a similar way with formaldehyde and that in this case the reaction is of great value, since it leads to the production of the "carbocyanines", substances used as sensitisers for the photographic plate. (Reference is made to pyrophthalone in dealing with quinophthalone, the corresponding compound from quinaldine and phthalic anhydride.)

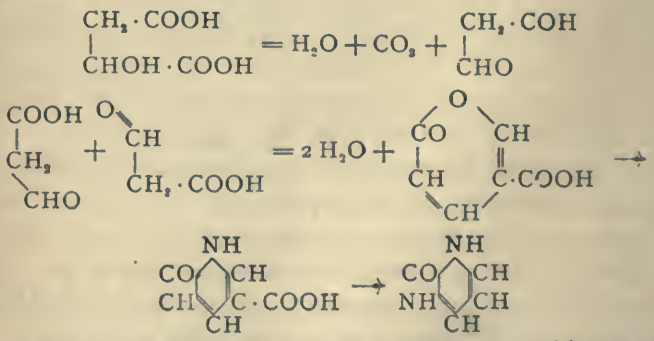
The other methylpyridines and higher homologues are not of interest with regard to dyestuff formation and will not be discussed here.

Pyridiones

The tautomerism of the hydroxypyridines was first elucidated in the 4- or γ-series. Lieben and Haitinger (*Monatsh.*, 1885, *6*, 300) obtained 4-pyridone (m. p. 148.5° when anhydrous) by heating chelidamic acid, and found that it gave a methyl derivative when treated with methyl iodide and caustic potash or silver oxide. The substance so obtained formed a crystalline, very deliquescent mass, and was not altered by heating with concentrated hydriodic acid to 150°. When however, 4-chloropyridine was heated to 100° with sodium methoxide, an isomeric compound was obtained, this was a liquid of b. p. 190.5—191°/738.3 mm. It had an alkaline reaction and on heating with hydriodic acid to 100° yielded methyl iodide and 4-pyridone. The chloropyridine from which the methoxypyridine was obtained resulted from 4-pyridone by the action of an excess of phosphorus trichloride at 150°. The following scheme shows the relationship of the four compounds.



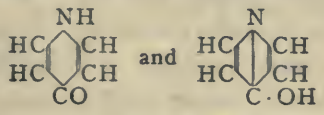
2–*Hydroxypyridine* or 2–*Pyridone* results when carbon dioxide is eliminated from hydroxyquinolinic acid (Königs and co-workers, *Ber.*, 1883, *16*, 2160; 1884, *17*, 590; 1886, *19*, 2433); 6-hydroxynicotinic acid (von Pechmann and Welsh, *Ber.*, 1884, *17*, 2391); and 2-hydroxy-3-nicotinic acid or *a*-isocinchomeronic acid (Weidel and Strache, *Monatsh.*, 1886, *7*, 297). Von Pechmann and Baltzer (*Ber.*, 1891, *24*, 3144) obtained 2-pyridone in fair amount from malic acid. When the latter is heated with sulphuric acid, the elements of formic acid are removed and it may be assumed that the half-aldehyde of malonic acid is formed as an intermediate product. Two molecules then condense giving coumalic acid which is converted into the methyl ester and transformed into hydroxynicotinic acid by the action of ammonia. By distilling the hydroxynicotinic acid, 2-pyridone (m. p. 107°, b. p. 280—281°) is obtained.



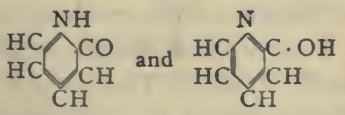
The hydriodides of methyl and ethyl pyridones were obtained by the direct action of methyl and ethyl iodides; the free bases boiled at 240° and 246—248° respectively.

If, however, 2-pyridone was dissolved in dilute caustic soda and precipitated by addition of silver nitrate, the resulting silver compound gave alkyloxypyridines on treatment with alkyl iodides. The formation of 2-methoxypyridine was accompanied by that of methylpyridone, but in the case of ethoxypyridine (b.p. 155—156°) the yield was nearly theoretical.

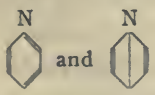
The proved tautomerism of 2-pyridone and 2-hydroxypyridine is of considerable theoretical interest. Lieben and Haitinger (*Monatsh.*, 1883, *4*, 339; 1885, *6*, 325) found that 4-pyridone and 4-hydroxypyridine were one and the same substance though giving rise to two sets of derivatives. To account for this tautomerism, they assumed that the relationship between the pyridone and hydroxypyridine structures was to be represented by the two formulae,



A similar argument applied to the case of 2-pyridone would necessitate the tautomeric structures.



Now just as 4-pyridone gives 4-chloropyridine, so does 2-pyridone give 2-chloropyridine (von Pechmann and Baltzer, *loc. cit.*, 3150), and as there is only one pyridine, it would have to possess the two constitutions



Von Pechmann interpreted the results as an argument in favour of a centric formula which had already been advocated by Bamberger.

Decker had found that quinoline methiodide when treated with alkali readily gives N-methylquinolone, especially if potassium ferricyanide be added as an oxidising

agent. Extending his work to the pyridine series, he found that when solutions of pyridine alkyl (methyl or ethyl) iodides were treated with alkali and a ferricyanide, the corresponding N-alkyl-2-pyridones, identical with the products obtained by von Pechmann and Baltzer were formed (*Ber.*, 1892, *25*, 444).

Many discrepant statements concerning the supposed alkyl-pyridinium (and -quinolinium) hydroxides must evidently be refered to the formation of pyridones (and quinolones), which had not been isolated in a state of purity.

Dyestuffs from Pyridine

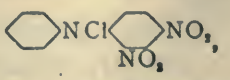
Pyrophthalone is dealt with under the head of Quinophthalone.

Rosol Scarlet and Rosol Red

Bayer & Co. introduced certain dyestuffs under these names; they are obtained from pyridine but the ring is no longer intact, and the colour must be connected with a long chain of conjugated double lingkages.

Vongerichten (*Ber.*, 1899, *32*, 2571) obtained 2:4-dinitrophenylpyridinium chloride whilst working out a quantitative test by which 0. 1 per cent of pyridine might be detected in aqueous or alcoholic solution. The method consists in treating an alcoholic solution of chlorodinitrobenzene with the liquid to be tested for pyridine, warming gently, shaking and adding caustic soda; presence of pyridine is shown by a reddish-violet coloration.

When 1-chloro-2:4-dinitrobenzene is dissolved in an excess of pyridine and the solution allowed to stand, dinitrophenylpyridinium chloride separates in the course of 12 hours as a white crystalline mass which may be recrystallised from methyl alcohol (long, flat prisms) or glacial acetic acid (concentrically grouped needles). The salt,



which is readily soluble in water and alcohol, was analysed

as well as the auri- and platini-chlorides; its aqueous solution, when treated with moist silver oxide, gave a red crystalline precipitate (no alkaline reaction), soluble in caustic soda with reddish violet colour. Sodium carbonate gave a brown precipitate which gradually turned scarlet and crystalline; the analysis pointed to the formula

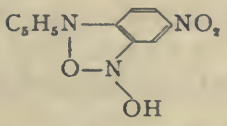
$$[C_5H_5N \cdot C_6H_3(NO_2)_2]_2O.$$

On boiling with hydrochloric acid, the precipitate went gradually into solution, dinitrophenylpyridinium chloride being regenerated.

Gail (*Dissertation,* Marburg, 1899) had also examined the reaction between chlorodinitrobenzene and pyridine; his analysis of the red substance obtained by the subsequent action of alkali agreed with the hydroxide formula,

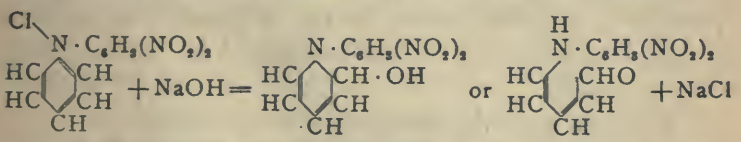
$$[C_5H_5N{:}C_6H_3(NO_2)_2]OH$$

This was confirmed by Spiegel (*Ber.*, 1899, *32*, 2835) who suggested a constitution



to explain the difference of properties from those of the expected ammonium salt.

Zincke (*Annalen,* 1904, *330*, 361) examined dinitrophenylpyridinium chloride and its transformation products at length; the red crystalline hydroxide appears to be the pseudo-base,



since it dissolves in alkali hydroxides and only slowly regenerates dinitrophenylpyridinium salts when treated with acids. This change is nearly quantitative when an acetic acid solution of hydrogen chloride is employed, but if treatment with aqueous hydrochloric acid is resorted to, dinitroaniline is eliminated, presumably with formation of a dialdehyde (II) which could not be isolated. This raises the question as to

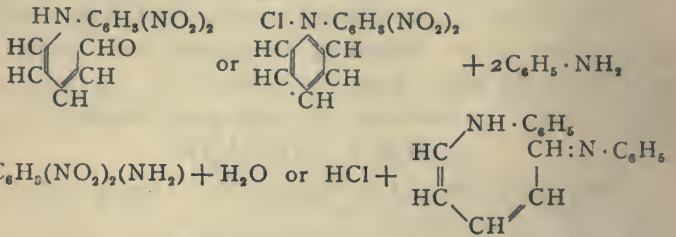
whether the red substance really contains the six-membered ring intact, but, as suggested in the above equation, is not rather to be given an alternative open-chain formula (I)

I. $C_6H_3(NO_2)_2 \cdot N : CH \cdot CH : CH \cdot CH_2 \cdot CHO$.

II. $CHO \cdot CH : CH \cdot CH_2 \cdot CHO$.

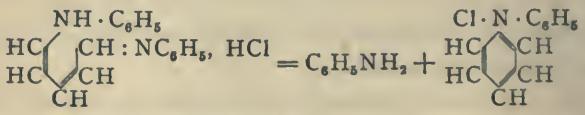
III. $C_6H_5N : CH \cdot CH : CH \cdot CH : CH \cdot NH \cdot C_6H_5$.

Although the dialdehyde (II) was not isolated, the corresponding dianilide (III) was obtained by the action of aniline on the red substance or on the dinitrophenylpyridinium chloride, dinitraniline being eliminated.



$= C_6H_3(NO_2)_2(NH_2) + H_2O$ or $HCl +$

The free dianilide crystallises in orange yellow leaflets, its hydrochloride in red needles: when the latter is heated, aniline is eliminated and phenylpyridinium chloride is formed.



An *anilinophenylhydrazide*,

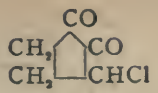
$C_6H_5(NO_2)_2N : CH \cdot CH : CH \cdot CH : CH \cdot N_2H_2C_6H_5$,

crystallising in shining black needles is obtained either from the pyridinium salt or the red compound by the action of phenylhydrazine.

Although the aldehyde-alcohol or dialdehyde

$HO \cdot CH : CH \cdot CH : CH \cdot CHO$ or $CHO \cdot CH_2 \cdot CH : CH \cdot CHO$

was not isolated, a monochloro-substitution derivative had been prepared some years previously. Hantzsch (*Ber.*, 1889, *22*, 1238) had obtained an acid, $C_6H_5O_4Cl$, by the decomposition of phenol by chlorine; this on elimination of carbon dioxide gave a compound, $C_5H_5O_2Cl$, thought at the time to be a monochlorodiketopentamethylene,



From the latter compound, Ince (*Ber.*, 1890, *23*, 1478) obtained coloured anilides and toluidides, and Zincke (*Annalen*, 1905, *339*, 193) showed that it is to be represented by the open chain formula,

$$HO\cdot CH:CCl\cdot CH:CH\cdot CHO,$$

i. e. it is the monochloro-substitution derivative of the hypothetical aldehyde-alcohol referred to previously.

In preparing the anilides, it is not necessary to isolate the compound, $C_5H_5O_2Cl$, but it is sufficient to treat the sodium salt, $C_6H_4O_4ClNa$, directly with a solution of aniline in hydrochloric acid when the dye separates as its hydrochloride,

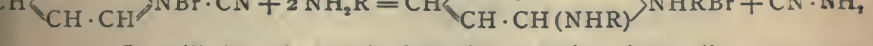
$$C_6H_5NH\cdot CH:CH\cdot CH:CCl\cdot CH:N\,C_6H_5),HCl.$$

This forms dark red leaflets, m. p. 128—129°, and is converted into phenylchloropyridinium chloride on boiling with hydrochloric acid. The dianilide gives rise to an oxime, yellow needles, m. p. 152°,

$$C_6H_5NH\cdot CH:CCl\cdot CH:CH\cdot CH:NOH,$$

and numerous other derivatives were prepared.

About the time of the appearance of Zincke's earlier paper, W. König (*J. pr. Chem.*, 1904, II, *69*, 105) published results concerning the addition of cyanogen bromide to pyridine. If these two substances are mixed in ethereal solution and a primary amine is added, a dyestuff is precipitated whilst cyanamide remains in the solution. The reaction was interpreted by the following equation, in which it is seen that an addition product (pyridinium salt) is assumed to be first formed; this then reacts with the amine, the nitrogen of the pyridine being split off with the cyanogen.



It will be observed that the reaction is really very similar to Zincke's, cyanogen taking the place of the dinitrophenyl radicle.

Shortly afterwards, König (*J. pr. Chem.*, 1904, ii, *70*, 19) admitted the possibility of an open chain formula. In the earlier paper it was shown that some of the dyestuffs crystallised in apparently very different forms from different solvents; at the time it was suggested that this might be due to stereoisomerism. In the later paper, desmotropy was looked on as a more probable cause, especially in view of the fluorescence of the dyestuffs. The two forms were written as

$$\begin{array}{l} CH{:}CH\cdot CH{:}NR \\ | \\ CH{:}CH\cdot NH_2RX \end{array} \quad \text{and} \quad \begin{array}{l} CH{:}CH\cdot CH\cdot NHR \\ | \qquad\quad | \\ CH{:}CH\cdot NHRX \end{array}$$

the first formula corresponding with that of Zincke.

König examined the behaviour of several dyestuffs which crystallised well from acetic acid and alcohol. Animal fibres took the dyes, vegetable fibres to a limited extent; fastness to washing was not good. The cyanobromide was caused to react with the following amines-, aniline, *m*-xylidine, α-cumidine, α- and β-naphthylamines, *p*-phenetidine, *p*-aminophenol, aminoazobenzene, methylaniline and sodium sulphanilate.

Zincke and Würker (*Annalen*, 1905, *341*, 365) subsequently examined the action of aliphatic amines on dinitrophenylpyridinium chloride, obtaining in the first instance amorphous substances the hydrochlorides of which were red in colour; dinitraniline was not eliminated. If the treatment were prolonged, dinitraniline and a quaternery pyridinium salt were produced.

$$C_6H_3(NO_2)_2N{:}CH\cdot CH{:}CH\cdot CH{:}CH\cdot NH\,Alk,\ HCl \longrightarrow$$

$$C_6H_3(NO_2)_2(NH_2) + \begin{array}{l} CH\cdot CH{:}CH \\ \| \qquad\quad | \\ CH\cdot CH{:}N\cdot AlkCl \end{array}$$

With excess of dimethylamine or piperidine, two molecules of the base entered into reaction and dinitraniline was eliminated, compounds of the structures

$$\text{and} \begin{array}{l} (CH_3)_2N\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}N(CH_3)_2Cl \\ C_5H_{10}N\cdot CH{:}CH\cdot CH{:}CH\cdot CH{:}NC_5H_{10}Cl \end{array}$$

being produced.

Reference may also be made to a further paper by Zincke and Schreyer (*Annalen*, 1907, *353*, 380).

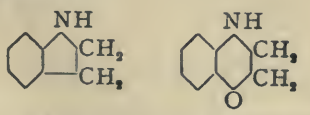
Besides chlorodinitrobenzene and cyanogen bromide, a number of other compounds have been found capable of producing the same rupture of the pyridine ring, e. g. picryl chloride, 1 : 3-dichloro-4 : 6-dinitrobenzene, diaryloxalimino chlorides, benzanilideimide chloride, carbodiphenylimide, phosgene, phosphorus oxytrichloride, phosphorus pentachloride but not phosphorus trichloride (Reitzenstein, *J. pr. Chem.*, 1908, II, *73*, 257; Bayer & Co., D. R. P. 218904; Reitzenstein and Breuning, *J. pr. Chem.*, 1911, II, *83*, 97; König and Bayer *ibid.*, 325). In several cases, isolation of the intermediate addition product has not been attained, but the fact that subsequent treatment with an amine gives a diarylamide of the general type

$$R{\cdot}NH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}NR$$

can only be taken as proof that the reaction follows the same general course.

The production of certain of the dyestuffs obtained by these reactions was protected by patent (D. R. P. 155782), most of the earlier colours proved of very little technical value as they lacked fastness to light; possibly some of them might find application as photographic sensitisers (Kieser, *Zeitschr. f. wissensch. Phot.*, 1905, III, 15).

Bayer & Co. (D. R. P. 218904/1908) afterwards found that if the primary or secondary bases hitherto used were replaced by cyclic secondary bases of the type of dihydroindole or phenmorpholine



the resulting dyestuffs were of value. König (*J. pr. Chem.*, 1904, ii, *70*, 56) had already noticed that the sustitution of tetrahydroquinoline for secondary open chain amines resulted in the formation of a dye the shade of which was redder than that of the dyes obtained from open chain secondary amines. The scarlet shade was however on the yellow side and the colour was only sparingly soluble. But using α-me-

thyldihydroindole in place of the isomeric tetrahydroquinoline, a dyestuff is obtained which is sufficiently soluble for convenient use; the shades dyed by it on tannined cotton resemble those given by Rhodamine 5 G, but are superior in clearness, intensity and fastness. Strong fluorescence is observed when dyed on silk or artificial silk.

Soon afterwards (Bayer & Co., D. R. P. 218616), it was found that very similar results were obtained by attaching the dihydroindole group at only one end of the open chain, some other secondary amine (e. g. methylaniline) residue being attached to the other end. The formation of such compounds is rendered possible by the fact that when the dyes from pyridine and secondary bases are treated with alkalies, they lose one molecule of secondary amine and give rise to substituted amino-aldehydes. Thus Zincke (*Annalen*, 1905, *338*, 127) found that the dyestuff from methylaniline and pyridine gives an aldehyde (m. p. 79°), in accordance with the equation,

$$(C_6H_5)(CH_3)N\cdot CH:CH\cdot CH:CH\cdot CH:N(CH_3)(C_6H_5)Cl + NaOH = NaCl + NH(CH_3)(C_6H_5) + (C_6H_5)(CH_3)N\cdot CH:CH\cdot CH:CH\cdot CHO$$

This may now be condensed with a cyclic secondary amine, e. g. methyldihydroindole, with formation of an asymmetrically substituted dyestuff.

$$(C_6H_5)(CH_3)N\cdot CH:CH\cdot CH:CH\cdot CHO + HCl,\ NH\cdot C_6H_4(CH_2\cdot CH_2) = H_2O + (C_6H_5)(CH_3)N\cdot CH:CH\cdot CH:CH\cdot CH:N\cdot C_6H_4(CH_2\cdot CH_2)\ Cl$$

When the pyridine dye prepared from methylaniline is treated with an excess of aniline, the reaction expressed by the following equation takes place,

$$(C_6H_5)(CH_3)N\cdot CH:CH\cdot CH:CH\cdot CH:N(CH_3)(C_6H_5)Cl + 2C_6H_5NH_2 = C_6H_5NH\cdot CH:CH\cdot CH:CH\cdot CH:NH\cdot(C_6H_5)Cl + 2C_6H_5\cdot NH\cdot CH_3$$

In this case, Zincke was unable to effect the reverse change.

The reaction appears to be fairly general; Bayer & Co. (D. R. P. 216991) state that the reversal may be effected at a higher temperature in the presence of sodium acetate, and further, that the replacement of one amine by another may be entire or only partial. Thus by acting on a dye of type (I) with a base NHRR′, one may possibly obtain the dyestuff (II) as well as the compound (III). (X = Halogen.)

I. NHR·CH:CH·CH:CH·CH:NHRX
II. NHR·CH:CH·CH:CH·CH:NHR′X
III. NRR′·CH:CH·CH:CH·CH:NRR′X

The colour of the dyestuffs of this class has attracted the particular attention of König *(Verh. Ges. deut. Naturforsch. u. Ärzte,* 1912, II [1], 221; König and Becker, *J. pr. Chem.,* 1912, II, *85,* 353). Bayer and Co. draw attention in their patents to the way in which the colour is altered by the use of cyclic in place of open chain secondary amines. König points out that the yellow or orange dyes of the methylaniline type, show only general absorption,[1]) whilst the dyes from cyclic secondary amines, which are reddish-orange to violet in colour, show well marked absorption bands. In the case of the dyestuffs from cyclic amines with a five-membered ring, the central band is resolved into two on dilution, this does not happen with compounds derived from amines with a six-membered ring. König considers this distinction to be specific.

Whilst cyclic secondary amines in place of methylaniline condition the formation of redder dyes than are formed when the open chain base is used, the colour is sent more in the green direction if, in the case of open chain bases, the side chain is lengthened by saturated alkyl groups, or, an ortho-substituent is introduced into the benzene ring.

König utilises Kaufmann's hypothesis involving subsidiary valencies, one or other of the following formulae being assigned to the dyestuffs:

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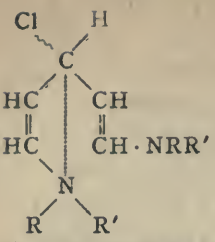
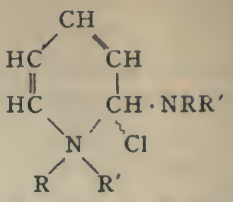
1) An examination of the ultra-violet spectrum would be of interest.





As the subsidiary valency (dotted line) is rendered stronger, so the colour is shifted towards the red.

Patent Literature

The reactions described have formed the subject matter of several patents.

König (D. R. P. 155782/1903) protected the preparation of dyestuffs made by the action of cyanogen halides in presence of pyridine on primary and secondary amines and their derivatives (*J. pr. Chem.*, 1904, II, *69*, 105). In the seven examples given in his patent, cyanogen bromide is allowed to react with pyridine and (I) aniline, (II) monomethylaniline, (III) *p*-aminophenol, (IV) sulphanilic acid, (V) 2-naphthylamine, (VI) benzidine and (VII) aminoazobenzene respectively.

The production of the same substances using 1-chloro-2:4-dinitrobenzene had already been described by Vongerichten (p. 18); novelty was however introduced when the primary bases previously used were replaced by secondary cyclic bases, and patents were obtained for the production of new dyestuffs from pyridine and methyldihydroindole or methylphenmorpholine, chlorodinitrobenzene being used as opener of the pyridine ring. (Brit. PP. 20367, 21585, 21911/1908; D. R. P. 218904/1908; Fr. P. 395793/1908; W. König, assignor to Bayer & Co., U. S. PP. 913513, 913514/1909.)

In the compounds of D. R. P. 218904, the residue of the same secondary base is attached to both ends of the open chain.

Example 1. 28.15 kilos of 2:4-dinitrophenylpyridinium chloride are heated on the water-bath for four hours under reflux with 60 kilos of ethyl or methyl alcohol and 26.6 kilos

of methyldihydroindole (Jackson, *Ber.*, 1881, *14*, 883). On pouring the deep crimson solution into very dilute hydrochloric acid, a thick red paste containing dyestuff and dinitroaniline separates, this is collected, extracted with hot water and the solution precipitated by the addition of hydrochloric acid or sodium chloride. After drying, the material consists of microscopic needles with a brownish-red, blue or green surface lustre, very easily soluble in alcohol or glacial acetic acid and also readily soluble in hot water. The shades obtained with the dye are very similar to those given with Rhodamine 6 G, but are clearer and faster to light. The same dyestuff is obtained when the addition products of picryl chloride or of 1 : 3-dichloro-4 : 6-dinitrobenzene with pyridine are allowed to react with methyldihydroindole, and it may also be obtained by using the aldehyde (pseudo-base) prepared by Zincke,

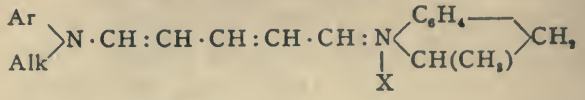
$$C_6H_3(NO_2)_2 \cdot N : CH \cdot CH : CH \cdot CH : CHOH$$

or an addition product of pyridine with a cyanogen halide.

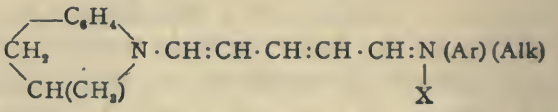
Example 2. 8 kilos of pyridine, 60 litres of methyl alcohol and 29.8 kilos of methylphenmorpholine (D. R. P. 97 242) are mixed and 50 kilos of 2 N solution of cyanogen bromide allowed to flow in in the course of half an hour. The mixture becomes warm and soon turns red. After some two hours at ordinary temperature, it is stirred and enough dilute hydrochloric acid added to give a thick paste whilst the supernatant liquid is only feebly coloured. The paste is filtered off and dried either at ordinary temperature or *in vacuo* at 100°, violet-brown microscopic needles possessing a blue lustre being obtained. The dyestuff is readily soluble in alcohol, glacial acetic acid and hot water, and dyes tannined cotton a bright red of yellower shade than that given by the dyestuff obtained according to Example 1. Various modifications are mentioned in the patent, such as the use of different solvents, aqueous solutions of cyanogen halide, and 3- and 4-substituted pyridines.

As previously stated, dyestuffs of the class now considered can be prepared in which the residues at the ends of

the chain are derived from different secondary amines. In D. R. P. 218616 (8. 3. 1908) methods are described for preparing such compounds, and it is remarked that the formulae



and II.

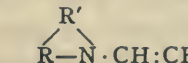


represent different substances which produce different shades in dyeing. One might have expected the formulae to be tautomeric and that in any case, solutions of the two forms would contain identical positive ions.

In preparing compounds of type I, an aldehyde possessing the structure

$$(Ar)(Alk)N \cdot CH:CH \cdot CH:CH \cdot CHO$$

is condensed with a cyclic secondary base; for compounds of type II, an aldehyde of the general formula



is condensed with a secondary amine NH (Ar) (Alk).

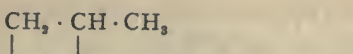
Example 1. 1.8 kilos of the aldehyde

$$(C_6H_5)(CH_3)N \cdot CH:CH \cdot CH:CH \cdot CHO$$

(Zincke, *Annalen*, 1905, *338*, 127) are heated for about four hours under reflux on the water-bath with 5 litres of alcohol, 2 litres of 30 per cent acetic acid and 1.33 kilos of α-methyldihydroindole until no further increase in the red colour is observed. The alcohol is then distilled off and the residue poured into an aqueous solution of hydrogen and sodium chlorides. The thick paste of needles is filtered off and dried. The dyestuff gives a clear scarlet (blue shade) on tannined cotton, fast to washing and light.

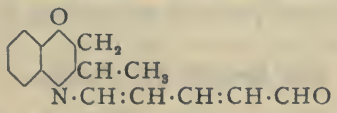
Modifications are mentioned; thus the reaction may take place in the cold, a longer time being occupied, also the oxime or the phenylhydrazone may be used in place of the aldehyde.

Example 2. 2.13 kilos of the aldehyde (m. p. 126.5°) obtained by the action of alkalies on the condensation product of pyridine and methyldihydroindole and possessing the constitution



are digested for some hours on the wather-bath with 5 litres of alcohol, 1 litre of 60 per cent acetic acid and 1.33 kilos of tetrahydroquinoline. The product is worked up as in the last example; the dyestuff gives a clear scarlet on tannined cotton.

The use of the aldehyde



derived from methylphenmorpholine (m. p. 150°) is also referred to.

The replacement of the residue of one base by another is illustrated by three examples in D. R. P. 216991/8. 3. 1908.

Example 1. 4.5 kilos of the dyestuff from pyridinium cyanobromide and sulphanilic acid (D. R. P. 155782, Ex. 4) are boiled for ten hours under reflux with 1.2 kilos of 50 per cent acetic acid, 2.7 kilos of methyldihydroindole and 15 litres of alcohol. When the reaction is finished, the sulphanilic acid is filtered off and the hot filtrate stirred into water containing hydrochloric acid and common salt, the dyestuff separating as a thick red paste which dries to a mass with a green metallic lustre. Various other reacting substances are mentioned.

Example 2. 4 kilos of the yellow pyridine dyestuff from methylaniline (D. R. P. 155782, Ex. 2), 1.4 kilos of tetrahydroquinoline, 1.8 kilos of 20 per cent hydrochloric acid and 15 litres of alcohol are heated under reflux on the water-bath until the reaction is finished (dye trial), this takes about 5 hours. The alcohol is then distilled off, and the dyestuff precipitated as microscopic red needles by pouring the residue into an aqueous solution of hydrochloric acid and salt.

The dye gives orange shades on tannined cotton, the colour is said to be fast.

If the quantities are compared, it will be found that slightly over one molecule of tetrahydroquinoline is used for one molecule of the dyestuff from methylaniline and pyridine. presumably the compound obtained has the constitution

$$(C_6H_5)(CH_3)N \cdot CH{:}CH \cdot CH{:}CH \cdot CH{:}N{:}C_9H_{10}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad Cl$$

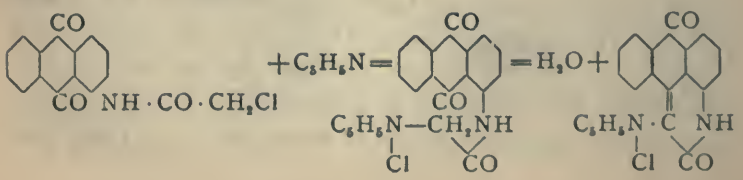
Example 3. 4.85 kilos of the dyestuff (m. p. 157°) from pyridine cyanobromide and 2:4-dichloroaniline, 3 kilos of methylphenmorpholine and 10 litres of alcohol are boiled for several hours and the product worked up as in Example 2.

Other Dyestuffs from Pyridine

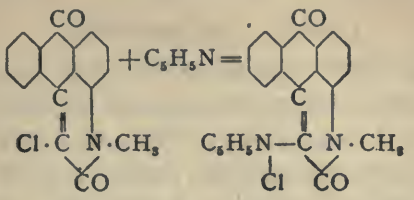
Reitzenstein and Breuning obtained a patent (D. R. P. 230 597/1909) for the production of red basic dyestuffs by allowing chlorine to act on pyridine in presence of a substance to further the reaction, e. g. zinc chloride, with or without an organic diluent, and then treating the mass with amino compounds. The patent was allowed to lapse in April 1911.

Pyridine has been used in conjunction with certain anthraquinone derivatives for the production of basic dyestuffs. Bayer & Co. (D. R. P. 290 984/1914) find that 1-chloracetylaminoanthraquinone adds on pyridine and that further condensation then takes place.

Example 1. 1 part of 1-chloracetylaminoanthraquinone is boiled with 20 parts of pyridine until the quantity of the pale yellow pyridinium compound shows no further increase. The substance dissolves easily in water and dyes tannined cotton yellow. The formation takes place apparently according to the scheme



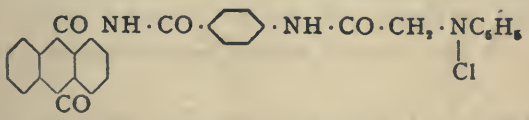
That this interpretation is correct is evident from the fact that Example 2 describes the production of a yellow dye from chloro-N-methylanthrapyridone (D. R. P. 264 010)



identical with that obtained according to Example 3 from pyridine and chloracetyl-N-methylaminoanthraquinone.

Examples 4 and 5 deal with the condensation of 1-α-bromobutyryl-4-benzoylaminoanthraquinone and of 1-chloracetylamino-4-benzoylaminoanthraquinone respectively with pyridine.

In Example 6 the chain is lengthened. 1-aminoanthraquinone is converted into the *p*-nitrobenzoyl derivative, this is reduced to the corresponding amino-compound, an α-chloracetyl group is introduced and the resulting substance united with pyridine. The dyestuff has the constitution



Tannined cotton and unmordanted wool are dyed a yellow (green shade) fast to chlorine and light.

In Example 7, trimethylamine takes the place of pyridine.

The properties of a number of related dyestuffs are tabulated, the shade being considerably altered in some cases. Thus 1-chloracetylamino-4-aminoanthraquinone and pyridine give a dyestuff producing a violet red on tannined cotton, whilst a blue dye is formed when *sym*-4 : 4 '-dichloracetylamino-1 : 1 '-dianthraquinonylamine is condensed with pyridine.

Chapter II

QUINOLINE, ITS HOMOLOGUES AND DERIVATIVES

Syntheses of the Quinoline Ring

The Quinoline nucleus occurs ready formed in several alkaloids, notably those derived from the various species of *Cinchona*. It is consequently found, together with homologous compounds, amongst the products of the distillation of quinine, (Gerhardt, *Annalen*, 1842, *42*, 310), cinchonine and strychnine (Gerhardt, *Annalen*, 1842, *44*, 276) with caustic potash (See also Williams, *Jahresb.* 1856, 533). It is also found in coal tar (Hofmann, *Annalen*, 1843, *47*, 76; O. Fischer, *Ber.*, 1883, *16*, 720; Jacobsen and Reimer, *ibid.*, 1084). brown coal tar (Döbner, *Ber.*, 1895, *28*, 106), and in Stuppfett, the oily product formed in the distillation of Idrian mercury ore (Goldschmidt Schmidt, *Monatsh.*, 1881, *2*, 17).

The following important syntheses of compounds containing the Quinoline ring may be mentioned.

1.-Quinoline is produced by passing the vapour of allylaniline over heated lead oxide (Königs, *Ber.*, 1879, *12*, 453).

2.-It is also formed by the dry distillation of acroleïn-aniline.

3.-Instead of acroleïn-aniline, it is more convenient to heat aniline (38 parts) with glycerine (120 parts), concentrated sulphuric acid (100 parts) and nitrobenzene (24 parts) (Skraup, *Monatsh.* 1880, *1*, 317; 1881, *2*, 141; Königs, *Ber.*, 1880, *13*, 911; Döbner and Miller, *Ber.*, 1881, *14*, 2816).

$$C_6H_5NH_2 + C_3H_8O_3 = C_9H_7N + 3\,H_2O + 2\,H$$
$$C_6H_5NO_2 + C_3H_8O_3 = C_9H_7N + 3\,H_2O + 2\,O$$

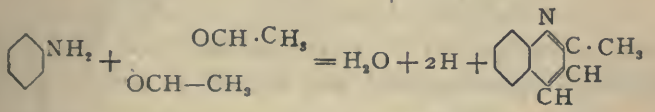
or $2\,C_6H_5NH_2 + C_6H_5NO_2 + 3\,C_3H_8O_3 = 3\,C_9H_7N + 11\,H_2O$

Various modifications of this reaction have been devised (See page 38).

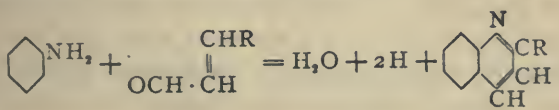
The above reactions show that quinoline contains a benzene ring; that it also contains a pyridine ring is evident from the fact that when oxidised it yields quinolinic (pyridine-

2 : 3-dicarboxylic) acid which gives nicotinic (pyridine-3-carboxylic) acid smoothly when heated. These reactions are only consistent with the following scheme

4. Homologues of quinoline (quinaldines are produced by the condensation of aldehydes containing the groupings $R \cdot CH_2 \cdot CHO$ and $R \cdot CH : CH \cdot CHO$ with aniline. Thus quinaldine proper (2-methylquinoline) is formed by gradually adding 80 parts of paraldehyde to a cooled mixture of 40 parts of aniline, 45 parts nitrobenzene and 100 parts of concentrated sulphuric acid (Döbner and Miller, *Ber.*, 1881, *14*, 2814).

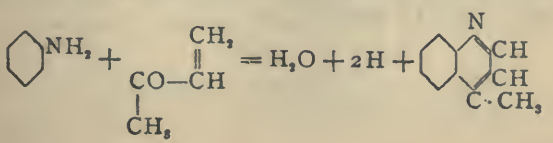


The same compound is also formed when aniline is condensed with aldol in presence of hydrochloric acid (Döbner and Miller, *Ber.*, 1883, *16*, 2465) and when aniline is heated with crotonaldehyde, nitrobenzene and sulphuric acid (Skraup, *Ber.*, 1882, *15*, 897). The corresponding reaction with cinnamaldehyde yields phenylquinoline



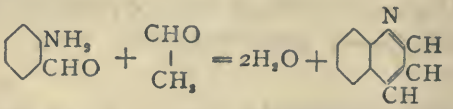
In the reaction with paraldehyde, the equation has been written as if condensation occurred between aniline and two molecules of acetaldehyde; we may correspondingly bring aniline into reaction with one molecule each of an aldehyde and a ketone (C. Beyer, *J. pr. Chem.*, 1888, II, *38*, 422).

$$H \cdot CHO + CH_3 \cdot CO \cdot CH_3 = CH_2 : CH \cdot CO \cdot CH_3 + H_2O$$

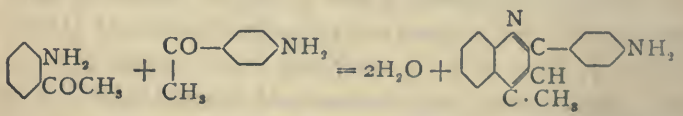


5. Acetylacetone and other β-diketones condense with aniline in presence of concentrated sulphuric acid to give homologues of quinoline (Combes, *Bull. soc. chim.*, 1888, *49*, 89).

6. Ortho-amino-aldehydes and ketones can be condensed with aldehydes and ketones cantaining the group $\cdot CH_2 \cdot CO$. Thus *o*-aminobenzaldehyde and acetaldehyde suffer alkaline condensation to quinoline (Friedländeer and Gohring, *Ber.*, 1883, *16*, 1883).

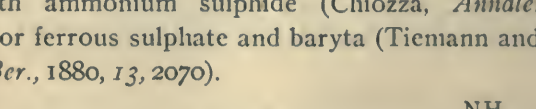


whilst a mixture of *o*- and *p*-aminoacetophenones gives flavaniline on heating with zinc chloride to 90° (O. Fischer. *Ber.*, 1886, *19*, 1038)



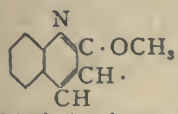
The production of the same compound by heating acetanilide with zinc chloride at 250° to 270° (O. Fischer and Rudolph, *Ber.*, 1882, *15*, 1500) is to be attributed to wandering of the acetyl group from the nitrogen atom into the nucleus and subsequent condensation of the aminoacetophenones thus produced. Partial isomerisation explains the formation of flavaniline from o-amino-acetophenone (Besthorn and O. Fischer, *Ber.*, 1883, *16*, 73).

7. 2-Hydroxyquinoline is tautomeric with carbostyril, the lactam resulting from the reduction of *o*-nitrocinnamic acid with ammonium sulphide (Chiozza, *Annalen*, 1852, *83*, 118) or ferrous sulphate and baryta (Tiemann and Oppermann, *Ber.*, 1880, *13*, 2070).



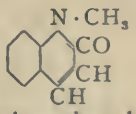
For the preparation of carbostyril, the ethyl ester is more suitable than *o*-nitrocinnamic acid itself (Friedländer and Ostermaier, *Ber.*, 1888, *14*, 1916).

Comparison of the absorption spectra of the two isomeric methyl derivatives



Methylcarbostyril

and

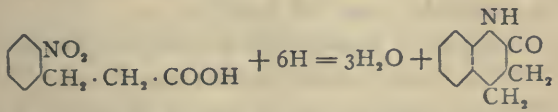


Methylpseudocarbostyril

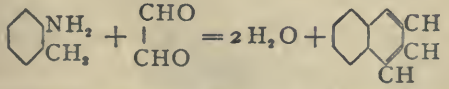
with that of carbostyril, point to a lactam constitution for the latter substance (Hartley and Dobbie, *Trans. Chem. Soc.*, 1899, *75*, 643). This result agrees with the conclusion arrived at by Knorr on chemical grounds (*Annalen*, 1896, *293*, 81).

By treatment with phosphorus pentachloride and phosphoryl chloride, carbostyril gives 2-chloro-quinoline, which may be reduced to quinoline by heating with a solution of hydriodic acid in glacial acetic acid to 240°.

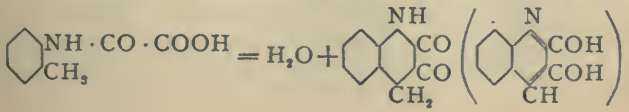
8. Similar ring formation takes place when *o*-nitrophenylpropionic acid (Glaser and Buchanan, *Zeitschr. f. Chem.*, 1869, 164) or its ethyl ester (Friedländer and Weinberg, *Ber.*, 1882, *15*, 1423) is reduced.

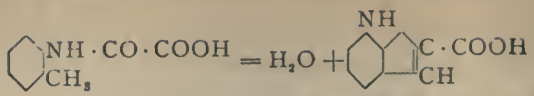


9. Quinoline is formed from o-toluidine and glyoxal by alkaline condensation (Kulisch, *Monatsh.*, 1894, *15*, 276; Hinsberg, *Annalen*, 1904, *337*, 327).

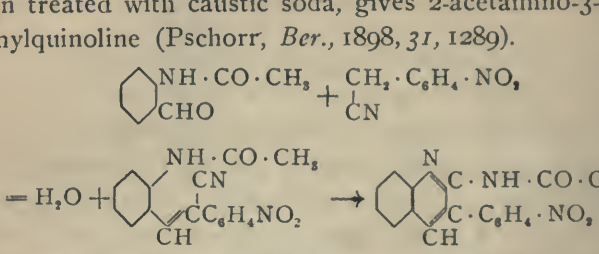


10. 2:3-Dihydroxyquinoline is obtained together with the isomeric indole-2-carboxylic acid by fusing oxotoluidic acid with sodium ethoxide (Madelung, *Ber.*, 1912, *45*, 3524).





11. *o*-Acetaminobenzaldehyde and *p*-nitrobenzyl cyanide are condensed by sodium ethoxide to a compound, which, when treated with caustic soda, gives 2-acetamino-3-*p*-nitrophenylquinoline (Pschorr, *Ber.*, 1898, *31*, 1289).

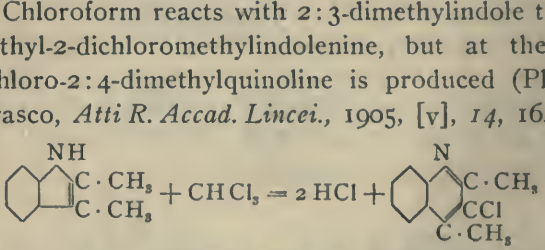


The migration of the acetyl group is noteworthy.

Besides these syntheses from benzene substituted with open chains, several reactions have been discovered whereby indole derivatives may be converted into quinoline compounds.

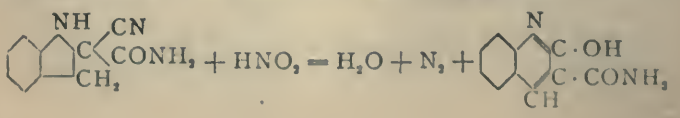
12. A small amount of quinoline is formed when 2-methylindole is heated with zinc chloride (E. Fischer and Städel, *Ber.*, 1887, *20*, 819). Pictet obtained a 17% yield by passing the vapour of 2-methylindole through a tube heated to dull redness (*Ber.*, 1905, *38*, 1946).

13. Chloroform reacts with 2:3-dimethylindole to form 2:3-dimethyl-2-dichloromethylindolenine, but at the same time 3-chloro-2:4-dimethylquinoline is produced (Plancher and Carrasco, *Atti R. Accad. Lincei.*, 1905, [v], *14*, 162).

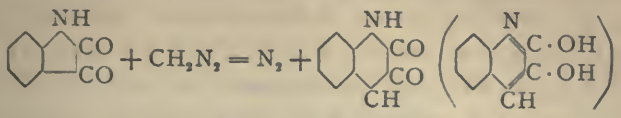


This may be compared with the production of chloropyridine from pyrrole and chloroform.

14. Nitrous acid converts 2-cyano-2:3-dihydroindole-2-carboxylamide into 2-hydroxyquinoline-3-carboxylamide (G. Heller and P. Wunderlich, *Ber.*, 1914, *47*, 1617).



15.-An extra carbon atom may be introduced into the isatin ring by the action of diazomethane; 2:3-dihydroxyquinoline is thus formed (G. Heller, *Ber.*, 1919, *52*, B. 741).



Quinoline, C_9H_7N

Quinoline occurs amongst the higher boiling bases of coal tar. By washing the oils with caustic soda and sulphuric acid in succession, phenols and basic substances are respectively extracted. The separation of pure quinoline from accompanying coal tar bases is a matter of considerable difficulty and cannot be effected by distillation alone; it is consequently more convenient to prepare the base synthetically, when, as for most purposes, freedom from homologues is essential.

In the original synthesis due to Skraup (*Monatsh.*, 1880, *1*, 317), a mixture of 24 grams of nitrobenzene, 38 grams of aniline, 120 grams of glycerine and 100 grams of concentrated sulphuric acid are heated together. The heating has to be carried out very carefully at first, otherwise the reaction is too violent; boiling is then continued for some hours under reflux. After dilution, excess of nitrobenzene is removed in a current of steam, the mixture is then rendered alkaline and the quinoline blown over, the distillate separating into two layers. The resulting quinoline usually contains some aniline. For purification the base may be dissolved in six parts of alcohol and precipitated as the acid sulphate by the addition of one molecular proportion of sulphuric acid.

Alternatively the quinoline may be treated carefully in acid solution with chromic acid, aniline being thus destroyed; or, aniline in acid solution may be diazotised and the diazonium compound decomposed by heating. In any case, the acid solution is subsequently rendered alkaline and the base blown over in a current of steam; it is finally purified by distillation.

For working on a larger scale, the following procedure is described (Friedländer, 1888, I, 174). A mixture of 600 parts of glycerine (28° Bé), 600 parts of concentrated sulphuric acid, 144 parts of nitrobenzene and 216 parts of aniline are heated for one day to 125°; the temperature is then raised to 180—200° to complete the reaction. To avoid trouble from the violence of the reaction (usually initiated by local overheating) the mixture is continuously stirred. The product is then worked up as in the case of small quantities, any aniline being removed by means of chromate or nitrite. The yield is said to be 70 per cent. On account of previous publication, Skraup was only able to obtain a patent in America U. S. P. 241 738/1881).

The function of nitrobenzene in Skraup's synthesis of quinoline should be considered. The equation for the formation of quinoline from aniline and glycerine

$$C_6H_5 \cdot NH_2 + C_3H_5(OH)_3 = C_9H_7N + 3\,H_2O + 2\,H$$

shows a surplus of hydrogen which ought to be eliminated. With nitrobenzene there is a surplus of oxygen as seen from the equation

$$C_6H_5NO_2 + C_3H_5(OH)_3 = C_9H_7N + 3\,H_2O + 2\,O$$

Skraup's method of compensating the hydrogen from the aniline condensation by using it for reducing nitrobenzene, which should thus give more aniline for the condensation, is quite rational in its object. At the same time it is somewhat doubtfoul whether the nitrobenzene really does more than furnish the necessary oxygen, i. e. it is not apparent that the nitrobenzene molecules themselves actually give rise to molecules of quinoline. From 38 grams of aniline and 24 grams of nitrobenzene about 40 grams of quinoline are obtained; if the whole of the aniline were quantitatively transformed into quinoline, the yield should be 52.7 grams.

It would appear then, that the nitro-groups simply furnish a convenient source of oxygen to get rid of excess of hydrogen which would convert quinoline into reduction products and so diminish the yield. Evidence of this is seen in

the case of nitro-compounds which do not correspond with the amino-compounds in the conversion of the latter into quinoline derivatives.

Thus in the preparation of quinoline-6-sulphonic acid from glycerine, sulphuric acid and sulphanilic acid, the practically inaccessible *p*-nitrobenzene sulphonic acid was replaced by nitrobenzene (Happ, *Ber.*, 1884, *17*, 192); whilst in the preparation of 7-nitroquinoline from metanitraniline, Claus and Stiebel employed picric acid in place of metadinitrobenzene (*Ber.*, 1887, *20*, 3095).

A mild inorganic oxidising agent in place of an organic nitro-compound should offer advantages, providing it were cheap and gave water-soluble products.

On account of the possible violence of the reaction, it is advisable to use a 2-litre flask when 38 grams of aniline are brought to reaction according to Skraup's original process. J. Walter found that twice the quantity could be worked in a flask of 800 c. c. by modifying the method (*J. pr. Chem.*, 1894, II. *49*, 549). The flask is provided with a reflux condenser and a dropping funnel from which the mixture of aniline, glycerine and sulphuric acid is added in the course of three-quarters of an hour to the heated nitrobenzene contained in the flask.

Margosches (*Jour. pr. Chem.*, 1904, II, *70*, 129) stated that the yield in Skraup's synthesis is increased by the presence of salts of copper and iron. The condensation takes place in absence of nitrobenzene if the oxides or sulphates of the rare elements obtained from commercial cerium oxalate are added, but the yield is not as good as when nitrobenzene is present.

Reference has been made above to the possibility of using inorganic oxidising agents in place of nitrobenzene. Knüppel (*Ber.*, 1896, *29*, 704) employed arsenic acid for the purpose; 76 grams of this acid, 140 grams of concentrated sulphuric acid, 155 grams of glycerine and 50 grams of aniline being slowly heated under reflux until the beginning of the reaction. When this has subsided, gentle boiling is

continued for $2^1/_2$ hours, the isolation of the quinoline is then effected in the manner previously described. According to Knüppel's patent (D. R. P. 87 334/1894), 50 grams of aniline, 76 grams of arsenic acid and 150 grams of glycerine are heated in an open pan to 170° with 150 grams of sulphuric acid 66° Bé.

According to Knüppel, the method has a slight advantage over Skraup's process in the case of converting aniline to quinoline, whilst considerably better yields of substituted quinolines are obtained when the process is applied to *o*-toluidine, *o*-, *m*-, and *p*-nitranilines, *m*- and *p*-dimethylphenylenediamines, *β*-naphthylamine and *β*-anthramine. The reaction can also be used for the preparation of alizarine blue from *β*-aminoalizarine.

Stannic compounds may also be used, thus J. G. F. Druce *(Chem. News,* 1918, *117,* 346) finds that anhydrous aniline stannichloride, $(C_6H_7N)_2, H_2SnCl_6$, may be employed in place of the mixture of aniline and nitrobenzene. More recently *(Chem. News,* 1919, *119,* 271), he has applied the method to the three toluidines; with the meta-compound the yield was only 25 %, with para-toluidine as high as 70 %.

The use of inorganic oxidising agents in the synthesis of quinoline is also described by E. de Barry Barnett *(Chem. News,* 1920, *121,* 205). In this case calcined ferric oxide was used, which formed ferric sulphate with the sulphuric acid. With approximately equimolecular quantities of aniline and glycerine about 40 to 50 per cent of the theoretical yield was attained. Increase in the quantity of glycerine (Skraup and Knüppel both use a great excess) did not materially improve the yield; its lowness is probably attributed to destruction of the aniline rather than of glycerine, for the course of the reaction was practically unaltered by the addition of boric acid.

By rapidly adding a mixture of 50 grams of aniline, 65 grams of glycerine and 100 grams of ferric oxide to 150 c. c. of sulphuric acid heated in an open dish, allowing the reaction to proceed for half-an-hour and working up the product, a

60 % yield of quinoline was obtained. Barnett subsequently raised the point as to whether it might not be possible to design a process in which oxygen under pressure would be employed together with ferric oxide or stannic sulphate as a catalytic agent.

Physical Properties of Quinoline

Density; 1.1081/0°, 1.0947/20°, 1.0699/50° (Skraup). 1.1055/0°, 1.0965/11.5° (Oechsner). M. P. —19.5° (Altschul and von Schneider; Pictet). B. P. 237.1°/746.8 (Skraup). 240.4—241.3°/750 (Kretschy). 104.8°/9.2, 113.3°/15.88, 118.2/20.18, 132.0°/40.54, 238°/760 (Kahlbaum).

Molecular Heat of Formation, —32.8 Cal; Molecular Heat of Combustion; v = c, 1122.3 Cal.; p = c, 1123.0 Cal. (Delépine, *Compt. rend.*, 1898, *126*, 964).

Magnetic Rotation, Perkin (*Trans. Chem. Soc.*, 1896, *69*, 1115) Absorption Spectrum, Hartley (*Trans. Chem. Sco.*, 1882, *14*, 47). Purvis (*ibid.*, 1910, *97*, 1035) extended the observations giving results for liquid and vapour as well as solutions of pyridine. Dielectric Constant, Dewar and Fleming (*Proc. Roy. Soc.*, 1897, A, *61*, 358).

Salts. Very many have been described. The *hydrochloride*, C_9H_7N, HCl, m. p. 93—94°, is very soluble in water, in fact, deliquescent; it is soluble in all proportions in chloroform and absolute alcohol, and is soluble in warm ether and benzene. The double salts with metallic chlorides are generally sparingly soluble.

The *acid sulphate*, C_9H_7N, H_2SO_4, m. p. 163.5—164.5°, requires 50 parts of absolute alcohol at 18° and 9 at 78° for solution.

The *picrate*, C_9H_7N, $C_6H_3O_7N_3$, m. p. 203°, separates from benzene in bright yellow needles.

Reactions of Quinoline

Quinoline is hygroscopic, and if allowed to stand over water under a bell jar, takes up an amount said to correspond with the formula $C_9H_7N + 1^1/_2H_2O$ (Hoogewerf and van

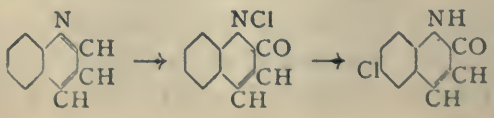
Dorp, *Rec. trav. chim.*, 1882, *1*, 9). Statements as to the occurence of such definite hydrates must be taken with caution; it is better to look on the liquid as a saturated solution of water in quinoline, for when very gently heated, it becomes turbid, i. e. the solubility of water in quinoline diminishes with rise in temperature.

By passing quinoline through a hot tube 3-diquinolyl is formed (Zimmermann and Müller, *Ber.*, 1884, *17*, 1965; O. W. Fischer, *Monatsh.*, 1884, *5*, 423).

Hoogewerf and van Dorp found that quinoline is attacked with difficulty by chromic acid mixture, Oechsner de Coninck (*Compt. rend.*, 1898, *128*, 682), found it was attacked, at any rate more readily than pyridine. The former authors (*Rec. trav. chim.*, 1882, *1*, 107) obtained ammonia, carbon dioxide, quinolinic and oxalic acids by oxidising with permanganate in alkaline solutions; this is confirmed by Golenkin and Klepikoff (*J. Russ. Chem. Soc.*, 1892, *22*, 535) who obtained no other crystalline acid on oxidising synthetic quinoline; the best yield of quinolinic acid was 28 per cent of the quinoline employed.

Bleaching powder solution both chlorinates and oxidises, chlorocarbostyril, C_9H_6ONCl, being formed; chlorine led into a dilute acetic acid solution of quinoline produces trichlorohydroxycarbostyril.

The reaction between bleaching powder and quinoline was effected by Einhorn and Lauch (*Annalen*, 1888, *243*, 343) who added a 20 per cent solution of the former to a very dilute aqueous solution of the latter in which boric acid had been dissolved. The product thus obtained contained chlorine attached to nitrogen and was readly transformed into carbostyril by a variety of agents, on boiling with alcohol, the chlorine migrated to the para-position in the benzene half of the nucleus.



Heated with sodium, 2-diquinolyl is formed; but when a hydroxylic solvent is present, the quinoline is reduced giving tetrahydroquinoline. This reduction has been effected by zinc or tin and hydrochloric acid (Wyschnegradsky, *Ber.*, 1879, *12*, 1481; 1880, *13*, 2400); by sodium amalgam (Königs, *Ber.*, 1881, *14*, 100); or by sodium (Weidel and Gläser, *Monatsh.*, 1886, *7*, 328).

Tetrahydroquinoline is also formed when quinoline is heated with hydrogen under pressure in presence of nickel oxide, but if the reaction is carried to completion (quinoline and one-tenth of its weight of nickel oxide for 12 to 20 hours at 110 atmospheres and 240°), practically the only product is decahydroquinoline (Ipatiew, *Ber.*, 1908, *41*, 992). By passing quinoline vapour and hydrogen through a tube containing reduced nickel at 260—280°, Padoa and Carughi obtained 2-methylindole, methyl-*o*-toluidine and *o*-toluidine. (*Atti R. Accad. Lincei*, 1906, [v], *15*, II, 113).

With bromine, quinoline gives a direct addition product, $C_9H_7NBr_4$, but on substitution, bromine enters the pyridine half of the quinoline nucleus. (La Coste, Claus and Collischonn. See especially Decker, *J. pr. Chem.*, 1892, II, *45*, 47; and Claus, *ibid.*, 222). As previously noted, chlorine behaves as an oxidising as well as a chlorinating agent in the presence of water (See Claus, *J. pr. Chem.*, 1893, II, *48*, 135). Quinolines, halogenated in the benzene nucleus, may be obtained by the application of Skraup's reaction to the halogenated anilines, or by replacement of amino-groubs in amino-quinolines using Sandmeyer's method.

Nitric and sulphuric acids attack the benzene half of the nucleus. A mixture of the two acids gives 5-(ana) and 8-(ortho) nitroquinolines (Königs, *Ber,*. 1879, *12*, 449; Claus and Cramer, *Ber.*, 1885, *18*, 1245; Nölting and Trautmann, *Ber.*, 1890, *23*, 3654; Dufton, *Trans. Chem. Soc.*, 1891, *59*, 756; 1892, *61*, 782).

6- and 7-Nitroquinolines are obtained by application of Skraup's synthesis to *p*-nitraniline (La Coste, *Ber.*, 1883, *16*, 669) and *m*-nitraniline (Claus and Stiebel, *Ber.*, 1887, *20*, 3095)

respectively. The production of dinitroquinolines from quinoline or its mononitro-derivatives is described by Claus (*Ber.*, 1885, *18*, 1243; *J. pr. Chem.*, 1896, *53*, 198); Kaufmann and Decker (*Ber.*, 1906, *39*, 3648); and Kaufmann and Hüssy (*Ber.*, 1908, *41*, 1735).

Aminoquinolines are obtained by reduction of the nitroquinolines.

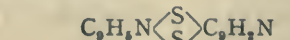
The course followed on sulphonation depends on the strength of the acid used and on the temperature at which the reaction is carried out. O. Fischer and Bedall (*Ber.*, 1882, *15*, 683, 1979) obtained a mixture of 5- and 8-quinoline-sulphonic acids.

Riemerschmied (*Ber.*, 1883, *16*, 721) found the proportion of the 5-acid was small at temperatures below 250°, but it increased at 270°. La Coste and Valeur (*Ber.*, 1887, *20*, 95) used $3^1/_2$ parts of fuming sulphuric acid, heating for one hour to 170°; in place of the separation by means of mercuric oxide which they employed, lime or baryta is more convenient (Claus, *J. pr. Chem.*, 1888, II, 37, 260), the calcium salt of the 8-acid crystallising out first.

The meta- or 6-quinoline sulphonic acid was obtained by Claus (*loc. cid.*, 261) by sulphonating quinoline with an acid of 10 to 20 per cent anhydride content at a temperature not above 125—130°.

Para or 6-quinoline sulphonic acid is obtained from sulphanilic acid, nitrobenzene, glycerine and sulphuric acid (Happ, *Ber.*, 1884, *17*, 192).

With sulphur dichloride at 160° mono- and tri-chloroquinoline are formed as well as a thio-substituted compound of the probable structure



(Edinger, *Ber.*, 1896, *29*, 2456; *J. pr. Chem.*, 1896, II, *54*, 340, 355; *Ber.*, 1897, *30*, 2418).

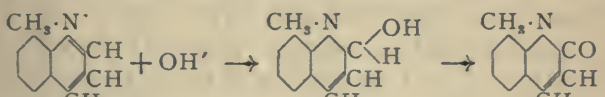
Quinoline like pyridine, in virtue of its tertiary nitrogen atom, forms addition products with alkyl magnesium halides

(B. Oddo, *Atti R. Accad. Lincei*, 1904, [v], *13*, II, 100; 1907, [v]) *16*, 538; Sachs and Sachs, *Ber.*, 1904, *37*, 3088).

Quinolinium Compounds and Quinolones

As a tertiary base, quinoline unites with an equimolecular proportion of an alkyl iodide or sulphate, thus Williams obtained quinoline methiodide or methylquinolinium iodide, $C_9H_7N \cdot CH_3I$ by the action of methyl iodide on quinoline (*Jahresb.*, 1856, 534).

The corresponding quaternary ammonium hydroxide is not known in a solid condition; apparently its ions exist in solution but unite to form a carbinol base which passes into 1-methyl-2-quinolone (N-methylcarbostyril) either by oxidation or decomposition. The changes involved may be represented by the following scheme,



this view of quinolone formation rests on the following evidence.

When moist silver oxide acts on aqueous quinoline methiodide, a strongly alkaline liquid is obtained: La Coste noticed that the solution was unstable, and further observed that caustic soda, added to a solution of the methiodide, produced a flocculent precipitate which dissolved easily in alcohol, and especially so in ether; to this compound he assigned the composition of a methylquinolinium oxide, $(C_9H_7N \cdot CH_3)_2O$ (*Ber.*, 1882, *15*, 192). La Coste's preparation melted to a reddish brown resin below 50°; Ostermayer (*Ber.*, 1885, *18*, 594) obtained a substance to which he assigned the same formula, but it crystallised in large, shining prisms, was soluble in ether and melted at 72—75°.

Decker discovered that solutions of (substituted) alkylquinolinium salts give quinolones on treatment with alkali and a ferricyanide (*J. pr. Chem.*, 1892, II, *45*, 161).

$$C_6H_3(NO_2)\left\langle\begin{array}{l} N(CH_3I):CH \\ \qquad\qquad\;| \\ CH = CH \end{array}\right. + 3KOH + 2K_3Fe(CN)_6$$

$$= C_6H_3(NO_2)\left\langle\begin{array}{l} N(CH_3)\cdot CO \\ \qquad\qquad\;| \\ CH = CH \end{array}\right. + 2K_4Fe(CN)_6 + KI + 2H_2O$$

and his attention was drawn (*Ber.*, 1892, *25*, 443) to the nearly identical melting points recorded by Ostermayer for the base from quinoline methiodide and alkali, and by Friedländer and Müller (*Ber.*, 1887, *20*, 2009) for methylpseudocarbostyril (72°) obtained by the action of methyl iodide and caustic soda on carbostyril.

$$C_6H_4\left\langle\begin{array}{l} NH\cdot CO \\ \qquad\;\;| \\ CH:CO \end{array}\right. + CH_3I + NaOH = H_2O + NaI + C_6H_4\left\langle\begin{array}{l} N(CH_3)\cdot CO \\ \qquad\qquad\;| \\ CH = CH \end{array}\right.$$

A supposed bromoquinolinium base described by La Coste had already proved to be the corresponding quinolone, and Decker now showed that methylquinolinium salts behave in the same way towards alkaline ferricyanide as the bromo- and nitro-substituted alkylquinolinium salts he used in his first experiments, and was thus able to isolate methylquinolone of m. p. 72°. Evidently this was the compound which Ostermayer had obtained, his analytical data must, as the result of Decker's work, be rejected.

This is in accordance with the scheme given above representing the formation of methylquinolone by the oxidation of a carbinol base, Decker seems to have rather doubted the accuracy of La Coste's observation as to the primary formation of a strongly basic quaternary hydroxide.

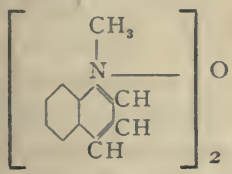
That methylquinolinium and hydroxyl ions can exist side by side in the same solution follows from the work of Hantzsch and Kalb (*Ber.*, 1899, *32*, 3109) on pseudoammonium bases. By shaking up a solution of methylquinolinium iodide with the exact quantity of silver oxide necessary to remove the whole of the iodine, an alkaline solution was obtained which, on determining its electric conductivity, gave $\mu_{32} = 207.5$. Practically the same result, $\mu_{32} = 209$, was obtained when a solution was prepared by mixing equivalent solutions of methylquinolinium sulphate and caustic baryta.

The gradual combination of the quinolinium and hydroxyl ions to form a non-electrolyte was shown by mixing equivalent solutions of methylquinolinium iodide and caustic soda and determining the value of $\mu_{32}/25^{\circ}$ at intervals.

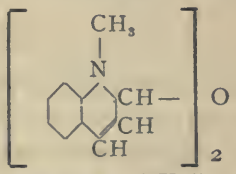
Time in minutes	0′	10′	30′	60′	2 hrs.	3 hrs.	19 hrs.
Conductivity	299,4	299,1	293	290	282,5	281,8	242

As the conductivity falls, so the precipitate described by La Coste increases in quantity. Hantzsch and Kalb analysed the material thrown out from solution after washing it thoroughly and drying to constant weight; the figures obtained agreed excellently with the formula given by La Coste.

But whilst La Coste, in accordance with the views held at the time, considered the substance to be an ammonium oxide, Hantzsch and Kalb regarded it as the ether of the carbinol pseudo-base



La Coste

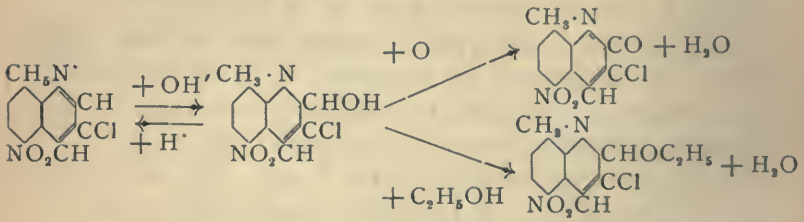


Hantzsch and Kalb.

We shall see below that both conceptions are wrong, the precipitate is really a mixture of methylquinolone and a reduced methylquinoline.

Decker admitted (*Ber.*, 1902, *35*, 2588, 2589) that the carbinol base may be first produced, in fact he was the first to use carbinol formulae for the bases obtained from the quaternary quinolinium salts. In certain cases the carbinol bases have been definitely isolated; thus a pseudo-base $C_{10}H_9O_3N_2Br$, is obtained by precipitating solutions of 1-methyl-5-nitro-3-bromoquinolinium salts with ammonia. When dried, this carbinol forms beautiful, glittering, yellow needles, it is evidently a chemical individual and not a mixture (*J. pr. Chem.*, 1892, II, *45*, 178). Decker confirmed these results at a later date (*Ber.*, 1903, 36, 1205) and showed that the corresponding methyl-nitro-chloroquinolinium salts behave in a perfectly similar manner.

These true carbinol bases on solution in acids regenerate the quinolinium salts from which they are obtained; when warmed with alcohols they give alkyl ethers, whilst oxidising agents readily convert them into quinolones. The relationships exhibited by these various negatively substituted compounds appear to be quite clear; on mixing solution of such quinolinium salts with dilute alkalies, the quinolinium and hydroxyl ions unite with the direct formation of the carbinol. This change and the subsequent transformations of the carbinol may be expressed by the scheme



For the precipitate produced by adding alkali to a solution of methylquinolinium iodide, both La Coste and Hantzsch and Kalb undoubtedly obtained analytical figures agreeing with the formula of an ether rather than with that of a carbinol. La Coste described the precipitate as flocculent; Hantzsch and Kalb adduced microcrystalline structure as further evidence of individuality, Decker (*loc. cit.*, 1208) found that whilst the precipitate appeared to be microcrystalline on casual inspection, no trace of crystals could be detected under the microscope, but merely small oily drops which had solidified to a brittle resin. Examination under polarised light also failed to reveal any trace of crystalline structure, whilst on digestion with N/20 hydrochloric acid, resinous particles were left undissolved and only 12 per cent of the acid necessary for re-formation of a quinolinium salt from carbinol or ether base was used.

On ultimate analysis, figures agreeing with the formula $(C_9H_7N\,CH_3)_2O$ were obtained, similar results having already been obtained by La Coste and Hantzsch and Kalb. But $C_{20}H_{20}ON_2$ is also the sum of $C_{10}H_{11}N$ and $C_{10}H_9ON$, so that

there is a possibility of the precipitate being a mixture of methyldihydroquinoline and methylquinolone with only a small amount of carbinol base present. By addition of four molecular proportions of N/2 caustic soda to methylquinolinium iodide and treatment with a current of steam, a distillate was obtained which after addition of 5 per cent sodium carbonate solution gave up methylquinolone and a base to benzene when shaken with this solvent, from the aqueous layer, methylquinolinium picrate (m. p. 169.5) was isolated.

The base dissolved by the benzene was taken to be methyldihydroquinoline; its picrate, which melted at 144 or 145°, was subsequently identified as that of methyltetrahydroquinoline (Kairoline), a base obtained some years earlier by Hofmann and Königs (*Ber.*, 1883, *16*, 732; 1885, *18*, 595. Ladenburg gives the melting point of kairoline picrate as 125°, *Ber.*, 1895, *28*, 1172).

From this it appears that methylquinolinium hydroxide is largely transformed in accordance with the equation

$$3\,C_9H_7N(CH_3)(OH) = C_9H_{10}N\cdot CH_3 + 2\,C_9H_6ON\cdot CH_3 + H_2O$$

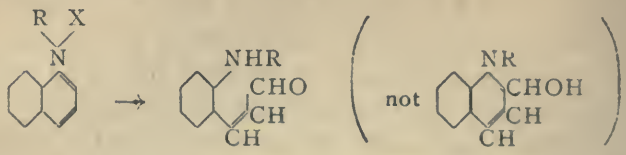
(Quite possibly the first change of the methylquinolinium hydroxide is into a mixture of methylquinolone and methyldihydroquinoline, the former is the lactam of methylaminocinnamic acid, the latter the internal anhydride of methylaminocinnamyl alcohol. Such a transformation is reminiscent of the Cannizzaro reaction; in such a case it would be necessary to assume the subsequent formation of methylquinolinium hydroxide and methyltetrahydroquinoline from the dihydro-compound

$$2\,C_9H_7N(CH_3)(OH) = C_9H_6ON\cdot CH_3 + C_9H_8N\cdot CH_3$$
$$2\,C_9H_8NCH_3 + H_2O = C_9H_7N(CH_3)(OH) + C_9H_{10}N\cdot CH_3$$

Author.)

Before leaving the subject of the pseudo-bases derived from quaternary cyclic ammonium salts, reference should be made to Roser's views (*Annalen*, 1892, *272*, 225). After studying cotarnine, the conclusion was reached that the pseudo-

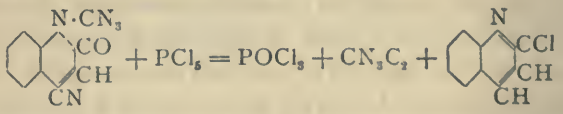
bases were ortho-amino substituted open chain aldehydes. simple quinoline derivatives would thus be represented in the following manner



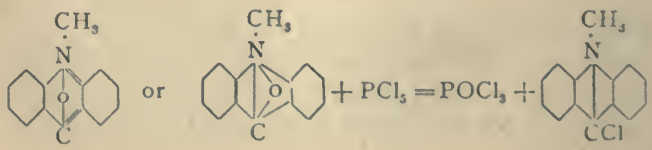
This view cannot be upheld according to Decker, for as he points out (*Ber.*, 1902, *35*, 2590), Pictet and Patry were able to decompose the pseudo-bases from methylacridinium iodide (methylacridol) into methyldihydroacridine and methylacridone, of which compounds the former may be volatilised in a current of steam (*Ber.*, 1902, *35*, 2536).

In this particular case, opening of the heterocyclic ring is very improbable.

An interesting reaction of the quinolones was discovered by O. Fischer (*Ber.*, 1898, *31*, 609). When methyl- or ethylquinolone is heated with a mixture of phosphorus oxychloride and pentachloride, alkyl chloride is eliminated and 2-chloroquinoline produced.



A similar reaction is observed with the α-pyridones (*loc. cit.* and *Ber.*, 1899, *32*, 1298); 1-methyl-2-pyridone giving 2-chloropyridine. γ-Pyridones behave differently, methylacridone heated with phosphorus oxychloride and pentachloride to 120—130° for some time yielding methylchloroacridinium chloride. In consequence, Fischer would represent alkylacridoned with a cross linked oxygen atom.



Nitro- and Amino-Quinolines

Of the very numerous substitution derivatives of quinoline, comparatively few have been practically employed for the synthesis of dyestuffs, and generally these have been homologues. Mills and Pope (*Phot. Journ.*, 1920, *60*, 183) have prepared acetamino- and amino-derivatives of isocyanine dyes, employing quinolinium salts prepared by the addition of alkyl iodides to acetamino-substituted quinoline and quinaldine; of these compounds some appear to possess useful properties. It is further quite possible that amino-quinolines may be used for other dyestuff syntheses, references to their literature as well as to that of the nitro-compounds from which they are obtained by reduction are therefore given below. It is only those compounds in which the amino-group is situated in the benzene half of the nucleus which are likely to have technical application.

5-*Nitroquinoline.* Obtained with 8-nitroquinoline by direct nitration of quinoline. M. P. 72°. Claus and Cramer. *Ber.*, 1885, *18*, 1243; Nölting and Trautmann, *Ber.*, 1890, *23*, 3654; Dufton, *Trans. Chem. Soc.*, 1891, *59*, 756; 1892, *61*, 782; Claus and Setzer, *J. pr. Chem.*, 1896, II, *53*, 390.

6-*Nitroquinoline.* From *p*-nitraniline by the Skraup reaction. M. P. 149—150°. La Coste, *Ber.*, 1883, *16*, 669; Knüppel, *Ber.*, 1896, *29*, 705.

7-*Nitroquinoline.*. From *m*-nitraniline. Claus and Stiebel, *Ber.*, 1887, *20*, 3095; Claus and Massau, *J. pr. Chem.*, 1893, II, *48*, 170; Knüppel, *Ber.*, 1896, *29*, 706.

8-*Nitroquinoline.* By nitration of quinoline or by applying Skraup's reaction to *o*-nitraniline. M. P. 88—89°. Königs, *Ber.*, 1879, *12*, 449; La Coste, *Ber.*, 1883, *16*, 673; Claus and Küttner, *Ber.*, 1886, *19*, 2887; Friedländer, *Jahresb.*, 1882, 367; Dufton, *Trans. Chem. Soc.*, 1891, *59*, 756; 1892, *61*, 782; Claus and Setzer, *J. pr. Chem.*, 1896, II, *53*, 390; Knüppel, *Ber.*, 1896, *29*, 705.

5-*Aminoquinoline.* M. P. 110°, B. P. 310°. Dufton, *Trans. Chem. Soc.*, 1892, *61*, 785; Claus and Setzer, *J. pr. Chem.*, 1896, II, *53*, 390; *Acetyl derivative.* M. P. 103°.

6-*Aminoquinoline.* M. P. 140° (La. C.), 109° (K), 114° (C. and S.). La Coste, *Ber.*, 1883, *16*, 670; Ziegler, *Ber.*, 1888, *21*, 863; Claus and Schnell, *J. pr. Chem.*, II, 1895, *53*, 106; Knüppel, *Annalen*, 1889, *310*, 75; Decker, *J. pr. Chem.*, 1911, II, *84*, 425. *Acetyl derivative.* M. P. 138°.

7-*Aminoquinoline.* M. P. 94°. Claus and Stiebel, *Ber.*, 1887, *20*, 3096; Claus and Massau, *J. pr. Chem.*, 1893, II, *48*, 170; F. M. Hamer, *Trans. Chem. Soc.*, 1921, *119*, 1436.

8-*Aminoquinoline.* M. P. 70°. Königs., *Ber.*, 1879, *12*, 450; Bedall and Fischer, *Ber.*, 1881, *14*, 2573; Claus and Cramer, *Ber.*, 1885, *18*, 1245; Claus and Setzer, *J. pr. Chem.*, 1896, II, *53*, 390. *Acetyl derivative.* M. P. 178°.

Methyl Derivatives of Quinoline

Of the homologues of quinoline employed in the manufacture of sensitising dyestuffs, distinction must be made between those which are substituted in the benzene and pyridine halves of the nucleus. The cyanines and isocyanines are obtained when homologues of quinolines are treated with an alkyl iodide, sulphate or *p*-toluenesulphonate and the resulting quinolinium compound boiled with alkali in alcoholic solution, two quinoline residues are thus united by means of a "grouping" carbon atom. This grouping atom is attached to the quinoline nuclei either in the 2- or 4-position; it is thus essential that one at least of the two molecules of quaternary salt employed should be derived either from quinaldine (2-methylquinoline) or lepidine (4-methylquinoline), though the other molecule may be a derivative of quinoline or of a homologue containing substituting methyl groups in the benzene ring. These latter compounds are obtained from the homologues of aniline by the action of glycerine, sulphuric acid and an oxidising agent, other processes having to be employed in the preparation of quinaldine and lepidine.

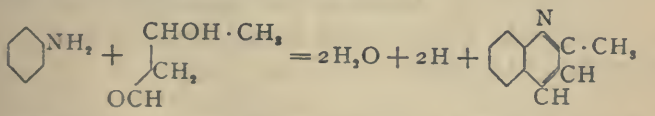
6-Methylquinoline (*p*-Toluquinoline) was obtained by Skraup (*Monatsh.*, 1881, *2*, 158) from a mixture of *p*-toluidine, *p*-nitrotoluene, glycerine and sulphuric acid. Modifications of Skraup's reaction could also be employed.

Liquid, smells like quinoline, D. 1.0815/0°, 1.0681/20°, 1.0560/50°, B. P. 257.4—258.6°/745 mm.

Various salts have been described; the methiodide was described by Skraup as fine, yellowish prisms.

2-Methylquinoline (Quinaldine). This base occurs in coal tar (Jacobsen and Reimer, *Ber.*, 1883, *16*, 1084) but is best prepared synthetically.

Döbner and Miller (*Ber.*, 1881, *14*, 2814) found it might be prepared by heating glycol (30 parts), aniline (40 parts) and nitrobenzene (14 parts) with concentrated sulphuric acid (38 parts), but that an easier method was to gradually add 80 parts of paraldehyde to a cooled mixture of 40 parts of aniline, 45 parts of nitrobenzene and 100 parts of sulphuric acid. This procedure was subsequently modified, a mixture of $1^1/_2$ parts of paraldehyde, 1 part of aniline and 2 parts of concentrated hydrochloric acid being heated for some hours on the water bath (Döbner and Miller, *Ber.*, 1883, *16*, 2465). It was shown at the same time that a mixture of aniline, aldol and hydrochloric acid might be employed, amongst the products of the latter reaction, ethylaniline and tetrahydroquinaldine were subsequently identified (*Ber.*, 1884, *17*, 1699). Quinaldine was also obtained by heating a mixture of crotonaldehyde, aniline, nitrobenzene and sulphuric acid (Skraup, (*Ber.*, 1882, *15*, 897). The reaction may be represented as follows when aldol is employed.



The excess hydrogen is used in reducing some of the aldehyde and, to a lesser extent, some of the quinaldine to tetrahydroquinaldine. H. O. Jones and P. E. Evans, who have studied the mechanism of the reaction, find that commercial samples of quinaldine always contain some of the tetrahydro base, 14 to 16 per cent being found in a sample from the A.-G. f. Anilin-Fabrikation (*Trans. Chem. Soc.*, 1911, *99*, 339).

Ristenpart (Weyl's *Einzelschriften zur chemischen Tech-*

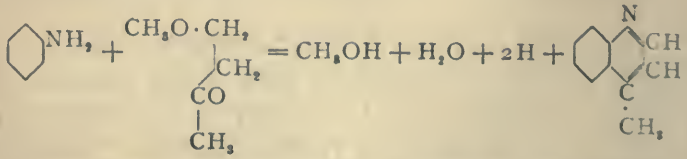
nologie, 1911, 4. Lieferung, 16) states that quinaldine is prepared technically by heating a mixture of 50 kilos of aniline, 100 kilos of hydrochloric acid and 75 kilos of paraldehyde for 5 hours under reflux, rendering alkaline and blowing over the base in a current of steam. The addition of a small amount of aluminium chloride to the reaction mixture was described by the Chem. Fabrik, Schering (Brit. P. 956/1883; U. S. P. 309 935/1883; Fr. P. 153 873/1883; D. R. P. 24 317/1882).

Of other syntheses, that from *o*-aminobenzaldehyde, acetone and caustic soda may be mentioned (Friedländer and Gohring, *Ber.,* 1883, *16,* 1835). Very similar is the reduction of *o*-nitrobenzylideneacetone (Meister, Lucius and Brüning, Brit. P. 3541/1882; U. S. P. 268 543/1882; D. R. P. 22 138/1882; B. P. 246—247°). Salts and alkyl iodides are described.

2 : 6-*Dimethylquionline* (*p*-Toluquinaldine) is also an intermediate for the formation of isocyanine dyes, and is obtained from *p*-toluidine, paraldehyde and hydrochloric acid (Döbner and Miller, *Ber.,* 1883, *16,* 2470). M. P. 60°, B. P. 266—267°. *Methiodide* (Möller, *Annalen,* 1887, *242,* 311).

4-*Methylquinoline* (Lepidine) is a product of the distillation of cinchonine with caustic potash (Williams, *Jahresb.,* 1855, 450). It was obtained synthetically by saturating a mixture of methylal and acetone with hydrochloric acid, and heating the product with a solution of aniline in concentrated hydrochloric acid (C. Beyer, *J. pr. Chem.,* 1886, II, *33,* 418).

Possibly the acetone and methylal condense to a methylmethoxyethyl ketone



The parent butanonol, $CH_3 \cdot CO \cdot OH_2 \cdot CH_2OH$ (b. p. 109—110°/30 mm) is prepared by condensing acetone and formaldehyde with aqueous potassium carbonate (Bayer & Co., U. S. PP. 981 668, 981 669, 989 993/1911; D. R. P. 223 207/

1909). Further details of the syntheses of lepidine and related compounds are given by Mikeska (*Jour. Amer. Chem. Soc.*, 1920, *42*, 2396).

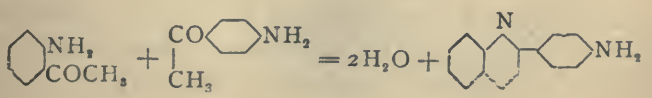
CHAPTER III.

QUINOPHTHALONE AND FLAVANILINE

DYESTUFFS FROM QUINOLINE

The production of the first dyestuff containing quinoline dates back to 1860, the first cyanine having been prepared in that year by the action of alkali on the addition product formed from amyl iodide and "quinoline" (containing lepidine) obtained by distilling cinchonidine with caustic potash. (Williams — — — — — — Hofmann — — —). The dyestuffs of this class found very limited technical application; they lacked fastness were expensive and were readily displaced by the cheaper and faster dyes of the triphenylmethane series. Use was made of cyanine at a much later date when it was found that it acts as a red sensitiser for the photographic plate.

In 1881, the Farbwerke vorm. Meister, Lucius and Brüning patented the production of yellow dyes which were obtained by heating acetylated bases with zinc chloride (Brit. P. 5427/1881; D. R. PP. 19766/1881; 21682/1882) the simplest member of the series, that produced from acetanilide, was examined by O. Fischer and co-workers and found to be 2-*p*-aminophenyl-4-methylquinoline; the action of the zinc chloride on the acetanilide causes the acetyl group to wander from the nitrogen atom into the nucleus giving *o*- and *p*-aminoacetophenones which condense according to the equation



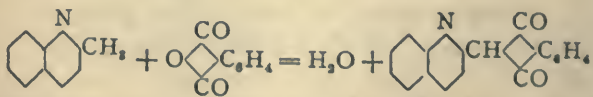
In fact a mixture of the aminoacetophenones can be condensed to flavaniline by the action of zinc chloride at as low a temperature as 90° (O. Fischer, *Ber.*, 1886, *19*, 1038).

About the same time, E. Jacobsen patented a process for making red and violet dyestuffs by acting on pyridine and quinoline bases with benzotrichloride Brit. P. 1362/1883; D.R.P. 19306/1882) or benzal chloride (D.R.P. 23967/1882). The dyestuffs described were of no particular value and the German Patents were allowed to lapse in 1886. It is of interest that Jacobsen found that synthetic quinoline did not give rise to violet dyes when acted on by benzal chloride or benzotrichloride, and he referred the dyestuff formation to the presence of quinaldine in the coal tar quinoline he employed. His view of the typical reaction is given by the equation

$$C_6H_5CCl_3 + C_9H_7N + C_{10}H_9N = C_6H_5CCl(C_9H_6N)(C_{10}H_8N) + 2\,HCl$$

and in the second patent he points out the advisability of using a quinoline or a quinoline substituted in the benzene nucleus with an equimolecular proportion of quinaldine or a derivative thereof.

E. Jacobsen discovered in 1882 that yellow colouring matters were obtained by the condensation of phthalic anhydride with coal tar "pyridine" and "quinoline" under the influence of zinc chloride; these were rendered available as dyestuffs by sulphonation (Brit. P. 1362/1883; D.R.PP. 23188/1882, 25144/1883). It was not ac first recognised that 2-methyl substituted pyridines and quinolines were essential for dyestuff formation, it will be seen later (p. 62) that this is the case and quinoline yellow is really produced from quinaldine according to the equation

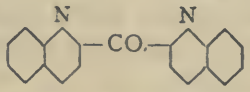


Quinoline red was introduced by the A.-G. für Anilinfabrikation (D. R. P. 40420/1886) who prepared it by heating a mixture of 10 parts of isoquinoline with 11 parts of quin-

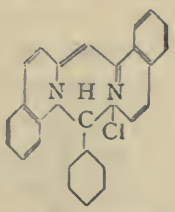
aldine (or 11.5 parts of toluquinaldine, 12 parts xyloquinaldine or 12.5 parts pseudocumoquinaldine) and 5 parts of zinc chloride to 120—130° and running in 15 parts of benzotrichloride.

Hofmann *(Ber.*, 1887, *20*, 4) found that a yield of 9 to 12% might be obtained with pure materials, the production of a red dye from coal tar quinoline (D. R. P. 19306) is probably to be assigned to the presence of isoquinoline as well as quinaldine.

Quinoline red gives benzaldehyde and a base $C_{19}H_{12}ON_2$ on oxidation, the latter compound probably possesses the constitution (Vongerichten and Krantz, *Ber.*, 1910, *43*, 128)



For the dyestuff itself, Krantz *(Chem. Weekblad*, 1914, *11*, 364) suggests the formula



Reference has already been made to the cyanines which had been considered to be products formed by the oxidation of alkylquinolinium salts. Hoogewerf and van Dorp *(Rec. trav. chim.*, 1883, 2, 28, 42, 318, 352) discovered that alkyllepidinium salts took part in the reaction, the quinoline obtained from cinchonine always containing some 4-methylquinoline or lepidine. The simplest cyanine is produced from a mixture of methylquinolinium and methyllepidinium iodides on treatment with alkali according to the equation

$$C_9H_7NCH_3I + C_9H_6(CH_3)NCH_3I + KOH$$
$$= KI + H_2O + H_2 + C_{21}H_{19}N_2I.$$

About the same time Spalteholz *(Ber.*, 1883, *16*, 1847) and Hoogewerf and van Dorp *(Rec. trav. chim.*, 1883, *2*, 41; 1884, *3*, 34) independently discovered that similar dyes were

formed when the alkyl halide addition products of quinoline and quinaldine (in place of lepidine) were treated with alkali, these compounds were called isocyanines.

The cyanines had been largely used as photographic sensitisers but were unreliable and had a tendency to veil and spot the plates. Miethe *(Chemische Industrie,* 1903, *26,* (3), 54) found a more powerful sensitiser in the "ethyl red" produced by condensing the ethiodides of quinoline and quinaldine; this showed fairly even sensitiveness from the ultraviolet to orange, and the plates sensitised with it worked cleanly.

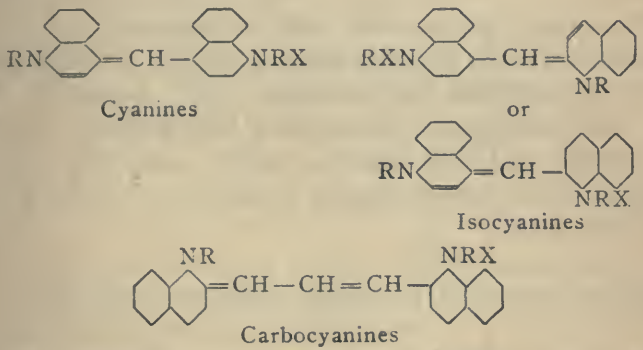
Shortly afterwards, König discovered still more active sensitisers of the isocyanine group; these were placed on the market by Meister, Lucius and Brüning under the names of Orthochrome T, Pinachrome and Pinaverdol (D. R. PP. 167 159 and 167 770/1903). Bayer and Co. introduced other sensitisers such as Perikol, Isokol and Homokol (D. R. PP. 158 078/1903, 170 648/1905, 170 649/1905). The sensitiveness conferred by these dyes extends into the red; they are used in the manufacture of panchromatic plates.

A new class of dyes was discovered by König and patented by Meister, Lucius and Brüning (Brit. P. 16 227/1905; D. R. P. 172 118/1905). These are formed from quaternary quinolinium salts (in presence or absence of quaternary quinolinium salts) and formaldehyde or substances producing formaldehyde in alkaline solution. Pinacyanol belongs to this class of dyes, which give blue solutions and sensitise further into the red than the isocyanines. The substances of this class have been called carbocyanines by Mills and Pope *(Phot. Jour.,* 1920, *60,* 184).

When quinaldinium salts are subjected to the joint action of alkali and an oxidising agent annother class of dyes is formed. Dicyanine belongs to this group, dicyanine "A" nitrate is obtained by bubbling air through an absolute alcoholic solution of 6-ethoxy-2:4-dimethylquinoline ethonitrate and sodium ethoxide, the corresponding dicyanine "A" iodide is obtained from the corresponding ethiodide of

6-ethoxy-2:4-dimethylquinoline and sodium methoxide in methyl alcoholic solution. The necessary ethoxydimethylquinoline is obtained by condensing *p*-phenetidine with paraldehyde and acetone (Mikeska, Haller and Adams, *Jour. Amer. Chem. Soc.*, 1920, *42*, 2392).

The constitutions of the cyanines, isocyanines and carbocyanines have been shown to be as follows (Mills and Pope, *Photh Jour.*, 1920, *60*, 183, 256; Mills and Wishart, *Trans. Chem. Soc.*, 1920, *117*, 579; Mills and Evans, *ibid.*, 1935; Mills and Hamer, *ibid.*, 1550).

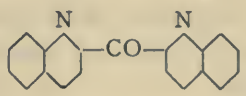


The observation of Adams and Haller (*Jour. Amer. Chem. Soc.*, 1920, *42*, 2389) that pure lepidinium salts give dyes of isocyanine type, similar to, but not identical with, those given by the corresponding derivatives of quinaldine, is confirmatory evidence in favour of the central carbon atom being attached to the two quinoline nuclei in positions 4 and 2' respectively; it further makes it probable that the two formulae given above as possible for the isocyanines are not tautomeric, but represented two distinct compounds.

Another class of quinoline dyestuffs is represented by the compounds obtained by acting on quinoline-2-carboxylic acids with acetic anhydride (Besthorn, *Ber.*, 1904, *37*, 1236) or by allowing quinaldinyl chloride to react with quinoline bases in a neutral solvent, e. g. benzene (Besthorn, D. R. P. 168948/1905). The reactions involved correspond with the equations

$$2\,C_9H_6N(COOH) = C_{19}H_{12}ON_2 + CO_2 + H_2O$$
$$C_9H_6N(COCl) + C_9H_7N = C_{19}H_{12}ON_2 + HCl$$

The substance produced from quinaldinic acid crystallisis in pointed needles, red by transmitted light and showing a green reflex. It sinters about 200° and melts between 230° and 240°. It might be expected that it possesses the constitution



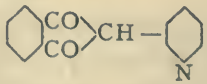
but a ketonic group could not be detected by means of hydroxylamine or phenylhydrazine, and the very slight basicity is inexplicable. The substance is very sensitive to light and oxidising agents; boiling with hydrobromic acid gives quinaldinic acid and quinoline whilst quinaldine acid and carbostyril are formed when it is warmed with concentrated sulphuric acid.

Compounds of this type do not seem to have received technical application, the patent lapsing in 1906.

Quinophthalone Group

Quinophthalone was discovered in 1883, and shortly afterwards it was found that pyridine bases were capable of condensation with phthalic anhydride. For convenience, consideration of the unimportant „pyrophthalone" has been deferred until this point as its constitution is similar to that of quinophthalone.

Pyrophthalone

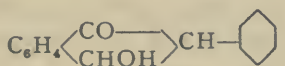


This was obtained by heating picoline from coal-tar (b. p. 133—140°) with phthalic anhydride and zinc chloride to 200° (Jacobsen and Reimer, *Ber.*, 1883, *16*, 2604). It crystallises from alcohol in bright yellow leaflets, is insoluble in

water, difficultly soluble in alcohol but easily in glacial acetic acid. Its melting point is given as above 260° by Jacobsen and Reimer, 280° by von Huber and 280° by Eibner and Löbering.

Von Huber *(Ber.*, 1903, *36*, 1653) found that a better yield was obtained when fractionated picoline (128—132°) was heated under reflux with an equimolecular quantity of phthalic anhydride and a little zinc chloride for some hours to 200°.

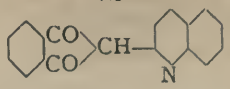
Pyrophthalone has feeble basic properties, it takes up two atoms of hydrogen when reduced with zinc dust and glacial acetic acid giving a substance which forms well crystallised salts and is probably a secondary alcohol. Von Huber represents the reduction product by the structure



Preparations melting at 280° were obtained by heating 2-picoline with phthalic anhydride and a little zinc chloride in sealed tubes at 230° or by the action of phthalyl chloride on 2-picoline in dry benzene solution; these were described by von Huber *(loc. cit.)* under the name of "isopyrophthalone", and given a phthalide constitution.

In repeating von Huber's work, Eibner and Hofmann *(Ber.*, 1904, *37*, 3023) found that both „pyrophthalone" and „isopyrophthalone" melted at 283°, not at 260° and 280° respectively, but on one occasion they obtained an isopyrophthalone melting at 195° from the mother-liquors of a preparation in which phthalyl chloride had been employed. This compound was converted by the action of alkali metal ethoxides into the compound of m. p. 283°. At a later date, Eibner and Löbering *(Ber.*, 1906, *39*, 2450) were unable to repeat the isolation of the compound melting at 195°, but fully established the symmetrical pyridyl-indandone formula for Jacobsen and Reimer's pyrophthalone to which they now assigned a slightly higher melting point, viz. 287°.

Quinophthalone (Quinoline Yellow)



Traub (*Ber.*, 1883, *16*, 298) obtained a condensation product by heating quinoline prepared from cinchonine with phthalic anhydride to 150°. The unused quinoline was extracted with dilute hydrochloric acid and the residue succesively crystallised from glacial acetic acid and benzene. The formula $C_{17}H_9O_2N$ had to be corrected to $C_{18}H_{11}O_2N$ as the compound proved to be identical with the quinoline yellow obtained by Jacobsen and Reimer from quinaldine (*Ber.*, 1883, *16*, 1082, 2603). Pure quinoline does not react with phthalic anhydride but the reaction

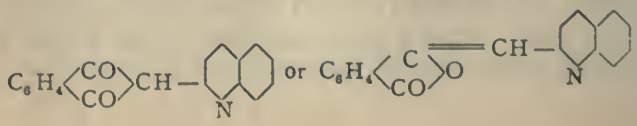
$$C_{10}H_9N + C_8H_4O_3 = H_2O + C_{18}H_{11}O_2N$$

can be effected by heating 2 parts of quinaldine with 1 part each of phthalic anhydride and zinc chloride for 4 or 5 hours at 200°. The product is dissolved in concentrated sulphuric acid at 100°, the solution poured into 20 times its volume of water and the precipitate successively crystallised from glacial acetic acid and alcohol.

Quinoline yellow melts at 234° (Jacobsen and Reimer) or at 238—240° (Eibner and Merkel, *Ber.*, 1904, *37*, 3006), it sublimes without decomposition, is insoluble in water, slightly soluble in ether, more easily in boiling alcohol and readily in glacial acetic acid. Neither basic nor acidic properties are marked, though mono-sodium and potassium derivatives may be prepared (Eibner and Merkel, *loc. cit.*, compare Eibner and Lange, *Annalen*, 1901, *315*, 345). The compound yields quinaldine and phthalic acid when heated with fuming hydrochloric acid to 240°. It is readily oxidised, nitric acid giving phthalic and quinaldinic acids.

Dilute solutions dye wool and silk yellow without the help of a mordant.

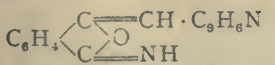
From the method of preparation, either of the formulae



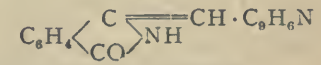
is possible. Jacobsen and Reimer at first inclined to the view that an oxygen atom of the phthalic anhydride united with two hydrogen atoms from the pyridine nucleus of quinoline or quinaldine since an analogous compound could apparently be obtained from pyridine. In this case, however, dyestuff formation was traced to the presence of 2-picoline, and it was recognised that a methyl group in position 2 (or possibly 4) was necessary for condensation with carbonyl groups (See *Ber.*, 1883, *16*, 1892, 2541, 2605, 2942).

Jacobsen now inclined to the first of the two formulae given above which represents quinoline yellow as a quinolylindandione, the second (phthalide) structure gradually came into favour without any definite proof being offered.

Eibner and Lange (*Annalen*, 1901, *315*, 306) attempted an experimental decision, the evidence seemed to be in favour of the phthalide formula, and apparent confirmation was afforded by the study of *p*-toluquinophthalone (Eibner and Simon, *Ber.*, 1901, *34*, 2303). The arguments adduced were that quinophthalone gives addition products with bromine and nitrogen peroxide (compare phthalide derivatives, Gabriel, *Ber.*, 1884, *17*, 2521; 1885, *18*, 2455; 1886, *19*, 837); that quinophthalone is produced from phthalyl chloride, $C_6H_4\langle^{CCl_2}_{CO}\rangle O$, and quinaldine and that isomeric quinophthalines are formed according to whether quinophthalone is condensed with ammonia, or, phthalimide, $C_6H_4\langle^{CO}_{CO}\rangle NH$, is condensed with quinaldine. The isomeric quinophthalines obtained by these reactions were represented by the following formulae.



α-Quinophthaline



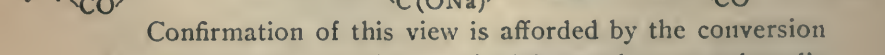
β-Quinophthaline

Doubt was cast on the correctness of Eibner's conclusions as a result of von Huber's examination of the condensation of 2-picoline with phthalic anhydride (*Ber.*, 1903, *36*, 1653). Jacobsen and Reimer (*Ber.*, 1883, *16*, 2603) had already examined the pyrophthalone produced in this way and thought that an isopyrophthalone was also formed from

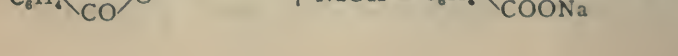
the reacting materials, but the occurence of an isomeride in the condensation of quinaldine with phthalic anhydride had not been observed until Eibner (*Ber.*, 1901, *34*, 2311) briefly mentioned a compound of m. p. 185° (corrected later to 187°) which he looked upon as the indandione derivative: he subsequently examined the new compound at greater length in conjunction with Merkel (*Ber.*, 1902, *35*, 2297). This „isoquinophthalone" is obtained by melting an equimolecular mixture of quinaldine and phthalic anhydride, heating slowly until the melt is just yellowish-red (160°) and after cooling, stirring energetically with not too much alcohol. Crystallisation may be effected by adding alcohol to the solution in chloroform until opalescence is observed.

As matters stood, Eibner attributed the phthalide structure to quinophthalone, whilst isoquinophthalone was represented as quinolylindandione. Further study of the mutual relationships of the two compounds led to the opposite conclusion.

Quinophthalone gives metallic derivatives, analysis showed that they were derived by replacement of one atom of hydrogen by sodium or potassium (Eibner and Merkel, *Ber.*, 1904, *37*, 3006). The same metallic derivatives were formed from isoquinophthalone, they yield quinophthalone on decomposition. The reaction is one which had already been utilised for the preparation of indandiones from substituted phthalides (Gabriel, *Ber.*, 1893, *26*, 951; Nathanson, *ibid.*, 2576); in the case we are now considering, the transformation from isoquinophthalone to quinophthalone is to be represented in the following way.

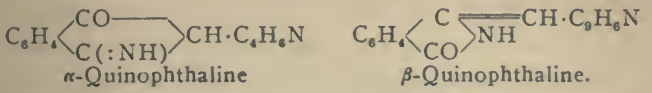


Confirmation of this view is afforded by the conversion of isoquinophthalone into quinolylacetophenonecarboxylic acid (m. p. 155°) on prolonged boiling with dilute alkalies (Eibner and Hofmann, *Ber.*, 1904, *37*, 3011).



From this acid, quinophthalone is obtained by heating above its melting point or by warming with concentrated sulphuric acid.

The isomerism of the quinophthalines must consequently be explained by the following formulae.



α-Quinophthaline *β*-Quinophthaline.

The *α*-compound was originally prepared by Jacobsen and Reimer as dark red leaflets; it is formed by heating quinophthalone with alcoholic ammonia: the *β*-compound is the substance of m. p. 213° which Eibner and Lange obtained as stout pale yellow prisms by heating quinaldine with phthalimide in presence of zinc chloride. Confirmation of this view is afforded by the conversion of the *β*-compound into quinolylacetophenone-*o*-carboxylic acid.

Quinoline yellow is fairly fast to light, some of the substitution derivatives containing chlorine in the benzene half of the quinoline nucleus are even faster (Meister, Lucius and Brüning, D. R. P. 286 237/1913).

Patent Literature

The production of yellow dyes of the Pyrophthalone and Quinophthalone series was patented by Emil Jacobsen (Brit. P. 1362/1883; D. R. P. 23 188/1882). The bases specifically mentioned as giving yellow compounds on heating with phthalic acid are pyridine *(sic.)*, picoline, the higher pyridine bases from coal-tar, the quinoline bases from coal-tar and boiling between 230 and 310°, quinaldine and the bases corresponding to quinaldine prepared from paraldehyde and toluidine, xylidine and naphthylamine. The process described consisted in heating one molecule of phthalic anhydride with two molecules of the base and one molecule of zinc chloride to 200° for 5 or 6 hours in the case of coal-tar bases and to about 250° for quinaldine and its homologues. The colouring matter was then isolated either by extracting excess of base and zinc chloride with dilute hydrochloric acid, or

by dissolving the melt in concentrated sulphuric acid and pouring into water. The precipitated dyestuff could be purified by crystallisation from boiling glacial acetic acid. The patent says nothing as to yield or formation of by-products, Eibner's isolation of isoquinophthalone shows that the reaction cannot be quantitative.

To obtain the dyes in a soluble form, they are sulphonated, preferably with chlorosulphonic acid at 100°, diluting, neutralising and salting out.

The use of chloro- and nitro-derivatives of phthalic anhydride as well as of phthalimide was also described by Jacobsen (D. R. P. 25 144/1883). The latter patent states that whilst pure synthetic quinoline does not give dyestuffs with phthalic anhydride, it may be made available for the purpose by methylation, ethylation &c.

The „Quinoline Yellow" which was actually used was the sodium salt of sulphonated quinophthalone, the greenish yellow shades produced by the dye are fast to light and soap.

The conversion of quinophthalone into basic dyes by heating with alcoholic ammonia or aliphatic amines for 40 hours at 200° was patented by Meister, Lucius and Brüning (D. R. P. 27 785/1883). The resulting quinophthalines, $C_6H_4\langle^{CO}_{C(:NR)}\rangle CH\cdot C_9H_6N$ do not seem to have found any practical application.

As mentioned above, Eibner has shown that the formation of quinophthalone is accompanied by that of isoquinophthalone, the amount of the latter is stated to reach 25 per cent of the total yield. Eibner finding that isoquinophthalone readily gives metallic derivatives of quinophthalone, utilised the reaction to obtain better yields of the latter substance (D. R. P. 158 761/1903). His method consists in treating the crude melt whilst warm with sufficient sodium ethoxide solution at water bath temperature to give an uniformly red mass; this is filtered and washed with alcoholic alkali until the filtrate is only bright yellow. The remaining

pure sodium compound is then decomposed by boiling water and the quinophthalone dried at 100°.

Eibner incidentally mentions the quinophthalones obtained by starting with 2:4-xylidine, 2:4:5-cumidine and 1- and 2-naphthylamines, converting these into quinaldines and condensing with phthalic anhydride. The two last are stated to be highly tinctorial.

Quinophthalones derived from chloroquinaldines have attracted some attention during more recent years. Bayer & Co. (Brit. P. 28 266/1908; U. S. P. 890 588/1908; D. R. P. 204 255/1907) heat 177.5 parts of *p*-chloroquinaldine (obtained from *p*-chloroaniline, acetaldehyde and hydrochloric acid) with 148 parts of phthalic anhydride to 210°. After 5 or 6 hours, the quinophthalone is washed with alcohol, dried and sulphonated with fuming sulphuric acid.

Wool and silk are dyed from an acid bath yellow (green shade); it is claimed that the yield of this dye is better than that of quinophthalone, it possesses greater tinctorial power and its lakes show greater fastness to light.

Meister, Lucius and Brüning (D. R. P. 286 237/1913) claim greater fastness to light for quinophthalones prepared from quinaldines containing chlorine and an ortho-substituent in the benzene nucleus. The chlorine may or may not be the ortho-substituent, the following are stated to be suitable bases for giving the necessary quinaldine; 2-chloroaniline, 3-chloro-4-toludine, 5-chloro-2-toluidine and 6-chloro-2-toluidine.

In employing orthochloroaniline, 13 parts of the base are heated for 5 hours at about 100° with 40 parts of hydrochloric acid and 10 parts of paraldehyde. 59 parts of the isolated chloroquinaldine (m. p. 68—70°) are heated with 50 parts of phthalic anhydride for 2 hours at 200—210°. The chloroquinophthalone is sulphonated by warming with 10 to 20 times its weight of 20 per cent fuming sulphuric acid.

The same firm also use the chloroquinaldine prepared from 3-chloroaniline in a similar manner.

It is possible to use certain derivatives of quinophtha-

lones as sulphur dyes, a quinaldine being condensed with a thiolphthalic acid (Ges. f. chem. Ind. Basel, Brit. P. 4159/1907; D. R. P. 189943/1906). The thiol group can be introduced into the phthalic acid either by replacement of an amino-group, or, more simply, by converting β-sulphophthalic acid into its acid chloride and reducing the sulphonyl chloride group by zinc dust. Thiolphthalic acid forms a yellow crystalline mass, it melts indefinitely about 160° or 170° and is soluble in organic solvents and hot water.

As an example of formation of colouring matter, equal weights of thiolphthalic acid and β-naphthoquinaldine are melted together at 150°, the temperature being raised to 200° in the course of 4 hours and maintained at 200° until the condensation is complete. The solidified melt can either be powdered and used directly, or purified by dissolving it in sodium sulphide solution, filtering and precipitating by hydrochloric acid.

The colouring matter may be used as a sulphur dye, thus unmordanted cotton is dyed orange yellow from a sodium sulphide bath, on oxidation (air or chromate) a very pure and fast yellow is obtained.

Flavaniline $C_{16}H_{14}N_2$

This compound is formed by heating acetanilide with zinc chloride and now only possesses theoretical interest. The patent taken out by Meister, Lucius and Brüning (D. R. P. 19766/1881) was allowed to lapse in 1883; in this patent the method given was to heat equal weights of acetanilide and zinc chloride, or, alternatively, 1 part of acetanilide, 2 parts of aniline hydrochloride and 2 parts of zinc chloride to 230—250°. The resulting melt was extracted by boiling with water, the resinous residue dissolved in hydrochloric acid and the colouring matter salted out. It was also claimed that the compound could be combined with alkyl halides or sulphonated.

An additional patent (D. R. P. 21682/1882) of the same firm claimed the use of amino-carboxylic acids in place of

amines; whilst the patents of Majert (D. R. P. 28 323/1882) and Baum (D. R. P. 27 948/1883) were obviously intended to circumvent the patents of Meister, Lucius and Brüning. Majert's method was to act on ethenyldiphenylamidine,

$$CH_3 \cdot C\begin{matrix} NH \cdot C_6H_5 \\ N \cdot C_6H_5 \end{matrix}$$

with zinc chloride; Baum's process consisted in heating aniline hydrochloride with an excess of acetic anhydride to 180—200° for 12 hours.

The use of flavaniline was abandoned as yields were bad, the dyestuff was not fast to light and the colouring power was small.

The constitution of this compound has already been dealt with (p. 55), other references are, Fischer and Rudolph, *Ber.*, 1882, *15*, 1500; Besthorn and Fischer, *Ber.*, 1883, *16*, 73.

CHAPTER IV.

THE CYANINE GROUP

Constitution of Isocyanines and Cyanines

The first dyes containing the quinoline nucleus were prepared by Greville Williams (*Trans. Roy. Soc. Edin.*, 1856, 1857, *21*, 309, 377), who subsequently suggested that they should be employed technically, Williams started with the crude quinoline obtained by the distillation of cinchonine, combined it with amyl iodide to a quaternary ammonium salt and boiled the aqueous solution of the latter compound with excess of ammonia in an open pan (*Chem. News*, 1860, *2*, 219). Cyanine dyes were exhibited in 1861 and placed on the market by Menier of Paris.

The composition of the cyanines was examined by Hofmann who recognised that the lepidine contained in quinoline derived from cinchonine was chiefly responsible for their

formation, his view of the reaction was that two molecules of lepidine amyliodide lost one molecule of hydriodic acid in presence of alkali, the residues being condensed (*Compt. Rend.*, 1862, *55*, 849; *Chem. News*, 1863, *7*, 85; *Proc. R. S.*, 1863, *12*, 410).

$$2\,C_{10}H_9N \cdot C_5H_{11}I = C_{30}H_{39}N_2I + HI$$

This view is incorrect, two atoms of hydrogen as well as hydrogen iodide being lost during the condensation. The resulting compound dissolves sparingly in water but easily in alcohol with deep blue colour, the crystals which show a metallic green lustre consist of monoclinic prisms (Arzruni and Traube, *Rec. trav. chim.*, 1885, *4*, 61).

The simplest of the cyanines was prepared by Hoogewerf and van Dorp (*Rec. trav. chim.*, 1883, *2*, 318), alkali being added to a boiling solution of the methiodides of quinoline and lepidine.

$$C_9H_7N \cdot CH_3I + C_{10}H_9N \cdot CH_3I + KOH$$
$$= KI + H_2O + C_{21}H_{19}N_2I + H_2$$

The resulting resin was boiled with alcohol, allowed to cool, and the residue repeatedly crystallised from dilute alcohol. The dye was thus obtained as needles showing a green reflex and melting at 291°. The aqueous solution is blue by reflected and violet by transmitted light.

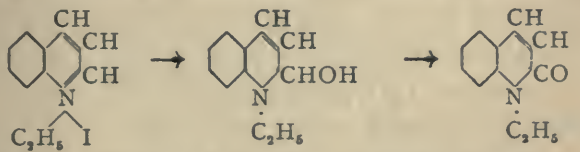
A number of the cyanines have been prepared, reference will be made to them subsequently.

The *isocyanines* were discovered independently by Spalteholz (*Ber.*, 1883, *16*, 1847) and Hoogewerf and van Dorp (*Rec. trav. chim.*, 1883, *2*, 41; 1884, *3*, 344). The quaternary ammonium iodides derived from quinaldine yield purplish red dyestuffs when treated with alkali, oxidation taking place simultaneously. For the preparation of an isocyanine it is necessary that equimolecular proportions of two quaternary ammonium salts be taken, of these one must be a quinaldinium, the other may be a quinolinium compound. Thus diethylisocyanine iodide obtained by the action of caustic potash on a mixture of the ethiodides of quinoline and

quinaldine was given the formula $C_{23}H_{25}N_2I$, $1^1/_2H_2O$ by Spalteholz, whilst Hoogewerf and van Dorp wrote the compound as $C_{23}H_{23}N_2I$, its formation being expressed by the equation

$$C_{12}H_{14}NI + C_{11}H_{12}NI = C_{23}H_{23}N_2I + HI + 2H$$

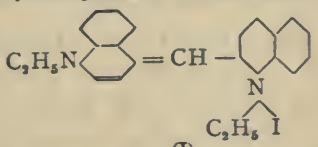
The constitution of the isocyanines may be regarded as settled. The action of alkali and an oxidising agent on the quaternary quinolinium salts whereby quinolones are produced



(Decker, *Ber.*, 1891, *24*, 692; 1892, *25*, 3326) suggests that a quinolone condenses with unaltered quinaldinium alkyl halide.

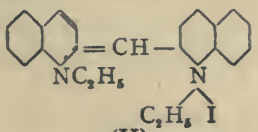
$$C_9H_6(NC_2H_5):O + CH_3 \cdot C_9H_6NC_2H_5I$$
$$= H_2O + C_9H_6(NC_2H_5):CH \cdot C_9H_6NC_2H_5I$$

Miethe and Bock (*Ber.*, 1904, *37*, 2012) assume that an intermediate γ-quinolone is produced, so that „Ethyl red", as they style the diethylisocyanine, would have the constitution



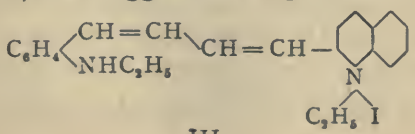
(I)

Decker (*J. pr. Chem.*, 1911, II, *84*, 235) supposing the condensation to take place in the α-position writes the isocyanines in the following manner



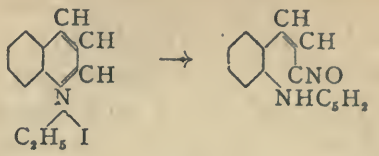
(II)

W. König (*J. pr. Chem.*, 1911, II, *86*, 166; compare *ibid.*, 1906, II, *73*, 100) has suggested an open chain formula



III

for the isocyanines, based on Roser's view (*Annalen*, 1892, *272*, 221; 1894, *282*, 363) that the pseudo-bases derived from the quinolinium alkyl iodides are aldehyde-amines

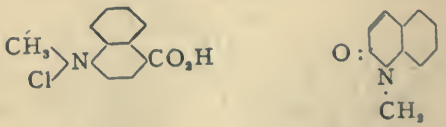


Although Roser's work has been supported by Gadamer (*Arch. Pharm.*, 1905, *243*, 12; 1908, *246*, 89) and Kaufmann and Strübin (*Ber.*, 1911, *44*, 680) the open chain formula must be definitely discarded for the isocyanines.

At present we are chiefly concerned as to whether condensation takes place in the α- or γ-position. The γ-condensation is rendered very probable by the observations of Kaufmann and Vonderwahl (*Ber.*, 1912, *45*, 1404) that quinolinium alkyl iodides substituted with chlorine in position 4 react with quinaldinium ethiodide with elimination of hydrogen chloride to give the same isocyanines as the unsubstituted compounds.

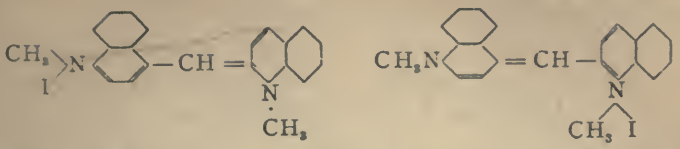
That the 2-methyl group reacts is rendered very probable by analogy with the formation of quinoline yellow, whilst Vongerichten and Höfchen (*Ber.*, 1908, *41*, 3054) have shown that benzylidene quinaldinium ethiodide and 2-isopropyl-quinolinium methiodide are incapable of taking part in the formation of isocyanines.

Mills and Wishart (*Trans. Chem. Soc.*, 1920, *117*, 579) oxidised dimethylisocyanine with permanganate and obtained cinchoninic acid methochloride and 1-methyl-2-quinolone.



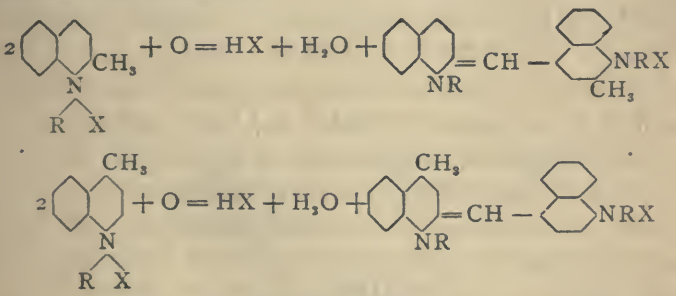
Since the dye had been prepared from quinolinium and quinaldinium salts, it is evident that the former must have given a 4-quinolone which condensed with the quinaldinium

salt thus leaving only the tautomeric formulae possible.



Which configuration is preferred probably depends on the relative positivity of the two quinoline nuclei. The value of these results is enhanced by the fact that Mills and Wishart obtained yields of the fission products amounting to 70 to 80 per cent of those theoretically possible.

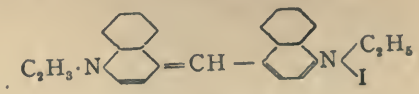
Additional proof that the two quinoline nuclei are linked in position 2 and 4 respectively by means of a CH group is afforded by the fact that either quinaldine alkyl iodides or lepidine alkyl iodides by themselves yield isocyanines when they undergo an alkaline oxidation (E. Q. Adams and H. W. Haller, *J. Am. C. S.*, 1920, *42*, 2389). Isomeric isocyanines are thus produced, their formation can only be explained by supposing that one molecule of the quinaldine alkyl iodide is attacked in poition 4, and one of the lepidine alkyl iodide molecules in position 2.



Whilst the dyes obtained from the ethiodides of quinaldine and lepidine have similar sensitising properties they are very different crystallographically. The authors cited submitted both the methiodides and ethiodides of lepidine and tolulepidine as well as the the methonitrate of the latter base to the reaction.

The cyanines, being derived in a similar way from lepi-

dine and quinoline alkyl iodides must almost certainly be represented with constitutions such as



Cyanines

The possibility of sensitising photographic plates to the less refrangible rays of the spectrum was discovered by Vogel (*Ber.*, 1873, *6*, 1302) who observed that the Wortley collodio-bromide dry plates which were stained with a yellow dye to prevent halation, showed sensitiveness in the green and not in the blue. If the dye were washed out, then the sensitiveness disappeared. Somewhat later, Vogel showed that the sensitiveness of collodio-bromide emulsions to the less refrangible rays was increased by a number of dyestuffs, amongst these being cyanine (*Ber.*, 1875, *8*, 95, 1635).

About the same time, Waterhouse discovered that eosine acts as a powerful green and yellow sensitiser and in 1884 the dye was used commercially in Edward's Isochromatic plates. Two dyestuffs nearly related to eosine, viz. Rose Bengal and Erythrosine (pp. 310, 311) are still used as sensitisers for the yellow and green.

Although cyanine was largely used as a sensitiser, it was found to be somewhat unreliable and had a tendency to veil and spot the plates. The discovery of the powerful sensitising action of certain of the isocyanines led to their rapid introduction. For an account of the application and properties of the isocyanine dyes, the paper by W. H. Mills and W. J. Pope should be consulted (*Phot. J.*, 1920, *60*, 183).

Dimethylcyanine. The iodide of the simplest cyanine, $C_{21}H_{19}N_2I$, was obtained by Hoogewerf and van Dorp (*Rec. trav. chim.*, 1883, *2*, 318) by adding caustic potash to a boiling solution of 2 parts of quinoline methiodide and 1 part of lepidine methiodide in 3 parts of water. The resulting resin was boiled with alcohol, allowed to cool, and the undissolved portion repeatedly crystallised from dilute alcohol. The

iodide was thus obtained as fine green needles melting at 291°, almost insoluble in ether and benzene, difficultly soluble in alcohol, somewhat soluble in water, acetone and chloroform. The aqueous solution is reddish blue, the alcoholic blue by reflected and violet by transmitted light.

The *chloride*, $C_{21}H_{19}N_2Cl$, 5 H_2O, is easily soluble in alcohol and melts with decomposition about 300°.

The *platinichloride*, $C_{21}H_{19}N_2(HPtCl_6)$, forms a yellow precipitate.

Diethylcyanine iodide, $C_{23}H_{23}N_2I$, forms green prisms, m. p. 271—273°. The corresponding *bromide* does not melt below 290° (Hoogewerf and van Dorp, *Rec. trav. chim.*, 1884, *3*, 340).

Diisoamylcyanine iodide, $C_{29}H_{35}N_2I$, $1^1/_2H_2O$, is obtained by dropping strong caustic potash solution into a mixture of 8 part of lepidine isoamyliodide and 2 parts of quinoline isoamyliodide in 20 parts of alcohol (Hoogewerf and van Dorp, *Rec. trav. chim.*, 1884, *3*, 352. Compare, *ibid.*, 1883, *2*, 28, 42, 324, and also Hofmann, *Compt. rend.*, 1862, *55*, 849; Nadler and Merz (*Zeitschr.*, 1867, 343). The iodide is easily soluble in hot alcohol and crystallises in cantharidine green, monoclinic tables (Arzruni, *Rec. trav. chim.*, 1884, *3*, 354). It is very sparingly soluble in water and ether. On rapid heating it fuses about 100°, whilst the periodide melts at 187—189°.

By treatment with moist silver oxide, it is stated that the free base, $C_{29}H_{36}N_2O$, may be obtained as a viscous, bronze coloured mass. Nadler and Merz prepared the chloride by the action of silver chloride on the iodide, it crystallises from hot water in blue prisms. Various other salts containing one, two or even three equivalents of acid radicle have been described. Thus $C_{29}H_{35}N_2I$, 2 HCl is colourless and $C_{29}N_{35}N_2I$, HCl is bronze coloured. By warming diissoamylcyanine nitrate in alcoholic solution with ammonium sulphide, Nadler and Merz obtained a reddish yellow compound, $C_{58}H_{68}O_2N_4S_3$, which is insoluble in water, but forms unstable salts with acids.

The cyanine, $C_{30}H_{39}N_2I$ (?), was said to be obtained by treating lepidine isoamyliodide with potash (Hofmann, *loc. cit.*, Arzruni and Traube, *Rec. trav. chim.*, 1885, *4*, 61). The compound described, dissolved easily in alcohol with a blue colour; silver oxide was stated to give the free base as a dark blue, indubitably crystalline mass. It will be noticed that the formula ascribed to the substance does not allow for oxidation to have occurred during its formation; further it should be noticed that a true cyanine could not be produced by the condensation of two molecules of lepidine as in this case both 4-positions would be occupied.

The blue colour of cyanine is destroyed by acids and restored by alkalies, salts with two equivalents of acid having a pale yellow colour; this led to a suggestion to use cyanine as an indicator.

Isocyanines

The formation and constitution of these compounds has already been discussed; the earliest members of the class in question being comparatively simple. It is evident that isocyanines of higher molecular weight may be prepared either by using quinolinium or quinaldinium salts containing heavier alkyl groups, or, alternatively, by replacing hydrogen by alkyl in the quinoline or quinaldine employed, substitution being effected in the benzene half of the nucleus. The simpler isocyanines possess certain advantages over the cyanines from a photographic point of view, but do not act as such efficient sensitisers for the red end of the spectrum.

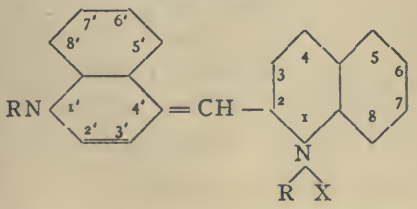
The possibility that isocyanines derived from toluquinolines and toluquinaldines might be more sensitive to red and yet possess the other advantages over the cyanines led to experiments on the part of Meister, Lucius and Brüning and the introduction of the Pinaverdol (isocyanine) type of sensitiser (Brit. P. 9598/1903; D.R.P. 167159/1903; F. P. 338780/1903). It was found that quinaldine alkyl iodides would not react with *o*-toluquinoline alkyl iodides, and only very bad yields were obtained from *o*-toluquinaldine alkyl

iodides and quinoline alkyl iodides. The hindering effect of substitution was not observed when meta or para toluquinoline or toluquinaldine alkyl iodides were employed and the eight possible condensations of quinaldinium salts with meta and para quinolinium salts, and of meta or para toluquinaldinium salts with quinolinium or meta or para toluquinaldinium salts were effected.

Several of the more complex isocyanines were introduced as sensitisers but no attention was paid to their preparation outside Germany.

The war prevented the use of these dyes by the allied Powers until methods were worked out for their preparation, the plates used for photographic work by the Allied Air Forces were sensitised by dyes actually made in the University Chemical Laboratory, Cambridge, where the constitutions of the more important isocyanines were determined. Work was also undertaken on an extensive scale in America, so that recently the patent descriptions have been amplified by an extensive scientific literature.

Mills and Pope number the positions in the isocyanine nucleus in the following manner



and give a list of the isocyanines which they have prepared and examined (*Phot. J.*, 1920, *60*, 186).

1. 1 : 1′-Dimethylisocyanine iodide.
2. 1 : 1′ : 6′-Trimethylisocyanine iodide.
3. 1 : 1′ : 6-Trimethylisocyanine iodide.
4. 1 : 1′ : 2′ : 6 : 6′-Pentamethylisocyanine iodide.
5. 1 : 1′-Diethyl-6-methylisocyanine iodide.
6. 1 : 1′-Di-*n*-propyl-6-methylisocyanine iodide.
7. 1 : 1′-Di-*n*-butyl-6-methylisocyanine iodide.

8. 1 : 1′-Diethylisocyanine iodide.
9. 1 : 1′-Diethyl-2′-methylisocyanine iodide.
10. 1 : 1′-Diethyl-β-naphthoisocyanine iodide.
11. 1 : 1′-Dimethyl-5-acetaminoisocyanine iodide.
12. 1 : 1′-Dimethyl-5-aminoisocyanine iodide.
13. 1 : 1′-Dimethyl-6-acetaminoisocyanine iodide.
14. 1 : 1′-Dimethyl-6-aminoisocyanine iodide.
15. 1 : 1′-Dimethyl-6′-acetaminoisocyanine iodide.
16. 1 : 1′-Dimethyl-6′-aminoisocyanine iodide.
17. 1 : 1′-Dimethyl-6-cinnamoylisocyanine iodide.
18. 1 : 1′-Diethyl-6-ethoxy-6′-methoxyisocyanine iodide.
19. 1 : 1′-Dimethyl-2′-cyanoisocyanine iodide.
20. 1-Ethyl-1′-methyl-2′-phenylisocyanine iodide.

1 : 1′-*Dimethylisocyanine iodide,* $C_{21}H_{19}N_2I$, has been found by Mills and Pope to be of relatively little use as a photographic sensitiser, though the homologous compound, substituted by methyl in position 6, is the very useful „Pinaverdol".

1 : 1′-*Diethylisocyanine iodide,* $C_{23}H_{23}N_2I$, was discovered by Spalteholz (*Ber.,* 1883, *16,* 1851) who assigned to it the formula $C_{23}H_{25}N_2I$, and almost simultaneously by Hoogewerf and van Dorp (*Rec. trav. chim.,* 1884, *3,* 346) who prepared the salt by dropping caustic potash lye (1 molecule) into a boiling mixture of 1 part of quinaldine ethiodide and 1.9 parts of quinoline ethiodide in 25 parts of alcohol. The solution was partially evaporated, the separated material dissolved in alcohol, precipitated by ether and recrystallised from 50 per cent alcohol.

The 1 : 1′-diethylisocyanine salts are referred to as „Ethyl Red" by Miethe and Bock. Miethe made the discovery (*Chemische Industrie,* 1903, *26,* (3), 54) that ethyl red was far more powerful in its effects than the cyanine dyes, sensitising fairly evenly from the ultra-violet to orange, also, that plates sensitised with it worked cleanly.

Pinaverdol or Sensitol Green is a salt of 1 : 1′ : 6-*Trimethylisocyanine* (Mills and Pope, *Phot. J.,* 1920, *60,* 188; Wise, Adams, Stewart and Lund, *J. Ind. Eng. Chem.,* 1919,

11, 460). According to D. R. P. 167 159, an alcoholic solution of 6 grams of caustic potash is added to a boiling solution of 28 grams of *p*-toluquinaldine methiodide and 55 grams of quinoline methiodide in about 800 cc. of alcohol.

Mills and Pope boiled 80 grams of quinoline methiodide and 41 grams of *p*-toluquinaldine methiodide with 6.65 grams of sodium hydroxide dissolved in 1600 cc. of alcohol. The isocyanine iodide crystallised on cooling and was purified by recrystallisation from methyl alcohol.

Two modifications are known, a labile one which separates as minute dark purple felted needles, the stable form consists of elongated rectangular plates showing an olive green metallic reflex. Crystallographic data are given by Wherry and Adams (*J. Wash. Acad. Sci.*, 1919, *9*, 396), spectrographs are given by Mills and Pope and also by Valenta (*Photog. Corresp.*, 1903, 359) and Newton and Bull (*Phot. J.*, 1905, *45*, 15).

Very similar sensitising effects are given by the isomeric 1 : 1' : 6'-trimethylisocyanine iodide obtained from *p*-toluquinoline methiodide and quinaldine methiodide.

Comparison of 1 : 1'-dialkyl-6-methylisocyanines in which the two alkyl groups are methyl, ethyl, *n*-propyl and *n*-butyl shows that the total induced sensitiveness steadily diminishes as the molecular weight of the dye is increased. This diminution of sensitiveness is especially marked in the green and red (Mills and Pope, *loc. cit.*, 191; compare Sheppard, *Phot. J.*, 1908, *48*, 311).

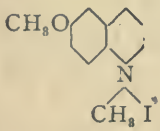
Pinaverdol is a better sensitiser than the simpler salts of 1 : 1'-dimethylisocyanine, the maxima shown in spectrographs being more nearly equal and less marked in the case of the higher homologues.

1 : 1' : 6 : 6'-*Tetramethylisocyanine iodide*, is obtained from *p*-toluquinoline methiodide and *p*-toluquinaldine methiodide. According to D. R. P. 167 159 it makes the photographic plate $2^1/_2$ times as sensitive in the red as the isocyanine from quinoline and quinaldine. The corresponding compound from the ethiodides was only $1^1/_2$ times as effective.

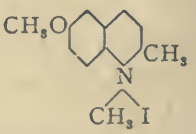
The following directions are given for the preparation of the dye. 30 grams of *p*-toluquinaldine ethiodide and 58 grams of *p*-toluquinoline ethiodide are dissolved in 800 cc. of hot alcohol and 6 grams of caustic potash dissolved in alcohol added. The formation of dyestuff is complete in a few minutes, it is precipitated by ether and purified by recrystallisation from water and alcohol.

Shining dark green prisms, easily soluble in hot alcohol, more difficultly in hot water and very sparingly in cold water, with reddish violet colour.

Shortly afterwards (D. R. P. 167 770) a further patent was taken for the use of meta and para alkyloxylated quinolinium and quinaldinium salts such as



and



For dyes derived from these, similar advantages were claimed. Two examples may be quoted from this patent.

1. 30 grams of *p*-toluquinaldinium ethiodide and 65 grams of *p*-methoxyquinolinium ethiodide are dissolved in 500 cc. of alcohol and the boiling solution treated with 6 to 8 grams of caustic potash dissolved in 100 cc. of alcohol. The colouring matter is precipitated by addition of ether and crystallised from alcohol. Shining brown leaflets, easily soluble in alcohol with a reddish violet colour.

2. 10 grams of *p*-methoxyquinaldine ethiodide and 20 grams of *p*-toluquinoline ethiodide are dissolved in 100 cc. of methyl alcohol. To the boiling solution a solution of 2.5 grams of caustic potash is added. The colouring matter is isolated by partially evaporating the methyl alcohol and then purified by repeated solution in alcohol and washing with ether.

Pinachrome has been stated to be 1 : 1'-Diethyl-6-ethoxy-6'-methoxyisocyanine iodide, this seems to be confirmed by the apparent identity of sensitising action effected by commercial Pinachrome and the product formed on heating 6-

methoxyquinoline ethiodide (12.6 grams), 6-ethoxyquinaldine ethiodide (6.86 grams) and sodium hydroxide (1.2 grams) in alcoholic solution (Mills and Pope, *Phot. J.*, 1920, *60*, 197).

Reference should be made to D. R. P. 154 448/1903 of Meister, Lucius and Brüning. It is stated that alkyl iodides of quinoline bases, not containing a methyl group in the pyridine ring, can give sensitising dyestuffs if acted on by alkali in alcoholic solution. Two examples are given, in the first, quinoline ethiodide is dissolved in methyl alcohol and treated with 10 per cent methyl-alcoholic potash; in the second, quinoline methochloride is used similarly.

It will have been noticed that no mention of the use of an oxidising agent has been made in any of the foregoing patents.

The A. G. f. Anilinfabrikation (D. R. P. 155 541/1903) definitely claimed the use of an oxidising agent when the alkyl halide addition products of quinoline, quinaldine and lepidine were treated with alkali in alcoholic solution. Amongst the oxidising agents to be thus employed in alkaline solution, potassium ferricyanide and ammonium persulphate are mentioned.

Bayer & Co. (U. S. P. 752 323/1903; F. P. 337 704/1903; D. R. P. 158 078/1903) obtained dyestuffs for use as sensitisers by the action of alkalies on the addition products formed from dialkyl sulphates and quinaldine (or with quinoline as well as quinaldine). Thus equimolecular quantities of quinaldine and dimethyl sulphate are combined, the product dissolved in five times the quantity of alcohol, warmed on the water-bath and half a molecular weight of alkali gradually added in 10 per cent aqueous solution.

An additional patent (D. R. P. 170 049/1904) describes the use of homologues of quinoline and quinaldine.

1. 156 parts of 2:7-dimethylquinoline and 126 parts of dimethyl sulphate are warmed on the water-bath until the product is soluble in water. It is then dissolved in 600 parts of alcohol 30 parts of caustic potash dissolved in 300 parts of alcohol added and the alcohol distilled off from the dark

red solution. The mass is dried, crushed and tarry matters extracted by ether; the residue is finally crystallised from alcohol or chloroform and ether. Steel blue crystals, soluble in chloroform, acetone, alcohol and water, insoluble in ether, benzene and ligroin.

2. 156 parts of 2:6-dimethylquinoline (i. e. *p*-toluquinaldine) and 125 parts of dimethyl sulphate are warmed on the water-bath giving 282 parts of methylquinaldinium salt, this is dissolved in 500 parts of alcohol and treated with 30 parts of caustic potash in 300 parts of alcohol. The procedure is then the same as that described in the other example.

Bayer & Co. (U. S. P. 780741/1904 of Berendes, D. R. P. 170048/1903) also used the addition products of quinoline bases with the alkyl esters of alkylsulphonic acids. The dyes obtained are said to be useful sensitisers as they do not produce fogging and have favourable absorption spectra. [1]) The following examples are given.

1. 143 parts of quinaldine and 138 parts of ethyl ethanesulphonate, $C_2H_5SO_2 \cdot OC_2H_5$, are heated on the water-bath until soluble in water, the product dissolved in 500 parts of alcohol and treated with a 10 per cent solution of 30 parts of caustic potash. The alcohol is then distilled off, resinous matter extracted by ether and the residue dissolved in chloroform and evaporated. Purification is effected by crystallisation from a mixture of alcohol and ether or other suitable solvent. Bronze green needles, difficultly soluble in water with reddish shade, the solutions in alcohol and chloroform are violet.

2. 143 parts of quinaldine and 186 parts of ethyl benzenesulphonate are combined at 140°, the product dissolved in 600 parts of alcohol and treated with an alcoholic solution of 30 parts of caustic potash. Then proceed as in the last example.

3. 143 parts of quinaldine and 279 parts of ethyl *p*-bromotoluenesulphonate are combined at 130—140°. The pro-

1) The absorption spectra will depend on the homologues or derivatives of quinoline which are employed, not on the fact that alkyl esters of alkylsulphonic acids are used.

duct is crystallised from alcohol. 42.2 parts of the salt are dissolved in twice its weight of alcohol and acted on by an alcoholic solution of 3 parts of caustic potash.

4. 155 parts of *p*-toluquinaldine are treated with 200 parts of ethyl *p*-toluenesulphonate.

5. 143 parts of quinaldine and 186 parts of methyl *p*-toluenesulphonate.

6. 20.8 parts of *p*-bromoquinoline are condensed with 20 parts of ethyl *p*-toluenesulphonate. 20.4 parts of the product so obtained together with 17.4 parts of the corresponding product from *p*-toluquinaldine and ethyl *p*-toluenesulphonate are dissolved in 75 parts of alcohol and treated with 3 parts of caustic potash in 300 parts of alcohol. Most of the alcohol is distilled off, water added, the mixture shaken with ether and then the procedure mentioned in the other cases followed.

Bayer & Co. introduced sensitisers under the names of Homokol, Isokol and Perikol.

It is remarkable that *α*-naphthoquinaldine alkyl iodides should be incapable of giving isocyanine dyes (A. G. f. Anilinfabrikation, D. R. P. 158 349/1904). The corresponding *β*-naphthoquinaldines give sensitisers, their solutions showing an absorption band more towards the red.

1. Add 2 parts of caustic potash dissolved in alcohol to a boiling solution of 7 parts of *β*-naphthoquinaldine ethiodide and 11.8 parts of quinoline ethiodide in 169 parts of alcohol. Formation of dyestuff is finished in 15 minutes. The compound thus produced is said to sensitise the photographic plate as far as the B line.

2. 7 grams of *β*-naphthoquinaldine ethiodide and 12.5 grams of *p*-toluquinaldine ethiodide are treated in the manner described.

3. Dissolve 6.7 grams of *β*-naphthoquinaldine ethiodide and 3 grams of quinaldine ethiodide in 100 cc. of alcohol. Add 1 gram of caustic potash in alcoholic solution and boil.

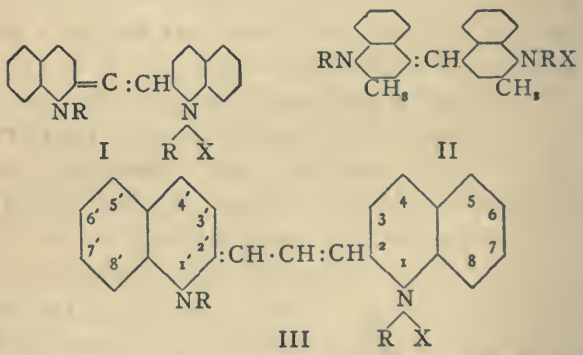
The general sensibility of plates prepared with aid of

these compounds and the shortening of the exposure for the red are claimed as great advantages.

Carbocyanines

Closely related to the Cyanines and Isocyanines are compounds such as Pinacyanol, introduced as a sensitiser by Meister, Lucius and Brüning (Brit. P. 16227/1905; F. P. 361686/1905; D. R. P. 172118/1905). Whilst isocyanines are formed from mixtures of quinoline and quinaldine alkyl halides, an intense reddish purple colour accompanying the change; a deep blue colouration is produced if formaldehyde is also present. Substances produced by such reactions will be referred to as Carbocyanines in accordance with the suggestion of Mills and Pope (*Phot. J.*, 1920, *60*, 256).

Three structures have been proposed for these compounds, viz.,



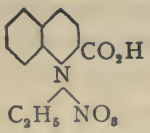
Formula I is due to O. Fischer (*J. pr. Chem.*, 1918, *98*, 204); it assumes condensation between equimolecular proportions of formaldehyde and quinoline and quinaldine alkyl iodides. Formula II was proposed by Wise, Adams, Stewart, and Lund (*J. Ind. Eng. Chem.*, 1919, *11*, 460), whilst the structure represented by III was adopted by Mills and Pope and confirmed by the work of Mills and Hamer (*Trans. Chem. Soc.*, 1920, 117, 1550).

Formulae II and III both assume condensation between two molecules of quinaldine alkyl iodide and one of formaldehyde, the quinoline alkyl iodide not entering directly into

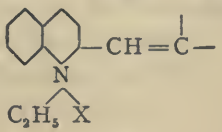
the reaction. Of these formulae, that of Mills and Hamer may be taken as definitely established. Very careful analysis showed that the iodide has a molecular weight of 479 ± 1 O. Fischer's formula is thus eliminated, formula II is very improbable as the structure is that of a cyanine.

That the quinoline ethiodide does not enter into the reaction was discovered by O. Fischer, whilst Mills and Hamer (compare also Mills and Pope) find that the same 1 : 1'-diethyl-6 : 6'-dimethylcarbocyanine iodide is produced from *p*-toluquinaldine ethiodide, formaldehyde and alkali, whether quinoline ethiodide be present or not.

By oxidation of diethylcarbocyanine bromide with dilute nitric acid, quinaldinic acid ethyl nitrate

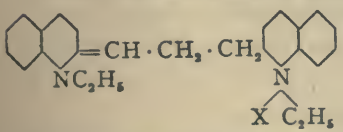
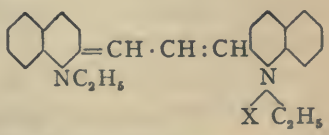


is formed the yield being about 90 per cent of that theoretically obtainable from one quinaldine residue of a pinacyanol molecule. This points to a probable grouping



After removal of the quinaldinic acid ethyl nitrate, the residue gives 1-ethyl-2-quinolone on oxidation with alkaline ferricyanide, i. e. union with the other residue must also be through position 2.

Of the alternative formulae

 and 

between which, analysis can scarcely decide definitely, the latter with its chain of conjugated double linkages is far more probable for a substance of the deep colour of pinacyanol, whilst the extra double linkage agrees better with

the actual nearly quantitative formation of quinaldinic acid ethyl nitrate.

The iodides of the carbocyanines are for the most part sparingly soluble, and are best crystallised from methyl alcohol in which they form deep blue solutions becoming reddish purple on dilution with water.

Although the carbocyanines are formed by condensation of two molecules of an alkylquinaldinium salt with one of formaldehyde, it is found that a better yield is obtained if a quinoline alkyl iodide is also present.

Mills and Pope have prepared the 18 following carbocyanines and tested their action (*Phot. J.*, 1920, *60*, 255).

1. 1 : 1'- Dimethylcarbocyanine iodide.
2. 1 : 1'- Dimethylcarbocyanine chloride.
3. 1 : 1'- Diethylcarbocyanine iodide.
4. 1 : 1'- Diethylcarbocyanine bromide.
5. 1 : 1' : 6 : 6'- Tetramethylcarbocyanine iodide.
6. 1 : 1'- Diethyl - 6 : 6'- dimethylcarbocyanine iodide.
7. 1 : 1'- Di - *n* - propyl - 6 : 6'- dimethylcarbocyanine iodide.
8. 1 : 1'- Di - *n* - butyl - 6 : 6'- dimethylcarbocyanine iodide.
9. 1 : 1' : 6 : 6'-Tetraethylcarbocyanine iodide.
10. 1 : 1'- Diethyl - 6 : 6'- dibromocarbocyanine iodide.
11. 1 : 1'- Diethyl - 5 : 5' (or 7 : 7') - dibromocarbocyanine iodide.
12. 1 : 1'- Diethyl - 6 : 6'- diacetaminocarbocyanine iodide.
13. 1 : 1'- Diethyl - 6 : 6'- diaminocarbocyanine iodide.
14. 1 : 1'- Diethyl - 6 : 6'- dimethoxycarbocyanine iodide.
15. 1 : 1'- Diethyl - 6 : 6'- diethoxycarbocyanine iodide.
16. 1 : 1'- Diethyl - 5 : 5'- diethoxycarbocyanine iodide.
17. 1 : 1'- Diethyl - 6 : 7 : 6' : 7'- dimethylenedioxycarbocyanine iodide.
18. 1 : 1'- Diphenoxyethylcarbocyanine iodide.

Pinacyanol or *Sensitol Red* is No. 3 of these compounds (Mills and Pope, *Phot. J.*, 1920, *60*,, 256), its preparation is also described by Wise, Adams, Stewart and Lund (*J. Ind. Eng. Chem.*, 1919, *11*, 460). Mills and Pope proceed as follows.

80 grams each of quinaldine and quinoline ethiodides, 21.6 grams of formaldehyde and 12.9 grams of sodium hydroxide are heated in alcoholic solution, the product crystallising from the reaction mixture in felted masses of lustrous green needles. The crystals are strongly pleochroic, deep blue and olive-green light being transmitted in two positions of the polarising Nicol.

In preparing the corresponding bromide, Mills and Pope dissolve equimolecular proportions of N-ethylquinolinium *p*-toluenesulphonate and N-ethylquinaldinium *p*-toluenesulphonate and add formaldehyde (2.7 mols) and alcoholic caustic soda (1.2 mols) to the boiling solution. After 12 hours the sodium *p*-toluenesulphonate is filtered off, and sodium bromide added to salt out the carbocyanine bromide which may be purified by crystallisation from methyl alcohol. The compound is a very efficient sensitiser for the red, sensitising down to 7000.

1:1'-*Diethyl*-6:6'-*dimethylcarbocyanine iodide* (No. 6 of Mills' and Pope's preparations, *loc. cit.*, 258) sensitises even further into the red than the lower homologue.

Of the remaining compounds described by Mills and Pope, the two bromo-derivatives (Nos. 10 and 11) are comparatively feeble sensitisers, whilst the introduction of acetamino-groups in positions 6 and 6' leads to extra sensitiveness.

In D. R. P. 172 118 it is expressly mentioned that formaldehyde may be replaced by methylal or ethylal or other substances readily splitting off formaldehyde, e. g. anhydroformaldehyde-aniline; that the quinaldinium alkyl iodide may or may not be mixed with quinolinium alkyl iodide and that one may effect the condensation in alcoholic, aqueous or pyridine solution. Examples of such condensations are given.

1. 30 parts of quinoline ethiodide and 30 parts of quinaldine ethiodide are dissolved in boiling alcohol, to the hot solution a mixture of 30 parts of 16 per cent sodium hydroxide solution and 20 parts of 40 per cent formaldehyde is added. In a few minutes the solution becomes deep blue,

heating on the water-bath is continued for half-an-hour. On cooling, the dyestuff separates as crystals with a green metallic reflex. The blue aqueous (sparingly soluble) or alcoholic solutions are not decolourised by carbon dioxide, but the colour disappears if dilute mineral acid or acetic acid is added in sufficient excess.

2. 20 parts of quinoline methochloride and 30 parts of toluquinaldine ethiodide are dissolved in 500 parts of hot water. 18 parts of 40 per cent formaldehyde and 25 parts of 16 per cent caustic soda are added in succession and the mixture heated for a short time to boiling.

3. Dissolve 30 parts of quinaldine ethoxide in 150 parts of hot pyridine, add 10 parts of 40 per cent formaldehyde, then 10 to 15 parts of 16 per cent caustic soda. Boil for some minutes, cool, dilute with 500 parts of water. Wash the dyestuff with water and crystallise from methyl or ethyl alcohol.

The patent recognises the possibility of converting the sparingly soluble halide salts into more soluble nitrates by double decomposition with silver nitrate.

The same ready solubility may be achieved (D. R. P. 175 034/1906, Addit. P. to 172 188) by using alkylquinolinium (and quinaldinium) alkyl sulphates. The following example is given.

a) 13 parts of quinoline are mixed with the calculated quantity of dimethyl or diethyl sulphate and heated to 120—150°. 15 parts of quinaldine are treated in a similar manner.

b) In place of dimethyl or diethyl sulphate, ethyl toluenesulphonate ($CH_3 \cdot C_6H_4 \cdot SO_2OC_2H_5$) may be used.

The mixture of both salts obtained according to procedure a) or b) is dissolved in alcohol, 10 parts of 40 per cent formaldehyde and 25 parts of 15 per cent caustic soda solution added, boiled a short time under reflux and poured into sodium sulphate solution. The dyestuff is then crystallised from alcohol or water.

Meister, Lucius and Brüning (D. R. P. 178 688/1906,

Addit. P. to D. R. P. 172 188) subsequently claimed that the alkali used to bring about the condensation might be advantageously replaced by alkali sulphite. Thus 57 parts of quinoline ethiodide, 60 parts of quinaldine ethiodide and 100 to 400 parts of sodium sulphite (or other sulphite) are dissolved in 1500 parts of hot water and 60 parts of 40 per cent formaldehyde added. Heating on the water-bath is continued until no further formation of dyestuff is observed, the material is then collected and crystallised from methyl alcohol.

The same firm took further additional patents to D. R. P. 172 118. In D. R. P. 189 942/1906 it is stated that formaldehyde may be replaced by glyoxylic acid, in this case a leuco- compound is first produced which is subsequently oxidised. Two examples are given.

1. Dissolve 5 parts of quinoline ethiodide and 6 parts of quinaldine ethiodide in 100 parts of water, add 4 parts of sodium glyoxylate and $2^1/_2$ parts of soda ash and warm for a short time on the water-bath drawing air through the solution. The precipitated dyestuff, identical with that of D. R. P. 172 118, is filtered off and crystallised from methyl alcohol.

2. 2.5 of soda ash are added to a solution of 11 parts of quinaldine ethiodide and 4 parts of sodium glyoxylate in 100 parts of water, the mixture heated for a short time on the water-bath, allowed to cool and a solution of 5.6 parts of potassium persulphate added slowly with continuous stirring.

In D. R. P. 200 207/1907 it is stated that the formaldehyde may be replaced by chloroform, bromoform or iodoform. As an example, 5 parts of quinoline ethiodide and 6 parts of quinaldine ethiodide are dissolved in 200 parts of alcohol, 7 parts of chloroform and 15 parts of 15 per cent caustic soda solution added and then boiled for 2 hours under reflux.

By the joint action of alkali and an oxidising agent, quinaldinium salts give another class of dyes, „dicyanine" belongs to this group. Dicyanine is not suitable for general photographic work but has been used for the lower region

(infra-red) of the spectrum (Mees and Wratten, *Phot. J.*, 1908, *40*, 25).

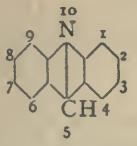
„*Dicyanine A*" is derived from 2:4-dimethyl-6-ethoxyquinoline. In order to prepare this base, Mikeska, Haller and Adams (*J. Am. Chem. Soc.*, 1920, *42*, 2392) condense 300 grams of acetone with 200 grams of paraldehyde by means of hydrochloric acid at 0° and add 300 grams of *p*-phenetidine dissolved in 600 grams of hydrochloric acid of sp. gr. 1.2. The mixture is then heated for two hours under reflux, cooled, caustic soda added and the bases extracted by ether. The extract is dried, the ether distilled off under reduced pressure and excess of phenetidine acetylated by acetic anhydride. The quinoline derivative is then dissolved out by hydrochloric acid, liberated by addition of caustic soda, extracted with ether, dried and distilled. Traces of phenetidine are removed by hydrochloric acid and sodium nitrite after which the base is once more liberated, extracted, dried and distilled. A final purification is effected through the sulphate, the base being dissolved in its own weight of 95 per cent alcohol and then treated with an equal weight of alcohol containing 10 per cent excess of the calculated quantity of sulphuric acid. The sulphate is collected, the base liberated and distilled. In this way 75 grams are obtained, b. p. 314—316°.

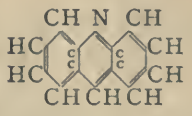
When the ethiodide of this dimethylethoxyquinoline is acted on by sodium methoxide, air being allowed access, Dicyanine A iodide (A IV) is produced. Dicyanine A nitrate (A VI) can be obtained by the action of sodium ethoxide in presence of air on the corresponding ethonitrate.

CHAPTER V.

SYNTHESIS OF ACRIDINE AND ITS DERIVATIVES

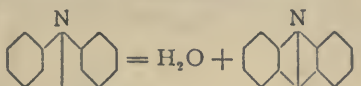
Acridine occurs in crude anthracene; its constitution may be expressed by one of the following formulae.





It has been obtained synthetically and numerous methods of building up the acridine nucleus have been devised.

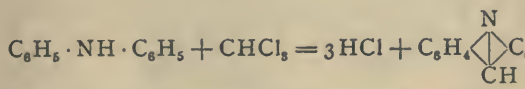
1. Acridine is obtained by heating diphenylamine with formic acid and zinc chloride (Bernthsen, *Annalen*, 1884, *224*, 3) or formyldiphenylamine with zinc chloride.



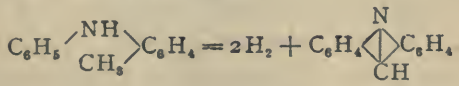
It alo results when oxalic acid, diphenylamine and zinc chloride are heated together.

Various modifications of this general reaction are known, thus if diphenylamine and zinc chloride be heated with benzoic acid, 5-phenylacridine is produced.

2. Chloroform, diphenylamine and aluminium chloride furnish acridine (O. Fischer and G. Körner, *Ber.*, 1884, *17*, 101).

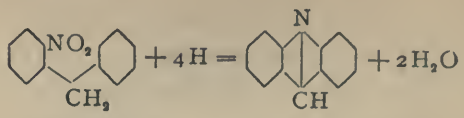


3. By passing phenyl-*o*-toluidine through a red-hot tube (Graebe, *Ber.*, 1884, *17*, 1370).

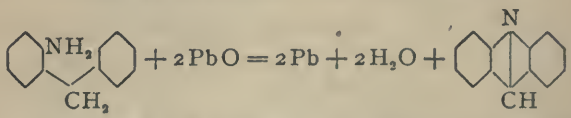


4. Acridine is formed in small quantities by heating benzaldehyde with aniline to 260° (Möhlau, *Ber.*, 1886, *19*, 2452).

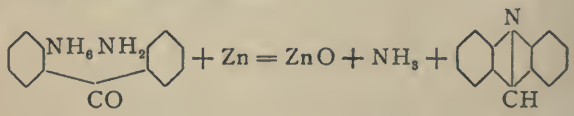
5. By reduction of *o*-nitro diphenylmethane (O. Fischer, *Ber.*, 1895, *28*, 1335).



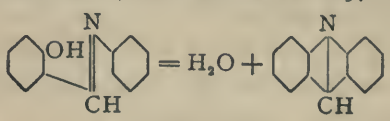
6. By distillation of *o*-aminodiphenylmethane over lead oxide (O. Fischer and Schütte, *Ber.*, 1893, *26*, 3086).



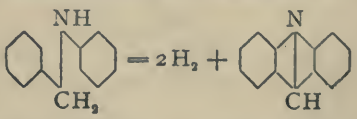
7. By heating 2 : 2'-diaminobenzophenone with zinc dust (Staedel, *Ber.*, 1893, *26*, 3364).



8. Heat 20 grams of salhydranilide with 25 grams of phosphorus pentoxide (Blau, *Monatsh.*, 1897, *18*, 124).



9. Pass the vapour of benzylaniline through a hot tube (H. Meyer and A. Hofmann, *Monatsh.*, 1916, *37*, 681).

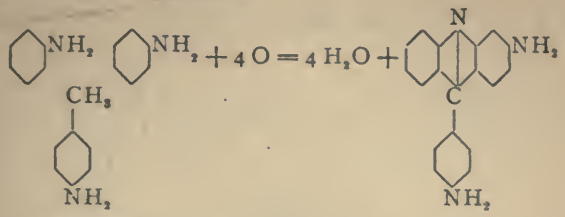


The reaction is said to go so easily as to be used with advantage in the preparation of acridine.

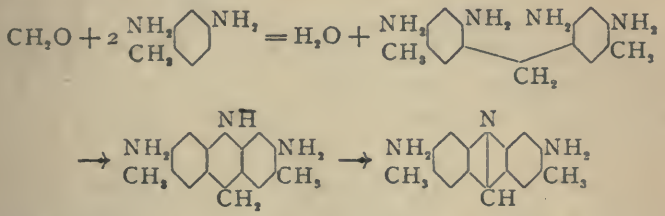
(The foregoing reactions establish the constitution assigned to acridine, confirmation being afforded by the fact that acridine yields acridinic acid (quinoline-dicarboxylic acid), Graebe and Caro (*Ber.*, 1880, *13*, 100) when oxidised.

10. Chrysaniline, a yellow dye formed as a bye-product in the rosaniline process, is a diaminophenylacridine formed

by the removal of hydrogen from one molecule of para-toluidine and two of aniline.

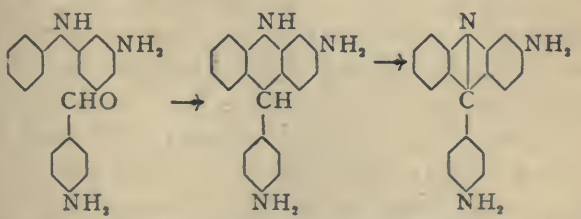


11. Aldehydes and *m*-diamines can, in many cases be condensed to derivatives of tetraaminodiphenylmethane; from these ammonia is removed by heating with hydrochloric acid and the resulting substituted dihydroacridine may be subsequently oxidised.



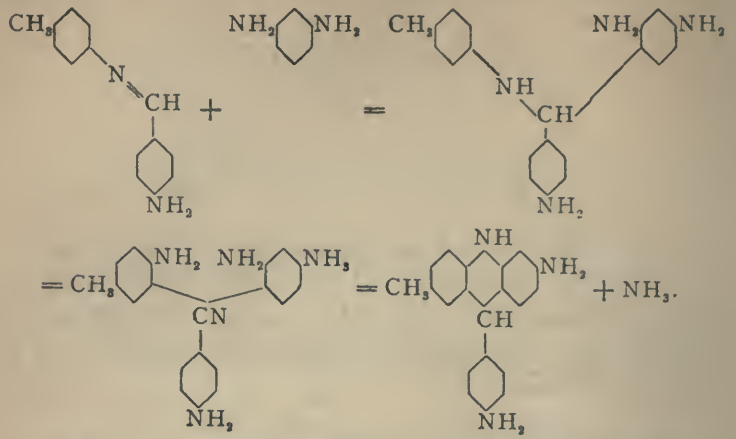
An analogous reaction consists in condensing formaldehyde with two molecules of aminocresol ($CH_3 : OH : NH_2 = 1 : 2 : 4$); by elimination of ammonia and removal of two atoms of hydrogen, dihydroxymethylacridine is formed (Cassella and Co., D. R. P. 120466/1900).

12. Paraminobenzaldehyde condenses with *m*-amino-diphenylamine and homologous compounds, yielding substances which may be oxidised to acridine derivatives (Badische Co., D. R. P. 102072/1897).



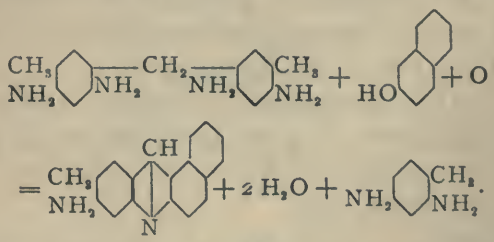
13. Analogous phosphine colouring matters are obtained

from *p*-aminobenzylidineaniline (or homologues), and a *m*-diamine



It should be noted that the first product of condensation is a leucoauramine. Alternatively, the *m*-diamine and the aldehyde may be condensed first and then heated with the monamine.

14. A very similar synthesis is due to Ullman and Naef (*Ber.*, 1900, *33*, 915). Formaldehyde and *m*-toluylenediamine are condensed to tetramethylditolylmethane, this when heated with 2-naphthol gives methylaminonaphthacridine.

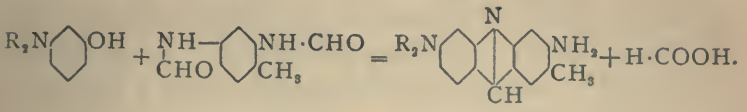


Alternatively, formaldehyde and 2-naphthol may be condensed to dihydroxydinaphthylmethane and one of the naphthol groups removed by heating with *m*-toluylenediamine and its hydrochloride (*loc. cit.*, 912 and D.R.P. 104748/1898).

Yet another variation is to condense anhydroformaldehyde, *m*-toluylenediamine and 2-naphthol in presence of ferric chloride (P. Julius and W. Reese, U.S.P. 644 324/1899)

or sodium acetate at 160—180° (Ullmann and Naef, *loc. cit.*, 916).

15. Dialkyl-*m*-aminophenols condense with diformyldiamines (J. R. Geigy, D. R. P. 161 699/1903).



Acridine

This base was discovered by Graebe and Caro (*Annalen*, 1871, *158*, 265) who found that it accompanied the crude anthracene obtained from coal tar. For its isolation, the portion of the tar distilling at 300—360° was extracted by dilute sulphuric acid and precipitated by potassium dichromate, the precipitate recrystallised from hot water and then decomposed by dilute ammonia. The free base was then dissolved in hot dilute hydrochloric acid, from this solution acridine hydrochloride was thrown out by addition of an excess of concentrated hydrochloric acid. From this salt the free acridine was liberated by ammonia.

The isolation of pure acridine from coal tar involves its separation from other basic compounds of a nearly related character; in the synthetic preparation from diphenylamine and formic acid (or by an equivalent process) a substance is obtained free from homologous bases. Bernthsen has described several syntheses (*Annalen*, 1884, *224*, 3).

(1.) *From formic acid and diphenylamine.* 50 grams of formic acid (s. g. 1.22), 175 grams of diphenylamine and about 100 grams of zinc chloride were warmed carefully. After shaking so as to obtain an uniform liquid, the melt was kept for some time at 150°, then at 210° and finally at 270°, care being taken to avoid evolution of carbon monoxide as far as possible.

After one or two days' heating, the melt was cooled, dissolved in alcohol and poured into excess of caustic soda solution. The upper alcoholic layer containing acridine and unaltered diphenylamine was evaporated and the residue

extracted several times with hot hydrochloric acid. The solution now contained acridine and diphenylamine as hydrochlorides, addition of alkali liberated the free bases which were taken up in ether and the ethereal solution shaken repeatedly with small quantities of hydrochloric acid. The resulting solution of acridine hydrochloride was precipitated with ammonia and the base recyrstallised from a large quantity of hot water.

Variations of the method of separating acridine from unchanged diphenylamine are described, they depend like the one given in detail above on the easier hydrolytic dissociation of diphenylamine hydrochloride. The yield from diphenylamine and formic acid is poor.

(II.) *From Formyldiphenylamine.* 23 grams of this compound and 45 grams of zinc chloride were heated first to 190—200°, then to 220°. Yield poor (Bernthsen, *loc. cit.*, p. 6).

(III.) *From oxalic acid and diphenylamine.* 75 grams of oxalic acid, 100 grams of diphenylamine and 150 grams of zinc chloride were melted together, the heating was regulated so that although steam and gas were evolved, very little formic acid escaped. In the course of two days, the temperature was gradually raised to 260°. From the resulting melt, acridine was liberated but was more difficult to purify than that obtained by other methods (*loc. cit.*).

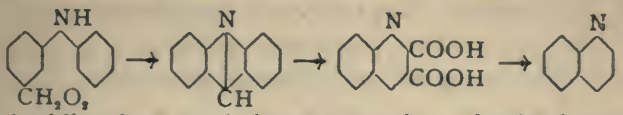
(IV.) *From chloroform and diphenylamine.* Zinc chloride was used as condensing agent (Bernthsen, *loc. cit.*, p. 10; compare O. Fischer, *Ber.*, 1884, *17*, 101).

Acridine crystallises from water in leaflets or broad needles, M. P. 107°, B. P. above 360°. It sublimes in needles and is fairly volatile in a current of steam. It dissolves easily in alcohol and other organic solvents, these solutions exhibit a blue fluorescence. It is slightly soluble in boiling water.

On oxidation with permanganate, acridinic acid is obtained (Graebe and Caro, *Ber.*, 1880, *13*, 100).

$$C_{13}H_9N + 9\,O = C_9H_5N(COOH)_2 + 2\,CO_2 + H_2O$$

Since this acid decomposes into carbon dioxide and quinoline-3-carboxylic acid when heated to 120—130°, the constitution of acridine as deduced from its synthesis from diphenylamine and formic acid or chloroform is fully confirmed



Acridine is a weak base, a number of salts have been described, e. g. (B, $C_{13}H_9N$),

B, HCl, H_2O. Colourless, easily soluble in water.

$(B, HCl)_2, HgCl_2$. Yellow, crystalline precipitate, insoluble in water.

$B_2H_2PtCl_6$. Yellow crystalline precipitate, scarcely soluble in water.

B, $HAuCl_4$. Yellow insoluble precipitate.

B, HI. B, HI, I_2.

B, HNO_3, 3 H_2O. Difficultly soluble in cold water.

$B_2H_2SO_3$. B, $NaHSO_3$.

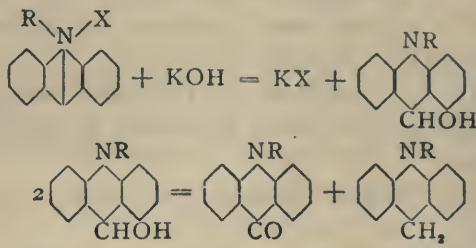
B, H_2CrO_4. Yellow precipitate, difficultly soluble in hot water and crystallising in yellow needles on cooling. It may be pointed out that the analytical figures would agree equally well with the formula $B_2H_2Cr_2O_7$, H_2O. The same remark applies to the chromates of several derivatives of acridine.

B, $C_6H_2(NO_2)_3(OH)$. Difficultly soluble. This picrate has been recommended for the detection and estimation of acridine (Anschütz, *Ber.*, 1884, *17*, 438).

Dihydroacridine, $C_6H_4\langle^{NH}_{CH_2}\rangle C_6H_4$, is obtained by reducing acridine with sodium amalgam in alcoholic solution (Graebe and Caro, *Annalen*, 1871, *158*, 278) or by boiling with hydrochloric acid and zinc dust (Bernthsen, *Ber.*, 1883, *16*, 1972). M. P. 169°; yields acridine and hydrogen at 300°.

Acridine combines with alkyl iodides to form quaternary ammonium salts. These are coloured, Graebe and Caro described two ethiodides, $(C_{13}H_9N)_2 \cdot C_2H_5I$ and $C_{13}H_9N \cdot C_2H_5I$, the former difficultly, the latter easily soluble in water.

Other addition products of alkyl iodides and acridine and its derivatives were subsequently described, they are all coloured compounds but when their solutions are treated with alkalies, colourless precipitates, soluble in organic solvents, are obtained. This behaviour is explained by the formation of pseudo-bases (carbinols) which then give a mixture of 5-alkylacridone and 5-alkyldihydroacridine.

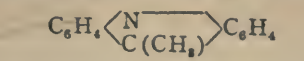


The chemical proof of this explanation was given by Pictet and Patry (*Ber.*, 1902, *35*, 2536). Acridine methiodide was treated with alkali and distilled in a current of steam. A non-volatile compound crystallising in long yellow needles and melting at 201° was thus obtained, it was identified as the methylacridone prepared by Decker (*J. pr. Chem.*, 1892, II, *45*, 161) and Graebe and Lagodzinski (*Annalen*, 1893, *276*, 47). The steam was found to have carried over a volatile compound of m. p. 96°, analysis showed this to be N-methyldihydroacridine.

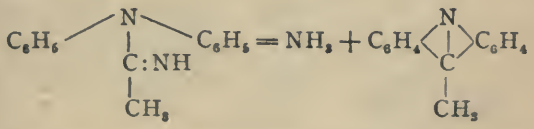
H. Bünzly and H. Decker (*Ber.*, 1904, *37*, 576) found that 5-methylacridone reacted with phenylmagnesium bromide giving a carbinol base from which 5-phenyl-10-methylacridinium salts could be obtained.

C. K. Tinkler (*Trans. Chem. Soc.*, 1906, *89*, 858) has further shown that whilst the absorption spectrum of 10-methylacridinium iodide closely resembles that of acridine hydrochloride, the character of the absorption is radically altered by addition of alkali to the solution and now resembles that of dihydroacridine (Compare also H. Decker, *J. Pr. Chem.*, 1893, II, *47*, *222*; Hantzsch, *Ber.*, 1899, *32*, 3109; Dobbie, Lauder and Tinkler, *Trans. Chem. Soc.*, 1904, *85*, 1005; 1905, *87*, 269).

5-*Methylacridine* or *Mesomethylacridine*,



is obtained from diphenylamine and acetic acid by heating with zinc chloride, the yield being far better than that of acridine when formic acid is employed. Bernthsen described a substance (*Annalen*, 1878, *192*, 29) obtained as a by-product in the preparation of isodiphenylacetamidine by heating acetonitrile with diphenylamine hydrochloride to 220°. The by-product was evidently produced from the isodiphenylacetamidine by loss of ammonia, it was probably identical with methylacridine.



E. Besthorn and O Fischer (*Ber.*, 1882, *15*, 1500; 1883, *16*, 74) obtained a crystalline base form diphenylamine and glacial acetic acid, but left the subject in the hands of Bernthsen, engaged at that time in working out the synthesis of phenylacridine.

Bernthsen (*Annalen*, 1884, *224*, 35) obtained the most satisfactory yield of methylacridine, 56 per cent of the theoretical, by heating 50 grams of diphenylamine, 30 cc. of glacial acetic acid and 85 grams of zinc chloride for 14 hours at 220°. The melt was dissolved in fairly concentrated sulphuric acid at 100°, poured into water and the resinous separation extracted 4 to 6 times with hot acidified water. The united filtered extracts were then precipitated by an excess of ammonia.

Methylacridine is obtained as quadratic tables by crystallisation from ligroin (Osann, *Ber.*, 1886, *19*, 427), m. p. 92—94° (Fischer and Besthorn), 114° (Bernthsen). Permanganate oxidises the compound to quinoline-tricarboxylic acid, nitric acid yields a trinitroacridine-carboxylic acid.

The *methiodide* crystallises from alcohol in bundles of

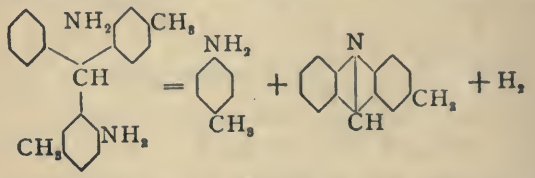
red needles, m. p. 185°, the corresponding carbinol base forms small white crystals melting at 187°.

The methyl group in 5-methylacridine is reactive, thus on warming a benzene solution with anhydrous chloral, aldol condensation takes place with formation of methylacridine-chloral,

$$(C_{13}H_8N)\cdot CH_2\cdot CHOH\cdot CCl_3.$$

(Bernthsen and Muhlert, *Ber.*, 1887, *20*, 1543).

3-*Methylacridine.* This compound was obtained by heating phenyldiaminoditolylmethane with zinc dust. M. P. 131.5° (Ullmann, *J. Pr. Chem.*, 1887, II, *36* 265).



5-*Isobuylacridine*, $C_{13}H_8N\cdot CH_2\cdot CH(CH_3)_2$, was obtained by heating 30 grams of diphenylamine, 30 grams of valeric acid and 50 grams of zinc chloride for 20 hours at 200—220° (Bernthsen, *Annalen*, 1884, *224*, 41). Isolation of the base from the resulting tar is difficult and Bernthsen records no melting point. The *hydrochloride* melts at 191°, the *nitrate* at 139°.

5-*Phenylacridine*, $C_{13}H_8N\cdot C_6H_5$, was first obtained by Bernthsen by heating benzonitrile with diphenylamine hydrochloride to 230—250° (*Annalen*, 1878, *192*, 19). He subsequently (*Annalen*, 1884, *24*, 12) prepared the compound by heating benzoyldiphenylamine with its own weight of zinc chloride for some hours at 210—230° and finally for 10 hours at 260—280°, or, alternatively, by heating 50 grams of benzoic acid with 70 grams of diphenylamine and 150 grams of zinc chloride for 10 hours at 260°. In the latter case, the solidified, brittle melt was powdered, dissolved in hot alcohol, poured into excess of strong ammonia and, after standing some time, considerably diluted. Diphenylamine was removed from the precipitate by washing with cold alcohol,

and the residue crystallised from hot alcohol in which it is somewhat soluble, or from benzene in which it is readily soluble. In the latter case the base separated with benzene of crystallisation. M. P. 181°; B. P. 403—405° (uncorr.).

Dunstan and Oakley (*Ber.*, 1906, *39*, 977) separate unaltered diphenylamine from phenylacridine by extraction with petroleum ether of low boiling point. A number of salts have been described (Bernthsen, Dunstan and Oakley).

Reduction of the hydrochloric acid solution with zinc dust gives *dihydrophenylacridine*, m. p. 163—164°, which has very slight basic properties; by chlorination and bromination, Dunstan and Oakley obtained *dichloro-* and *tribromo*-derivatives (*Ber.*, 1906, *39*, 981).

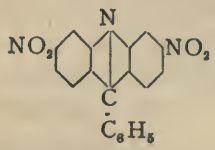
5-*p*-*Chlorophenylacridine*, obtained from *p*-chlorobenzoic acid, diphenylamine and zinc chloride, does not melt below 270° (Dunstan and Hilditch, *Trans. Chem. Soc.*, 1907, *91*, 1661). This compound gives a dibromo-derivative.

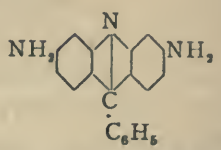
5-*p*-*Bromophenylacridine*, m. p. 234° (uncorr.) is obtained by condensation of *p*-bromobenzoic acid with diphenylamine (Dunstan and Stubbs, *Ber.*, 1906, *39*, 2402). On bromination, two further atoms of bromine are taken up. (Dunstan and Hilditch, *loc. cit.*, 1663).

By energetic nitration, Bernthsen (*Annalen*, 1884, *224*, 29) probably obtained a trinitro-compound (the analysis is unsatisfactory) the complete reduction of which furnishes a leuco-base which readily passes into a dyestuff (triaminoacridine) capable of dyeing silk yellow.

A dinitro-compound results when 2.5 grams of phenylacridine are dissolved in 7.5 cc. of sulphuric acid and treated with 1.45 cc. of nitric acid mixed with 5 cc. of sulphuric acid. This compound still possesses fairly marked basic properties which the trinitro-compound does not. It may be reduced to a diaminophenylacridine which Bernthsen considered was an isomeride of chrysaniline. The latter compound had been shown to be a diaminophenylacridine by O. Fischer and G. Körner phenylacridine being obtained after removal of two amino groups (*Ber.*, 1884, *17*, 203; *Annalen*, 1884, *226*, 184).

Dunstan and Oakley *(loc. cit.)* assume that the nitro groups enter positions 2 and 8, i. e. that the dinitrophenylacridine and the diamino compound formed from it by reduction have the respective formulae





On *sulphonation* with three times its weight of a mixture of concentrated and fuming sulphuric acids, phenylacridine yields a disulphonic acid, isolated by Bernthsen as the sodium salt *(Annalen,* 1884, *224,* 32). By alkaline fusion a compound was obtained in poor yield, possibly a dihydroxyphenylacridine.

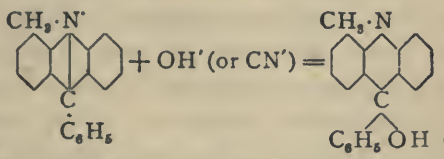
Phenylacridinium compounds. When phenylacridine is heated with an excess of methyl iodide in a sealed tube to 70—100°, phenylacridine methiodide is produced, this separates from hot alcohol in brownish black crystals (Bernthsen, *Annalen,* 1884, *224,* 20). It is characterised as a quaternary iodide by the fact that it decomposes into its components on heating; this decomposition is however incomplete (Decker, *Ber.,* 1905, *38,* 1155). Phenylacridine, like other tertiary bases, may be converted into methylacridinium salts by the use of methyl sulphate (Decker, *loc. cit.,* 1148).

The carbinol base, precipitated from aqueous solutions of the iodide by addition of caustic soda, crystallises from alcohol in triclinic prisms (Osann, *Ber.,* 1886, *19,* 427) and melts at 108° with development of a red colour. Bernthsen assigned to the carbinol base the formula of a quaternary ammonium hydroxide, as he considered the salts and the base must have analogous constitutions.

Decker (*J. Pr. Chem.,* 1892, II, *45,* 161) also examined this compound, but strangely enough did not assign to it a carbinol formula, although he had recognised the fact that when quinolinium salts are acted on by alkali, the hydroxyl wanders from nitrogen to carbon. A. Hantzsch and M. Kalb

(Ber., 1899, *32*, 3121) showed however that when an equivalent of caustic soda was added to a solution of 10-methyl-5-phenylacridinium chloride, the solution at first possessed the electrolytic conductivity of a hydroxide but this gradually sank to the value required for sodium chloride. This fall in conductivity is accompanied by the precipitation of 10-methyl-5-phenylacridol.

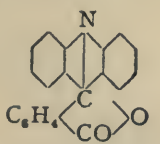
Hantzsch and Kalb *(loc. cit.*, 3126) further found that the addition of potassium cyanide to a solution of a methylphenylacridinium salt led to the precipitation of a colourless, crystalline cyanide of m. p. 176°. The union of hydroxyl or cyanogen ions with methylphenylacridinium ions may therefore be expressed by the equation



Confirmatory spectroscopic evidence has been given by Dobbie, Lauder and Tinkler *(Trans. Chem. Soc.*, 1905, *87*, 270).

3-*Methyl*-5-*phenylacridine* is obtained by heating 10 grams of phenyl-*p*-toluidine, 14 grams of benzoic acid and 30 grams of zinc chloride for 15 hours at 260° (Bonna, *Annalen*, 1887, *239*, 60). M. P. 135—136°.

5-*o*-*Carboxyphenylacridine* or *Acridylbenzoic acid* (Diphenylaminephthalein).



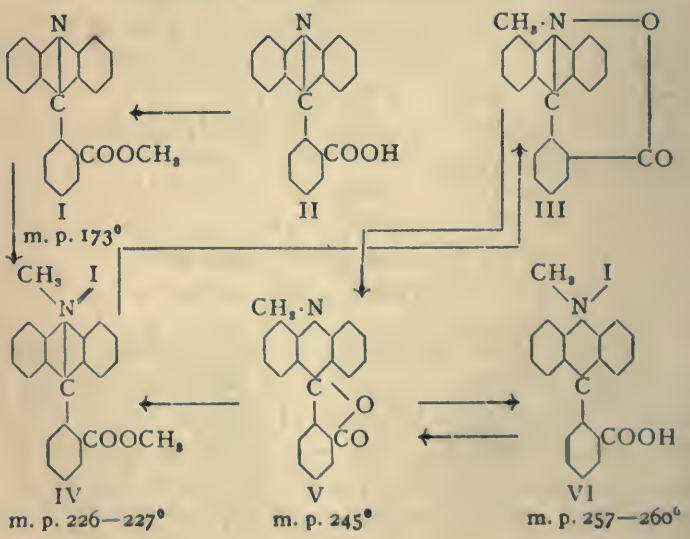
Bernthsen obtained this compound by heating 30 grams of phthalic anhydride, 45 grams of diphenylamine and 75 grams of zinc chloride for 10 to 14 hours at 180—200° (*Annalen*, 1884, *224*, 45). The melt was extracted with hot alcohol, the alcoholic solution poured into water and the precipitate thus obtained, together with the undissolved portion

of the melt, dissolved in a small amount of caustic soda, largely diluted (several times), filtered and the boiling solution treated with excess of hydrochloric acid. A small amount of a flocculent by-product was removed by filtration and the hydrochloride of the acridylbenzoic acid obtained as small crystals by concentration and cooling. The substance was purified by recrystallisation from hot dilute hydrochloric acid, it decomposes with partial fusion at 163°.

The free acridylbenzoic acid was obtained by decomposing the hydrochloride with an equivalent of soda, or by carefully adding hydrochloric or acetic acid to a solution of the sodium salt, $C_{20}H_{12}O_2NNa$.

Acridylbenzoic acid is almost insoluble in boiling water and but sparingly soluble in organic solvents. M. P. 347° (Decker and Hock, *Ber.*, 1904, *37*, 1006). The acid solutions show a green fluorescence, those in alkalies are colourless but give a beautiful blue fluorescence when strongly diluted.

In addition to the structure given above, acridylbenzoic acid may be represented as a phthalein or an internal salt. Derivatives of the various forms have been obtained by Decker and Hock *(Ber.*, 1904, *37*, 1002).



Methyl iodide adds on to acridylbenzoic acid to give the hydriodide of the methyl ester (I. Compare H. Meyer, *Ber.*, 1903, *36*, 614). This methyl ester in turn gives the methiodide (IV) when it is treated with dimethyl sulphate and the solution of the resulting methylsulphate precipitated by addition of potassium iodide. Addition of caustic soda to solutions of these salts (IV) causes gradual precipitation of the lactone (V), the betaine (III) being intermediately formed. The lactone (V) gives salts of the betaine (VI) when treated with acids.

The colours of the various compounds may be noted.

Ester (I) Bright yellow needles.

Free acid (II) Yellow needles.

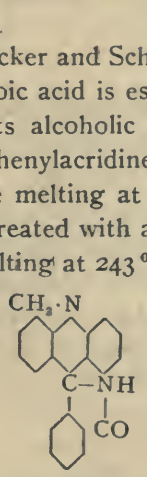
Methiodide (IV) Red needles.

Lactone (V) Colourless leaflets or cubes.

Betaine hydriodide (VI) Bright yellow leaflets.

Flaveosine (D. R. P. 49850) is probably derived from the betaine form and some of the dyestuffs of D. R. PP. 73334 and 75933 partly from this form and perhaps from types IV and VI.

In a later paper, Decker and Schenk *(Ber.*, 1906, *39*, 748) showed that acridylbenzoic acid is esterified by the action of hydrogen chloride on its alcoholic solution. The resulting ethyl acridylbenzoate (phenylacridine-*o*-carboxylate) of m. p. 161° gives a methiodide melting at 220° (compare formula IV above) which when treated with ammonia yields a lactam as colourless needles melting at 243°,

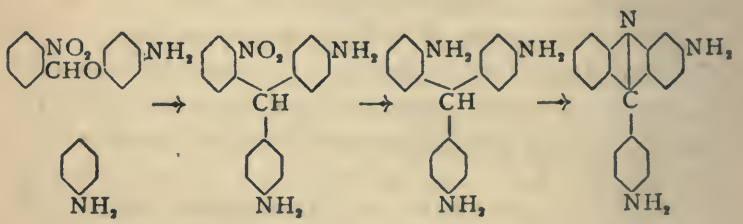


5-*Phenylacridine*-3-*carboxylic acid* is isomeric with acridylbenzoic acid, it was obtained by oxidising 3-methyl-5-phenylacridine with chromic acid mixture (Bonna, *Annalen*, 1887, *239*, 62).

CHAPTER VI.

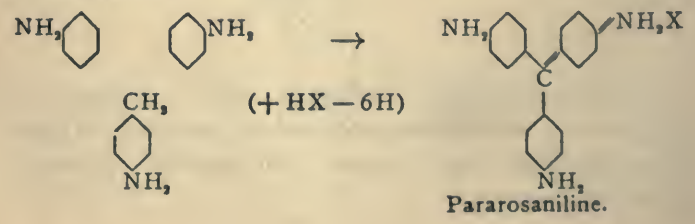
GENERAL ACCOUNT OF THE ACRIDINE DYESTUFFS

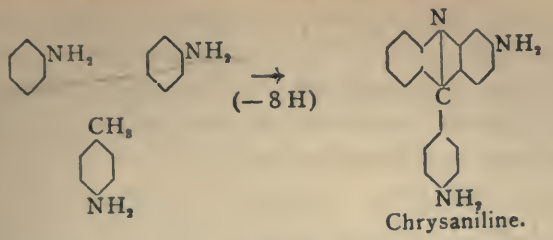
Chrysaniline or Phosphine is a by-product of the manufacture of fuchsine (rosaniline) by either the arsenic acid or the nitrobenzene process. It was discovered by Nicholson in 1863 and introduced as a yellow dye, the constitution of this compound was finally settled by its synthesis (O. Fischer and G. Körner, *Ber.*, 1884, *17*, 207). *o*-Nitrobenzaldehyde and aniline were condensed to *o*-nitro-di-*p*-aminotriphenylmethane, which was then reduced to the triamino-compound and the latter oxidised to chrysaniline. The changes may be represented by the following scheme.



Confirmation of this constitution is afforded by the production of 5-phenylacridine when the amino groups in chrysaniline are replaced by hydrogen.

Whilst pararosaniline results from the condensation of one molecule of *p*-toluidine with two molecules of aniline, both of which are attacked in the para position to the amino group, chrysaniline results from a condensation in which one molecule of aniline is attacked in the ortho-, the other in the para-position.

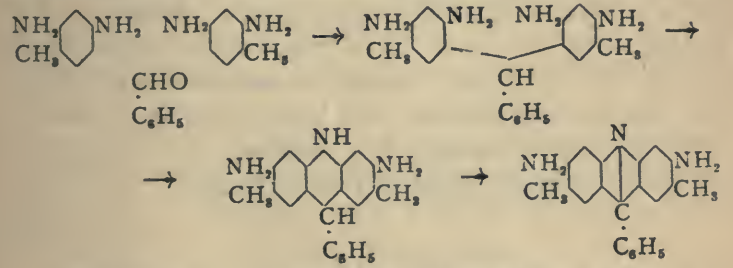




Chrysaniline.

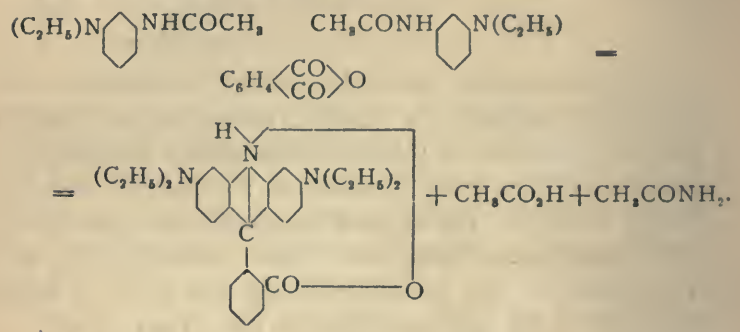
Little technical use was made of these observations, but in 1887 Oehler applied for a patent to protect the production of diamino derivatives of phenylacridine and its homologues, both amino groups being situated in the acridine nucleus (positions 2 and 8). The dyestuff produced with the aid of *m*-toluylenediamine, which reacts more smoothly than *m*-phenylenediamine, was introduced under the name of Benzoflavine (D. R. PP. 43 714, 43 720, see also 45 294, 45 298).

Two molecules of the diamine were condensed with one of benzaldehyde to give a tetraamino-derivative of triphenylmethane from which ammonia was removed by heating with hydrochloric acid. The resulting dihydroacridine was then oxidised to the corresponding acridine which formed the dyestuff.



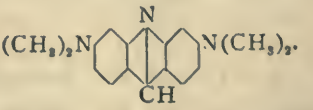
Chrysaniline (in its time) and Benzoflavine found considerable application as dyes for leather. Soon after the discovery of the latter, a yellow cotton dye, Acridine Yellow, was introduced by Leonhardt and Co. (D. R. P. 52 324/1889). This was a derivative of acridine (not of 5-phenylacridine) produced by similar reactions from *m*-toluylenediamine and formaldehyde, the latter compound having become technically available.

Slightly before this, application was made for the protection of Flaveosine (D. R. P. 49 850/1899), a derivative of 5-phenylacridine-*o*-carboxylic acid, obtained by the condensation of phthalic anhydride with two molecular proportions of *m*-acetylaminodimethylaniline.



At a later date, the Badische Co. (D. R. P. 141 356/1902) protected the direct condensation of phthalic anhydride with a mixture of a *m*-diamine and its hydrochloride.

The use of alkylated *m*-diamines for the synthesis of acridine dyes was extended by the condensation of *asym.*-dialkyl-*m*-diamines with formaldehyde (A. Leonhardt & Co., Brit. P. 8243/1890; D. R. P. 59 179/1889; Bender, U. S. P. 503 305. See also D. R. PP. 67 609, 68 908, 70 065, 70 935, 71 362). The resulting tetramethyltetraaminodiphenylmethane lost ammonia on heating with hydrochloric acid and the resulting leuco-compound was oxidised in the usual way with ferric chloride giving Acridine Orange

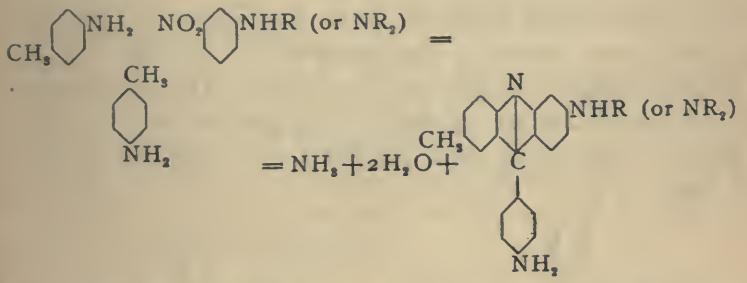


An interesting point is that Bernthsen's direct acridine synthesis was utilised by Leonhardt & Co. (D. R. P. 67 126/1890), *m*-dimethylaminoaniline beeing condensed either with formic acid or a mixture of oxalic acid and glycerine.

A similar idea underlies the method of heating the formyl derivatives of *m*-diamines (either by themselves or in

admixture with free *m*-diamines) with ammonium salts at a high temperature (J. R. Geigy, D. R. PP. 149 409/1903, F. P. 330 487/1903). Another way of introducing the formyl group consists in heating the metadiamine with the formyl derivative of a primary amine such as aniline (J. R. Geigy, D. R. P. 149 410/1903).

The next few years saw considerable activity in the synthesis of acridine dyestuffs and at last the knowledge of the constitution of chrysaniline was utilised in the working out of methods for the production of its homologues. A methylchrysaniline results when *p*-toluidine is heated to a high temperature with *m*-nitraniline in presence of ferrous chloride and hydrochloric acid; the ferrous salt reducing the nitro group whilst the ferric salt produced acts simultaneously as an oxidising agent (Meister, Lucius and Brüning, D. R. P. 65 985/1892).



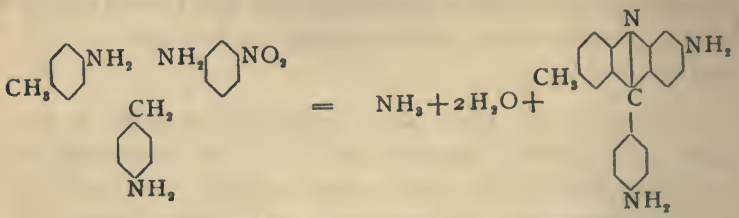
If the *m*-nitraniline is replaced by *m*-nitrophenol (D. R. P. 78 377/1894) or *m*-nitrophenetol (D. R. P. 79 263/1894) the corresponding reactions

$$2\,C_7H_9N + C_6H_4\,(OH)\,(NO_2) = C_{20}H_{17}N + 3\,H_2O$$
$$2\,C_7H_9N + C_6H_4\,(OC_2H_5)\,(NO_2)$$
$$= C_{20}\,H_{17}N + 2H_2O + C_2H_5OH$$

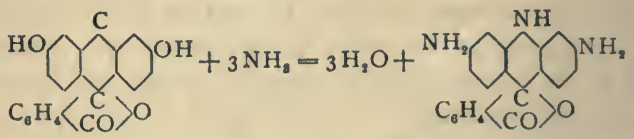
take place.

It would seem that the rôles of the amino and nitro groups in the equations given above in which *m*-nitraniline is involved may be interchanged, for homologous dyestuffs,

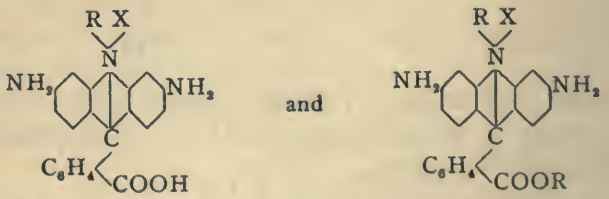
alkylated on one amino group, are obtained when *p*-toluidine is brought to reaction with mono- or di-alkylated *m*-nitraniline (Meister, Lucius and Brüning, D. R. P. 79877/1894).



The observation of R. Meyer and Oppelt (*Ber.*, 1888, *21*, 3376) that fluorescein underwent the reaction



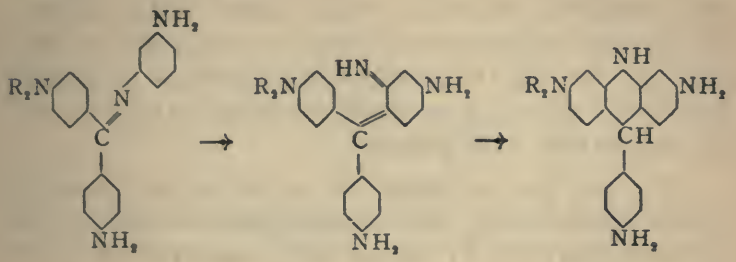
when heated with ammonia under pressure to a high temperature was utilised by the Badische Co. (D. R. PP. 73334, 75933 of 1893) who alkylated the product. This was effected by heating with an alcohol and an acid or with an alkyl halide. The actual salts produced are probably of such types as



where R = alkyl, X = acid radicle (Decker and Hock, Decker and Schenk).

In 1894, application was made by the Badische Co. (D. R. P. 82989) for protecting the conversion of certain substituted auramines, viz.- those derived from *m*-phenylene- and toluylene-diamines, into dyestuffs resembling phosphines. This was effected either by heating them by themselves or

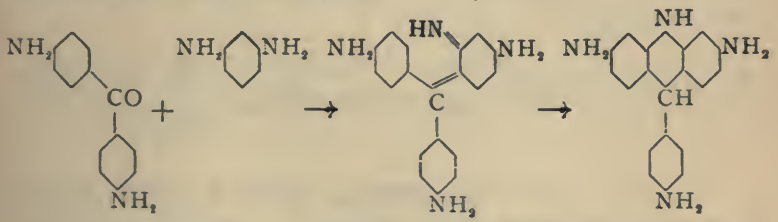
with a *m*-diamine, either free or as hydrochloride, with or without a condensing agent (e. g. zinc chloride) being present to 170—210°. In this case one may suppose the following changes to take place,



the leuco-compound undergoing oxidation to dyestuff.

Shortly afterwards, similar dyes were obtained by a modified process, tetraalkyldiaminobenzhydrols being condensed with *m*-diamines to the leuco bases of triphenylmethane dyes, which on heating underwent further condensation (and oxidation).

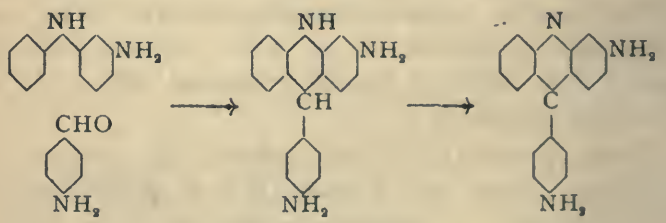
Faster dyes of a more purely yellow shade were obtained by Meister, Lucius and Brüning (D. R. P. 89660/1895) by the condensation of diaminobenzophenone or its diacetyl derivative with metadiamines. The patentees expressly state that the product from *m*-phenylenediamine has the properties of an aminobenzoflavine.



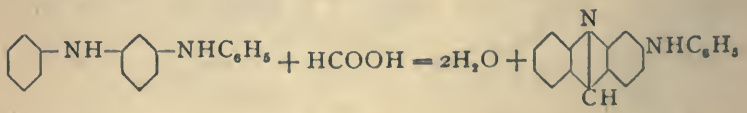
The alkylation of benzoflavine was effected by the Gesellschaft für chemische Industrie in Basel (D. R. P. 79703/1894 and P. A. G. 9475/1895) by heating with an acid and an alcohol; the resulting dyes had a more orange shade than the original benzoflavine.

The symmetrical diaminoacridines were never the equal of chrysaniline and its analogues as far as fastness and eveness of dyeing were concerned so that syntheses of dyestuffs with amino groups in the chrysaniline positions were always desirable. But whilst acridine yellow and benzoflavine are obtained by smooth reactions, the production of phosphine like dyestuffs by heating *p*-toluidine with *m*-nitroamines and ferrous chloride gave indifferent yields, so that new synthetical methods were desirable.

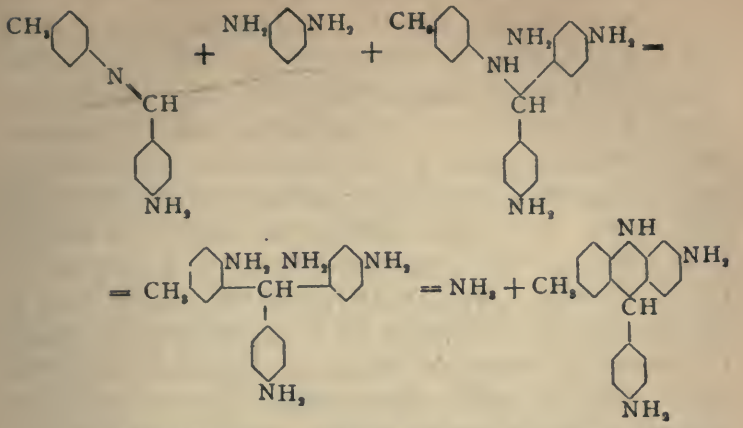
The Badische Co. struck out a new line in condensing *p*-aminobenzaldehydes with phenyl-*m*-phenylenediamine and its derivatives (Brit. PP. 14 920/1897, 21 496/1898; U. S. PP. 617 340, 619 577; F. P. 267 848/1898; D. R. PP. 94 951/1897, 102 072/1898).



The reaction may be compared with that between formic acid and diphenyl-*m*-phenylenediamine which results in the formation of anilinoacridine Besthorn and Curtman, *Ber.*, 1891, *24*, 2042).

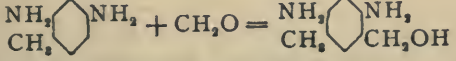


Meister, Lucius and Brüning obtained nearly related diaminophenylacridines by condensing an aminobenzylideneamine with a *m*-diamine; in this case a leuco-auramine was first produced and then underwent transformation, loss of ammonia and oxidation (D. R. P. 106 719/1898). The successive changes as far as leuco-base may be represented in the following manner

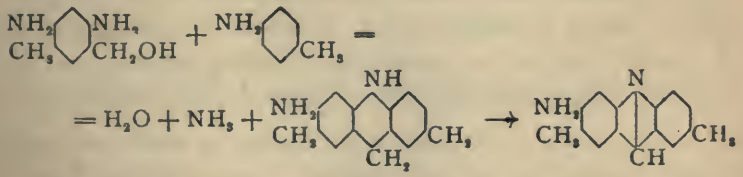


It will have been noticed that the dyestuffs hitherto mentioned all contain two or three amino groups; in 1898 acridine dyestuffs with only one amino group were described from several sources.

Henri Terrisse and Georges Darier of Geneva were first in the field (Brit. P. 20063/1898, D. R. P. 107517 of 13. 2. 1898; patent transferred to the Badische Co), condensing a *m*-diamine with formaldehyde and heating the resulting product with a para-substituted monamine. Terrisse (*Chem. Z.* 1899, *23*, 286) supposed the first product to be a diaminotolylcarbinol resulting from the reaction,

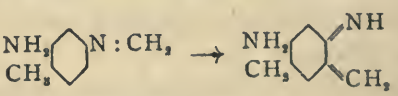


the subsequent condensation with *p*-toluidine giving primarily a monaminodimethyldihydroacridine which oxidises readily to the acridine dye.

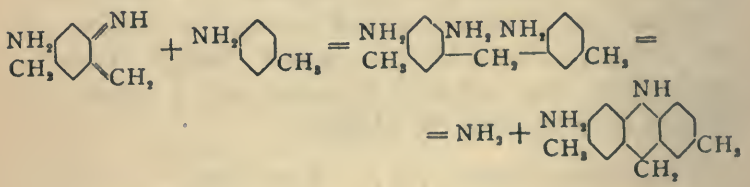


Terrisse appears to have been wrong in assuming the composition of a diaminotolylcarbinol for the substance pro-

duced from *m*-toluylenediamine and formaldehyde. Schiff (*Ber.*, 1891, *24*, 2130) obtained a crystalline compound which he did not analyse. Ullmann and Naef (*Ber.*, 1900, *33*, 914) found that when the toluylenediamine and formaldehyde underwent condensation in a neutral medium (alcoholic solution or aqueous suspension) a substance was formed which gave figures on analysis agreeing far better with the formula $C_8H_{10}N_2$. The compound behaved as if it possessed the constitution $C_6H_3(CH_3)(NH_2)(N:CH_2)$ rather than as the anhydride of an alcohol, for it was found to be capable of yielding formaldehyde which was identified by Tollens' phloroglucin test (*Ber.*, 1899, *32*, 2841). One may, perhaps, assume a transformation of the anhydroformaldehyde-*m*-toluylenediamine in the following sense



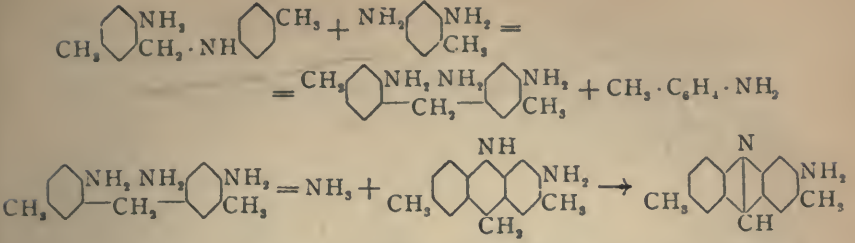
when it reacts with *p*-toluidine.



Further developments of the reaction were patented by the Badische Co. (D. R. PP. 118076, 125697/1898).

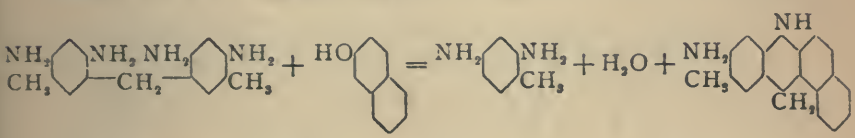
Meister, Lucius and Brüning (D. R. P. 107626 of 13. 2. 1898) utilised *o*-aminobenzylarylamines (D. R. P. 105797/1898). These substances were obtained by condensing in the cold a salt of a *p*-substituted primary aromatic amine with the anhydroformaldehyde compound of the same amine.

When these compounds were heated to 180—190° with a *m*-diamine (alone or in presencee of an oxidising agent), primary amine was split off and as final product a mono-aminoacridine obtained.

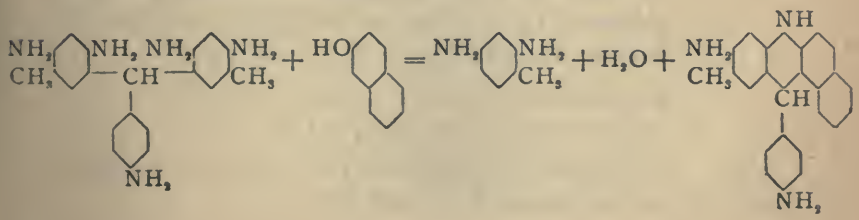


It will be noticed that the processes of Terrisse and Darier and of Meister, Lucius and Brüning lead to identical products.

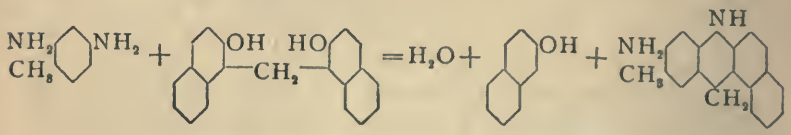
Ullmann arrived at monoamino(naphth)acridines in a different manner. Acid condensation of *m*-toluylenediamine with formaldehyde gives rise to tetraaminoditolylmethane (D. R. P. 52 324, Ullmann and Naef, loc. cit. 915). On heating this compound with 2-naphthol, one molecule of *m*-toluylenediamine is split off and the leuco-base, viz. aminomethyldihydronaphthacridine, m. p. 195—198°, produced (Brit. PP. 16 474, 16 475/1898; F. P. 280 164/1898 of the A. G. f. Anilinfabr.; D. R. P. 104 667/1898).



Ullmann (D. R. P. 108 273/1898) extended the method to the reactions between 2-naphthol and the condensation products of benzaldehyde and *p*-aminobenzaldehyde (see D. R. P. 45 294) with *m*-toluylenediamine. In the first case one obtains a monoaminomethylphenylnaphthacridine, in the latter, a diamino-derivative of chrysaniline type.

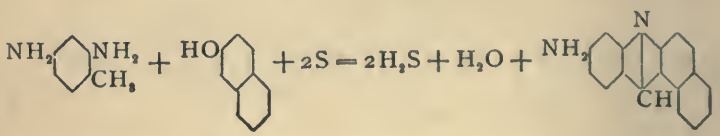


A very interesting production of dyestuffs of this class depends on the condensation of formaldehyde with 2-naphthol to dihydroxydinaphthylmethane and then heating the latter with *m*-toluylenediamine. In this case the diamine displaces one molecule of the naphthol.



More simply, one may condense anhydroformaldehyde-*m*-toluylenediamine with 2-naphthol by heating with sodium acetate (Ullmann and Naef, *Ber.*, 1900, *33*, 916). The same reaction, but with addition of ferric chloride, is described by Julius and Reess in U. S. P. 644 324/1899, assigned to the Badische Co.

Aminonaphthacridines have also been obtained by J. R. Geigy (D. R. P. 130 360) by melting together *m*-toluylenediamine, 2-naphthol and sulphur.



Here, the methyl group of the toluylenediamine furnishes the meso-carbon atom.

Ullmann extended his work in many directions and protected the preparation of unsubstituted tolunaphthacridines &c. Thus in D. R. P. 117 472/1898 derivatives of naphthacridine are obtained by reacting with 2-naphthol on

(a) a mixture of *p*-toluidine and an aldehyde (in the case of formaldehyde, trioxymethylene is employed):

(b) the condensation product of one molecule of *p*-toluidine with one molecule of an aldehyde: or,

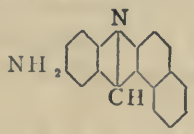
(c) the condensation product of two molecules of *p*-toluidine with one molecule of an aldehyde.

(a) $C_6H_4(CH_3)(NH_2) + CH_2O + C_{10}H_7OH =$
$= CH_3 \cdot C_6H_3\langle^{NH}_{CH_2}\rangle C_{10}H_6 + 2H_2O$

(b) $C_6H_3(CH_3)(N:CHR) + C_{10}H_7OH =$
$= CH_3 \cdot C_6H_3\langle^{NH}_{CHR}\rangle C_{10}H_6 + H_2O$

(c) $\begin{matrix}CH_3 \cdot C_6H_4 \cdot NH\\ CH_3 \cdot C_6H_4 \cdot NH\end{matrix}\rangle CH_2 + C_{10}H_7OH =$
$= CH_3 \cdot C_6H_3\langle^{NH}_{CH_2}\rangle C_{10}H_6 + C_6H_4(CH_3)(NH_2) + H_2O$

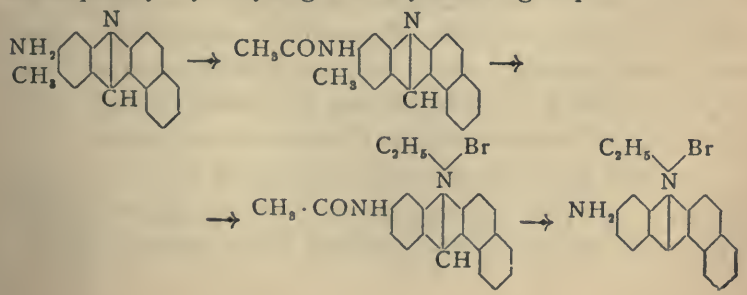
Other bases can be used in place of *p*-toluidine (D. R. P. 123 260/1898) and employing acetyl-*p*-phenylenediamine and subsequently hydrolysing, an aminonaphthacridine is produced.



It should be noticed that in this compound, the two nitrogen atoms are situated para (not meta) to one another (*Ber.*, 1902, *35*, 2670).

Tolunaphthacridine was also prepared by the action of *p*-toluidine on *β*-dihydroxydiphenylmethane. Using bases such as dimethyl-*m*-phenylenediamine gives rise to dimethyl-aminonaphthacridines (D. R. P. 128 754/1898).

The acridine dyestuffs are not always easily soluble, and further, not being very basic, their salts undergo hydrolysis somewhat easily. Ullmann remedied this defect (Brit. P. 17 426/1899; F. P. 292 151/1899; D. R. P. 118 439/1899) by acylating the amino group, adding on alkyl halide to the ring nitrogen, so obtaining a quaternary acridinium salt and subsequently hydrolysing the acylamino group.

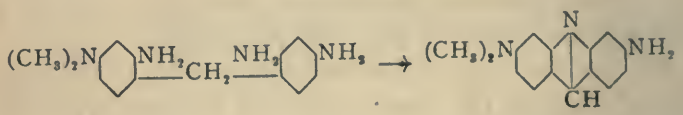


In Ullmann's British Patent (17427/1899) the use of dimethyl sulphate as alkylating agent is recommended, for solvents, benzene or nitrobenzene are employed (Ullmann, *Ber.*, 1902, *35*, 322; Ullmann and Naef, *Ber.*, 1900, 2470; Ullmann and Maric, *Ber.*, 1901, *34*, 4307). The dyestuffs obtained in this manner are more soluble and faster to alkalies, on the other hand, their fastness to light is slight.

The A. G. f. Anilinfabr. followed this up with other patents dealing with the alkylation of acridine dyestuffs (Brit. P. 1820/1900; F. PP. 296628, 304442/1900; D. R. PP. 117065/1899, 129479/1900).

Meister, Lucius and Brüning (D. R. P. 133788/1901; F. P. 316721) employed monochloracetic acid, this probably acted as a methylating agent, carbon dioxide being lost. (See Friedländer, VI, 475.)

Nastvogel (Bayer & Co. Brit. P. 11035/1900; D. R. P. 113709/1900; U. S. P. 675568/1900; F. P. 301256/1900) found that asymmetrically alkylated 2:8-diaminacridines resulting from the condensation and oxidation of asymmetrically alkylated derivatives of tetraminodiphenylmethane



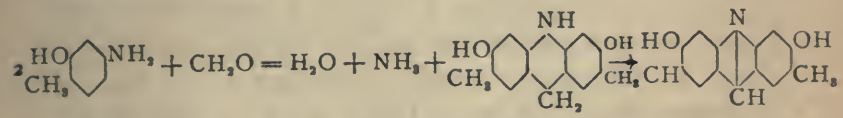
possessed valuable properties as leather dyes (yellow shade, easy solubility, eveness), the coriophosphines (Bayer & Co.) appear to be made by this process.

The Gesellschaft für chemische Industrie in Basel (D. R. P. 136617/1901) found that dyestuffs giving brownish orange shades on leather could be obtained by heating the neutral condensation product of one molecule of formaldehyde and one molecule of a metadiamine with acid under pressure. An explanation of the reaction was not given in the patent.

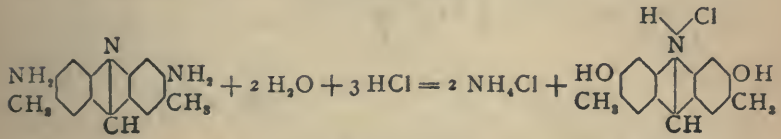
It may be noted that L. Cassella & Co. (Brit. P. 15064/1901; F. P. 312771/1901; D. R. P. 131365/1901) obtained new, easily soluble dyestuffs from acridine yellow

(diaminodimethylacridine) or its leuco-compound by condensation with formaldehyde and a metadiamine; the products dye in orange or brownish yellow shades. A supplementary patent (D. R. P. 132 116/1901) claimed the condensation of acridine yellow or its leucocompound with monamines (aniline etc.) and formaldehyde.

Derivatives of acridine containing hydroxyl in place of amino groups were obtained by Cassella & Co. (D. R. P. 120 466/1900; F. P. 306 146/1900) by condensing aminocresol with formaldehyde.



An alternative method of preparing such compounds is by removal of amino groups from acridine yellow by heating with mineral acids under pressure (L. Cassella & Co., D. R. P. 120 466/1900; F. P. 306 146/1900).

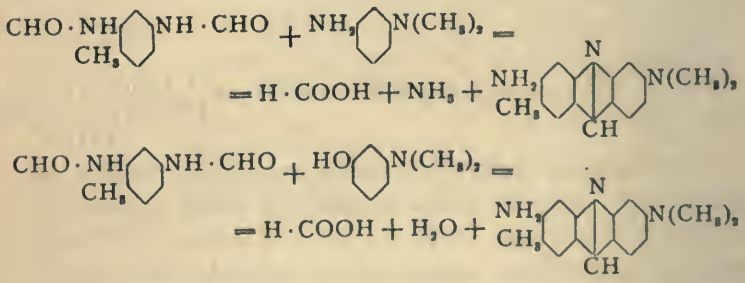


In preparing dialkylrhodamines by heating phthalic anhydride with monoalkyl-*m*-aminophenols, alkali soluble by-products are obtained, these are possibly hydroxylated acridine derivatives. Their isolation is described by the Badische Co. (D. R. P. 121 688/1899; F. P. 290 452/1899: see also Durand, Huguenin & Co., Brit. P. 7025/1899).

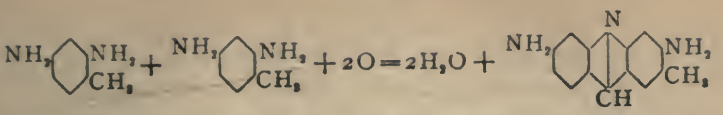
About 1900—1903, several patents were taken out for the modification of already known acridine dyestuffs. Generally the object was to alter the shade or secure a greater basicity or solubility, and for these purposes, alkylation (Meister, Lucius and Brüning, P. A., F. 16037, F. 16045; Leonhardt & Co., D. R. PP. 131 289/1901, 144 092/1902), treatment with formaldehyde (which probably acted as an alkylating agent, Meister, Lucius and Brüning, D. R. P. 152 662/1903; Cassella & Co., D. R. P. 135 771/1901), acet-

aldehyde (Leonhardt, D. R. P. 144 092/1902), glycerine (Badische Co., D. R. PP. 151 206, 151 207/1903), chloracetic acid or ester (Meister, Lucius and Brüning, D. R. PP. 133 738/1901, 136 729/1902), conversion into salts of organic acids (Bayer & Co., D. R. PP. 140 848, 142 453/1902) or sulphonation (Bayer & Co., D. R. P. 141 297/1902) were resorted to.

It will have been noticed that in the majority of cases, formaldehyde has been used to supply the carbon atom of the middle ring of acridine compounds. J. R. Geigy (D. R. P. 149 409/1903) described a method in which the formyl derivatives of *m*-phenylenediamine or its homologues were heated by themselves or with *m*-diamines in presence of ammonium salts. This was extended (D. R. P. 161 699/1904) to the case where the formyl-*m*-diamine was heated with alkylated *m*-diamine or mono- or dialkylaminophenols, glycerine being used as a diluting agent.

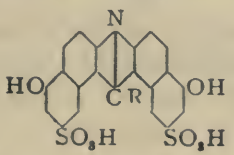


For some years, very little was done in the way of introducing new accridine dyestuffs. In 1912, L. Cassella & Co. (D. R. P. 258 560, F. P. 453 880/1912) found that brown basic dyestuffs, suitable for leather dyeing, are formed when *m*-toluylenediamine (or other diamine containing at least one methyl group ortho to an amino group) is heated with a nitro compound and hydrochloric acid to a high temperature. In this case, the nitro compound plays the part of an oxidising agent and the necessary orientation of the diamine points to the meso-carbon atom being derived from a methyl group of the *m*-diamine. Possibly a reaction such as



takes place, this being followed by a further condensation.

Meister, Lucius and Brüning (D. R. P. 272612/1912) obtain dialkylaminophenyldihydroxydinaphthacridinedisulphonic acids from a dialkylaniline, formaldehyde and an aminonaphtholsulphonic acid. The constitution of the latter must be such that if the amino group occupies position 1 in the naphthalene nucleus, position 2 must be free and vice versa; e. g. a compound of the constitution



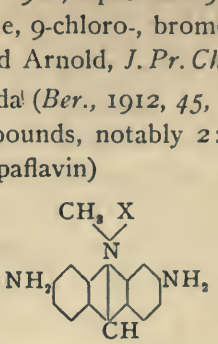
is obtained from dimethylaniline, formaldehyde and 6-amino-1-naphthol-3-sulphonic acid. (Referred to in the patent as 2-amino-5-oxynaphthalin-7-sulfosäure.)

Use has also been made of certain bases containing sulphur which were described by Kalle & Co. (D. R. P. 86096/1894). Metadiamines were heated with sulphur in presence of a solvent (e. g. alcohol) alkali might or might not be added. The product obtained in this way from *m*-phenylenediamine has m. p. 73°, that from *m*-toluylenediamine, m. p. 145°. These substances were intended for the manufacture of dyestuffs, and the A. G. f. Anilinfabr. (D. R. P. 288841/1914) finds that a whole series of dyes related to the phosphines may be produced if these sulphurised bases are heated with diaminodiarylmethanes. In the latter, the amino groups may be primary, secondary or tertiary. Attention is also called to D. R. PP. 82989 and 85199 relating to the preparation of dyestuffs from tetraalkyldiaminobenzophenones (or benzhydrols) and metadiamines.

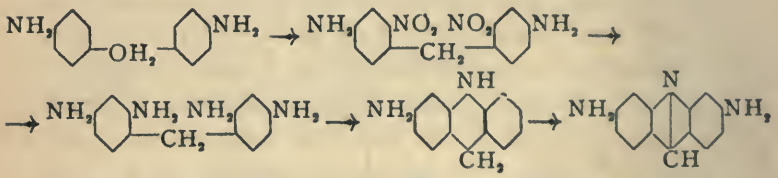
Acridine compounds have not only been used as dyestuffs but have found their way to some extent into medi-

cine. Three patents of Kalle & Co. (D. R. PP. 120 586, 122 607, 126 795 all of 1900, lapsed in 1902) deal with the production of thioacridine, 9-chloro-, bromo- and iodo-acridines. (See also Edinger and Arnold, *J. Pr. Chem.*, 1901, II, *64*, 169.)

Ehrlich and Benda (*Ber.*, 1912, *45*, 1787) discovered that certain acridine compounds, notably 2:8-diamino-10-methylacridinium salts (Trypaflavin)



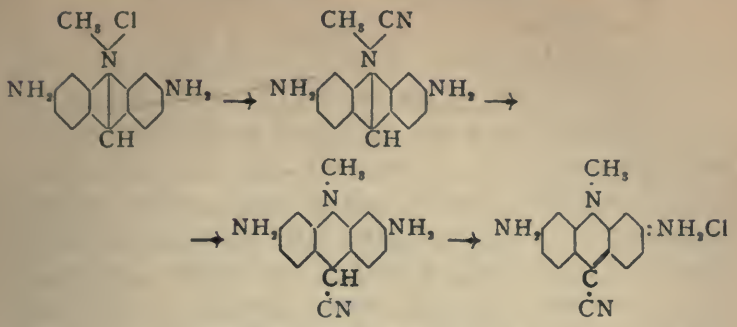
possess marked trypanocidal properties and processes for the production of 2:8-diaminoacridine, easier than that described by Schöpff (*Ber.*, 1894, *27*, 2120) were desired. L. Cassella and Co. (Brit. P. 24 652/1910; U. S. P. 1 005 176 of Ehrlich and Benda; F. P. 433 079/1910; D. R. P. 230 412/1910) abandoned Schöpff's reduction of diaminoacridone and starting with diaminodiphenylmethane, carried out the reactions shown in the following scheme.



After protecting the amino groups by acetylation, the acridine nitrogen atom can be methylated and the acetyl groups subsequently removed.

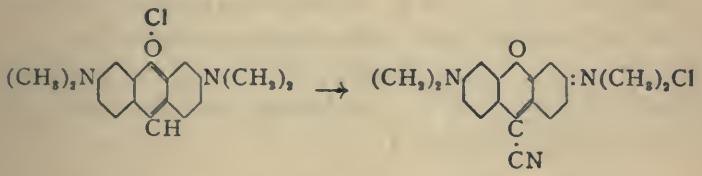
Browning's advocacy of this compound as a disinfectant has led to renewed interest, and the direct production of 2:8-diaminoacridine from *m*-phenylenediamine has been patented.

Trypaflavin and its analogues furnish dyestuffs if treated first with a cyanide and then oxidised (Cassella, D. R. P. 269 802/1913). The reactions involved are expressed by the scheme (*Ber.*, 1913, *46*, 1931),



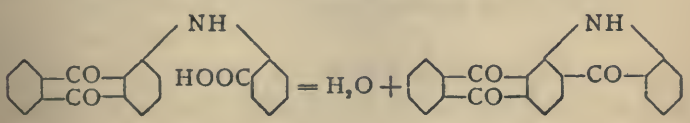
The compound obtained from diaminomethylacridinium chloride dyes silk or cotton mordanted with tannin an intense and lively red, a clear violet is produced with the corresponding dye from tetramethyldiaminomethylacridinium chloride (For preparation, see Ullmann, *Ber.*, 1901, *34*, 4316).

It is interesting that a corresponding dye can be obtained from pyronine



which gives shades similar to those given by Capri Blue.

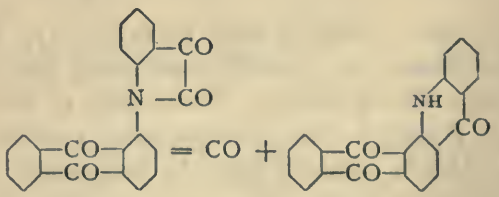
Anthraquinone vat dyestuffs containing the acridone ring have also been described. Compounds of such mixed type can be prepared from anthraquinone-1-anilino-*o*-carboxylic acid which is obtained either by condensing *o*-chlorobenzoic acid with 1-aminoanthraquinone or, better, from 1-chloroanthraquinone and anthranilic acid. By loss of water, the anthraquinone-1-anilino-*o*-carboxylic acid is transformed into anthraquinone-1 : 2-acridone (Ullmann, D. R. P. 221 853/1909; F. Ullmann and P. Ochsner, *Annalen*, 1911, *381*, 1; see also Ullmann and P. Dootson, *Ber.*, 1918, *51*, 9).



Several patents for the manufacture of vat dyes by similar processes were taken by the A. G. f. Anilinfabr. (D. R. PP. 233 038, 236 441, 238 977, 238 978, 241 442 all of 1910). Reactions of this type have also been used by the Badische Co. for the manufacture of vat dyestuffs some of which contain two acridone rings (D. R. PP. 234 977/1909; 237 236, 237 237, 237 546, 240 002 of 1910; 242 063, 243 750, 248 170 of 1911; 272 296, 272 287, 275 671, 285 724 of 1913; 287 614, 287 615 of 1914). *Indanthrene Red BN extra, Indanthrene Violet* and *Indanthrene Violet RN* extra of the Badische Co. belong to the anthraquinone- (mono or bis) acridone series.

Other vat dyes prepared by introduction of radicles into the amino group of 4-amino-1 : 2-anthraquinoneacridone have been patented by Meister, Lucius and Brüning (D. R. P. 239 540/1909; see also D. R. PP. 240 327/1909, 245 875/1910, 244 705/1911).

Bayer & Co. (D. R. P. 286 095/1914) obtain anthraquinone-1 : 2-acridone from 1-phenylaminoanthraquinone by acting on it with oxalyl chloride and treating the resulting antraquinonylisatin with a condensing agent (aluminium chloride, sulphuric acid etc.)



For further particulars concerning dyestuffs of this class, reference may be made to the volumes on vat colours and Anthracene Dyestuffs in this series.

CHAPTER VII.

AMINO DERIVATIVES OF ACRIDINE

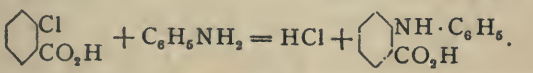
It will be evident from the last chapter that practically all the acridine derivatives which have been found useful as dyestuffs are amino derivatives of acridine or phenylacridine or of quaternary ammonium salts obtained by further alkylation. In the following account an attempt at a systematic survey will be made, not only of the dyestuffs, but, in a briefer manner, of the simpler amino compounds.

The simple aminoacridines may be obtained by the reduction of nitroacridones, the synthesis of the latter compounds leaving no doubt as to their constitution.

Ullmann and Sponagel (*Ber.*, 1905, *38*, 2211) discovered that copper powder (Naturkupfer C) accelerated reactions between alkaline phenoxides and bromo-derivatives of aromatic hydrocarbons such as

$$C_6H_5OK + C_6H_5Br = KBr + C_6H_5 \cdot O \cdot C_6H_5$$

Later (*Annalen*, 1907, *355*, 312) it was found that copper powder added to a boiling solution of *o*-chlorobenzoic acid in aniline led to the production of phenylanthranilic acid.



Phenylanthranilic acid decomposes into diphenylamine and carbon dioxide at higher temperatures, but this decomposition can be avoided by adding potassium carbonate. Copper is the best catalyst, but the reaction is also promoted by salts of iron, nickel, platinum and zinc; salts of manganese and tin are ineffective. Ullmann (*Annalen*, 1907, *355*, 316) estimates that 1 gram of copper as cuprous chloride is sufficient to effect the condensation of 2000 kilos of *o*-chlorobenzoic acid with aniline to phenylanthranilic acid.

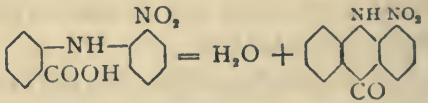
If *o*-bromo- or *o*-iodo-benzoic acids are used, a catalyst is unnecessary.

This reaction may be extended, nitranilines being used instead of the unsubstituted base. The resultant nitrophenyl-

anthranilic acids undergo condensation when warmed with concentrated sulphuric acid, nitroacridones being produced.

$$C_6H_4\begin{cases}CH\cdot C_6H_4\cdot NO_2\\COOH\end{cases} = H_2O + C_6H_4\begin{cases}NH\\CO\end{cases}C_6H_3\cdot NO_2.$$

1-*Aminoacridone* and 1-*aminoacridine*. — 2'-Nitrodiphenylamine-2-carboxylic acid (m. p. 219°) is prepared by heating potassium *o*-chlorobenzoate, *o*-nitraniline, copper acetate, potassium carbonate and amyl alcohol. Alternatively it may be prepared by condensation of *o*-nitrobromobenzene with anthranilic acid in presence of copper powder (Ullmann and Maag, *Ber.*, 1907, *40*, 2522; compare I. Goldberg, *Ber.*, 1906, *39*, 1691). Water is eliminated when the compound (6 grams) is warmed to 100° in concentrated sulphuric acid (42 cc.) solution for 15 minutes.



1-Nitroacridone is isolated by pouring into water, filtering, boiling with dilute ammonia, again filtering, drying and crystallising from toluene. M. p. 262° (Ullmann and Bader, *Annalen*, 1907, *355*, 328). The solution in concentrated sulphuric acid is yellowish brown. It should be noted that Ullmann and Bader refer to this compound as 4-nitroacridone.

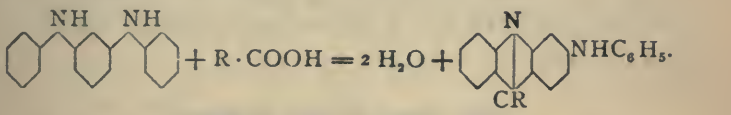
1-*Aminoacridone* is formed by boiling an alcoholic solution of 1-nitroacridone with sodium sulphide, it crystallises from alcohol in dark yellow needles melting at 355° with decomposition. The solution in concentrated sulphuric acid is yellowish green and shows a blue fluorescence.

1-*Aminoacridine* is obtained by reducing an amyl alcoholic solution of 1-aminoacridone with four times its weight of sodium and is isolated as the picrate, m. p. 206° (decomp.). The free base (no analysis) forms yellow brown needles soluble in alcohol with yellow colour and green fluorescence. The colour of the solution in concentrated sulphuric acid is yellow, the fluorescence green; solutions in dilute hydro-

chloric acid are reddish violet (Ullmann and Maag, *Ber.*, 1907, *40*, 2522).

2-*Nitroacridone* (Ullmann and Wagner, *Annalen*, 1907, *355*, 364) is obtained by condensing 2-chloro-4-nitrobenzoic acid to 5-nitrodiphenylamine-2-carboxylic acid (m. p. 239°) and acting on this with aluminium chloride.

2-*Anilinoacridine*. This compound was obtained by E. Besthorn and W. Curtmann (*Ber.*, 1891, *24*, 2042) by heating 5 grams of diphenyl-*m*-phenylenediamine with 10 grams of zinc chloride and 5 grams of 90 per cent formic acid for 4—5 hours to 250° in a sealed tube. After isolation and purification, the compound forms thick, brownish red, flat needles, m. p. 175—176°. The salts with mineral acids are red in colour, easily soluble in alcohol but sparingly in water. It is interesting that only one pyridine ring is formed from diaryl-*m*-diamines and an excess of acid.



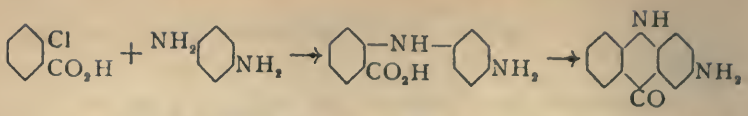
2-*Hydroxyacridine* is formed from the preceding compound (2 grams) by heating it with 20 per cent hydrochloric acid (25 cc.) to 250°. The salts formed with acids and alkalies are easily soluble in water.

2-Anilino-5-methylacridine (*loc. cit.*, 2044), m. p. 215 to 216° and 2-*hydroxy*-5-*methylacridine* were also described.

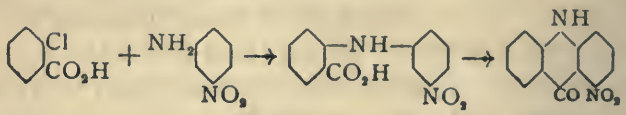
3-*Aminoacridone* (Ullmann and Bader, *loc. cit.*, 335) is obtained by the following steps.

o-Chlorobenzoic acid and *p*-phenylenediamine are condensed to 4'-aminodiphenylamine-2-carboxylic acid; m. p. 205° (decomp.) after crystallisation from xylene.

On condensation by sulphuric acid, 3-aminoacridone is produced, this crystallises from alcohol in yellow needles and melts at 298°. The solutions in alcohol and acetone are yellow with green fluorescence, the solution in concentrated sulphuric acid shows a bluish green fluorescence.



4-Nitroacridone and *4-aminoacridone* (Ullmann and Bader, *loc. cit.*, 332). Metanitraniline and *o*-chlorobenzoic acid are condensed to 3'-nitrodiphenylamine-2-carboxylic acid, yellow needles, m. p. 218°. By warming with concentrated sulphuric acid, 4-nitroacridone (referred to as 1-nitroacridone) is produced; it crystallises form nitrobenzene in yellow needles, the solution in concentrated sulphuric acid is non-fluorescent; no melting point is given.



Reduction gives 4-aminoacridone which crystallises from alcohol in yellow needles, m. p. 285°. The solution in concentrated sulphuric acid is yellow and exhibits a bluish green fluorescence.

Other simple Acridone Derivatives

Before passing on to the technically useful aminoacridines, reference may be made to a few substituted acridones obtained from derivatives of anthranilic acid.

Several halogenated acridones have been obtained by Ullmann and Tedesco (*Annalen*, 1907, *355*, 336). By condensing potassium *o*-chlorobenzoate with a halogenated aniline in amyl alcoholic solution, a trace of copper powder being used as catalyst, a substituted diphenylaminecarboxylic acid is produced which can be condensed to a substituted acridone by warming with concentrated sulphuric acid. 1-, 3- and 4-*Chloroacridones* have been prepared in this manner, they all occur as yellow needles which melt above 360°. 2-*Chloroacridone* is obtained by the action of concentrated sulphuric acid on 5-chlorodiphenylamine-2-carboxylic acid (m. p. 207°), a compound produced from 2 : 4-dichlorobenzoic acid and aniline.

1 : 3-*Dichloro-* and 3-*Bromoacridones* have also been described.

Acridone-1-carboxylic acid (Ullmann and H. Hoz, *Annalen*, 1907, *355*, 354). Diphenylamine-2 : 2'-dicarboxylic acid (m. p. 295°, decomp.) is obtained from *o*-chlorobenzoic acid by the action of anthranilic acid or ammonia. By the action of concentrated sulphuric acid it is condensed to acridone-1-carboxylic acid, dark yellow needles melting at 325° with decomposition. The yellow alkaline solution shows a blue fluorescence, the solution in concentrated sulphuric acid a green fluorescence. The *methyl ester* forms yellow needles, m. p. 172°.

Acridone-3-carboxylic acid (*loc. cid.*, 356) is a yellow crystalline powder melting above 350°. *Methyl ester*, colourless needles, m. p. 339°.

1-*Hydroxyacridone* (Ullmann and Kipper, *Annalen*, 1907, *355*, 345), is obtained by the action of concentrated sulphuric acid on 2'-hydroxydiphenylamine-2-carboxylic acid (m. p. 190°). The latter compound is formed by condensing potassium *o*-chlorobenzoate and *o*-aminophenol, the yield being omly 40 per cent.

On the other hand, *o*-anisidine gives an 85 per cent yield when amyl alcohol is used as a solvent. The resulting 2'-methoxydiphenylamine-2-carboxylic acid (m. p. 176°) condenses to 1-*Methoxyacridone*, m. p. 293°, and this compound may be demethylated to the hydroxyacridone by the action of aluminium chloride on its solution in xylene.

1-Hydroxyacridone crystallises as yellow needles from dilute acetic acid, it sinters at 290° and melts at 300°. The alcoholic solution exhibits a blue fluorescence, the solution in concentrated sulphuric acid is yellowish brown and fluoresces green. As a phenol, hydroxyacridone dissolves in dilute caustic soda, the solution is yellow.

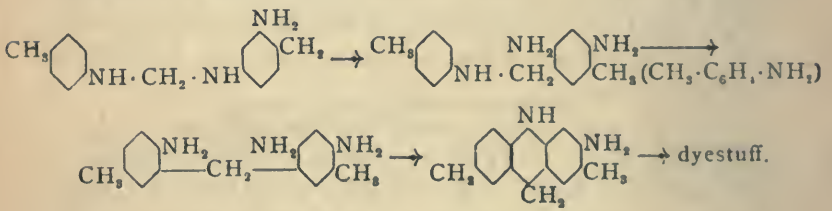
3-*Hydroxyacridone* (Ullmann and Kipper, *loc. cid.*, 346), melts indefinitely about 345—350°. It is obtained from *p*-phenetidine and *o*-chlorobenzoic acid by the usual steps, the resultant 3-ethoxyacridone being de-ethylated.

Homologues of 2-Aminoacridine.

2-Amino-3:7-dimethylacridine. — Terrisse and Darier (Brit. P. 20063/1898; D. R. P. 107517/1898, rights transferred to the Badische Co., *Chemiker Zeit.*, 1899, *23*, 86) first discovered that a single amino group introduced into the acridine nucleus in position 2 sufficed for the formation of a dyestuff. To obtain such compounds, equimolecular proportions of a metadiamine and formaldehyde are allowed to react and the product treated with a monamine, substituted in the para position. In this way, intermediate products ("imides") are formed to which the patentees assign constitutions such as

$$NH_2 \cdot X \cdot NH \cdot CH_2 \cdot NHY$$ [1])

Such an imide reacts with a para-substituted monamine to give a monoaminoacridine, the dihydroacridine first formed undergoing oxidation. The changes involved may be expressed by the scheme



Intermediate isolation of the "imide" may or may not be effected.

Example 1. 122 parts of finely divided *m*-toluylenediamine in 2 to 3 litres of water are stirred for some hours with 40 per cent formaldehyde solution, the product filtered, pressed, dried, ground and dissolved in 3 or 4 times its weight of *p*-toluidine at 100°. 143.5 parts of *p*-toluidine hydrochloride are then added, the mass solidifies and the reaction is completed by heating for a further half-hour on the water bath. After neutralisation with caustic soda,

1) The metadiamine reacts in the first place with formaldehyde to give an anhydroformaldehyde compound, e. g. $C_6H_3(CH_3)(NH_2)(N:CH_2)$. Ullmann and Naef, *Ber.*, 1900, *33*, 914.

excess of *p*-toluidine is removed in a current of steam and the yellow granular "imide" isolated.

1 part of the imide is dissolved in 6 parts of *p*-toluidine at 100°, 2 to 4 parts of *p*-toluidine hydrochloride added and the mixture heated with stirring for 3 hours at 120—160°.

The melt is poured into water, *p*-toluidine removed in a current of steam, the remaining solution cooled and filtered and the dyestuff precipitated from the filtrate by the addition of saltpetre. The corresponding base melts at 245° after crystallisation from alcohol.

Example 2. 108 parts of *m*-phenylenediamine are condensed in aqueous solution with 1 molecular proportion of formaldehyde (40 per cent). 1 part of the condensation product obtained in this manner is dissolved in 4 parts of *p*-toluidine at 100°, 3 parts of *p*-toluidine hydrochloride added and the mixture kept for 2 hours at 150—160°.

Whilst the hydrochloride of acridine yellow is sparingly soluble in water, the hydrochlorides of these monoamino-dyes are easily soluble; caustic soda gives a yellow precipitate and cotton (tannin and antimony mordant) is dyed yellowish orange.

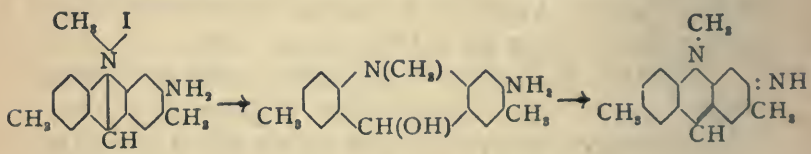
The Badische Co. (D. R. P. 107626/1898) obtained the same dyes by the action of metadiamines on bases of the type of *o*-aminobenzylaniline.

Example 1. Equal weight of *o*-aminobenzylaniline and *m*-toluylenediamine hydrochloride are stirred and heated to 180—190° until the mixture is thick and no further dye formation observable. After treatment with hot water and steam, the solution is filtered and salted out.

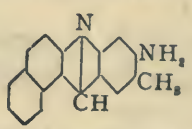
Example 2. 22 parts of *o*-aminobenzyl-*p*-toluidine (from anhydroformaldehyde-*p*-toluidine and *p*-toluidine, Meister, Lucius and Brüning, D. R. PP. 87934/1895, 104239, 105797/1898), 15 parts of *p*-toluidine, 20 parts of *m*-phenylenediamine hydrochloride, 4 parts of nitrobenzene and 1 part of ferric chloride are stirred and heated to 180—190° until dyestuff formation is complete. The isolation is effected as in the last example.

2-Amino-3:7-dimethylacridine has also been obtained by Ullmann (*Ber.*, 1903, *36*, 1125) by heating 60 grams of *p*-toluidine, 24 grams of tetraaminoditolylmethane and 36 grams of *p*-toluidine hydrochloride for 2 to 3 hours at 160—170°; in this case one molecule of *m*-toluylenediamine is eliminated.

Fox and Hewitt (*Trans. Chem. Soc.*, 1904, *85*, 532) obtained a methiodide of the acetyl derivative. This was hydrolysed and the carbinol base precipitated by ammonia. Freshly prepared, the compound gave figures on analysis corresponding with the formula $C_{16}H_{18}ON_2$, but if heated for some time in nitrobenzene, water was eliminated and addition of light petroleum precipitated a substance of the formula $C_{16}H_{16}N_2$. This change may probably be expressed by the scheme



A corresponding naphthacridine dye



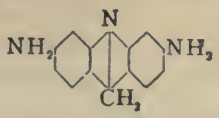
described by Ullmann has already been mentioned. These naphthacridine dyes do not seem to have found much application; the base whose structure is shown above forms lemon yellow needles, m. p. 240°, the acetyl derivative melts above 300°. Cotton is dyed (tannin mordant) in clear reddish yellow shades similar to those given by phosphine.

Diaminoacridines

1:3-*Diaminoacridone.* F. Jourdan (*Ber.*, 1885, *13*, 1450) condensed 1-chloro-2:4-dinitrobenzene with anthranilic acid to 2:4-dinitrodiphenylamine-2'-carboxylic acid, m. p. 280—282°. On reduction with tin and alcoholic hydrochloric acid, the hydrochloride of 1:3-diaminoacridone was obtained;

the free base formed feebly coloured, flat needles, m. p. 222—223°.

2:8-*Diaminoacridine.*



This base is important for it is not only the parent substance of a number of dyestuffs, but the quaternary ammonium salts obtained by alkylating the ring nitrogen atom exhibit remarkable properties with regard to the lower organisms.

The base was first obtained by M. Schöpff (*Ber.*, 1894, *27*, 2316) from diphenylmethane, the process was roundabout but left no doubt as to the constitution of the compound. Diphenylmethane [1]) gives a tetranitro-derivative on energetic nitration, m. p. 172° (Dorp, *Ber.*, 1872, *5*, 795; Städel, *Annalen*, 1883, *218*, 339), which is oxidised by chromic acid mixture to tetranitrobenzophenone, m. p. 225° (Dorp, *Ber.*, 1873, *6*, 725; Städel, *loc. cit.*, 341).

Schöpff gives the following directions for the preparation. 50 grams of diphenylmethane are added to a mixture of 70 grams of concentrated sulphuric acid and 130 grams of potassium nitrate at 10—25°, the mixture being well stirred. After all the diphenylmethane is added, the mixture is heated for half an hour to 70°, stirring being continued.

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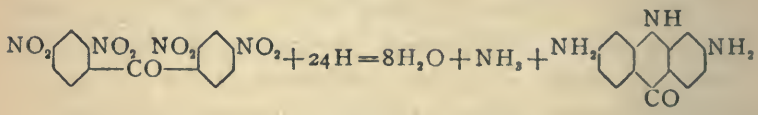
1) The literature regarding the preparation of diphenylmethane is extensive. Jena, *Annalen*, 1870, *155*, 86; Zincke, *Annalen*, 1871, *159*, 374; Baeyer, *Ber.*, 1873, *6*, 221; Meyer and Wurster, *ibid.*, 963; Graebe, *Ber.*, 1874, *7*, 1624; Zincke and Thörner, *Ber.*, 1877, *10*, 1473; E. and O. Fischer, *Annalen*, 1878, *194*, 253; Staedel, *ibid.*, 307; H. Schwarz, *Ber.*, 1881, *14*, 1526; Friedel and Crafts, *Bull. soc. chim.*, 1884, II, *41*, 324; *Ann. chim. phys.*, 1884, VI, *1*, 478. Friedel and Balsohn (*Bull. soc. chim.*, 1880, II, *33*, 337) prepared the compound by gradually adding 30 to 40 parts of aluminium chloride to a mixture of 100 parts of benzyl chloride and 500 parts of benzene. M. p. 26—27°, p. b. 261—263°.

After cooling, the mass is poured into a large excess of water, the product collected, boiled with not too much alcohol and the residue crystallised from glacial acetic acid. Yield about 72 per cent.

Städel's directions were followed (*loc. cit.*) for oxidising to tetranitrobenzophenone. Tetranitrodiphenylmethane is dissolved in glacial acetic acid and the solution heated for some time with the calculated amount of chromic acid. The product crystallises on cooling, after recrystallisation from boiling glacial acetic acid (sparingly soluble) it melts at 223°.

2:8-Diaminoacridone is formed when tetranitrobenzophenone is reduced (Schöpff, *loc. cit.*, 2318).



A solution of 270 grams of stannous chloride in 270 grams of hydrochloric acid (s. g. 1.19) was warmed to 100° and 36 grams of tetranitrobenzophenone added whilst the mixture was shaken. The beginning of the reaction was hastened by adding a little alcohol, the mixture becoming warmer. Soon after all the solid was dissolved, the tin double salt began to separate, its quantity was increased by boiling for a further half hour. After cooling, the crystals were filtered off over glass wool and a further quantity recovered from the filtrate by strong cooling and saturation with hydrogen chloride (gas).

The tin double salt was warmed for some time with a large quantity of water, the precipitated metastannic acid removed by filtration, the solution of diaminoacridone hydrochloride decolourised with animal charcoal, and the base precipitated as colourless, or at most, feebly yellow needles by addition of alkali or ammonia. One further crystallisation and analytically-clean diaminoacridone was obtained.

The melting point was found to be above 350°, Schöpff

also prepared and analysed the hydrochloride and the platinichloride.

2:8-Diaminoacridine was obtained (*loc. cit.*) by adding sodium amalgam to an alcoholic solution of the acridone until the violet fluorescence had disappeared and a sample, when poured into water, no longer separated unaltered acridone but gave an intesely yellow coloured solution with green fluorescence. This alkaline alcoholic solution was then evaporated on the water bath, water added and the undissolved diaminoacridine filtered off. By crystallisation from alcohol, after treatment with animal charcoal, yellow needles melting at 281° were obtained. The solution in concentrated hydrochloric acid is orange red, this turns yellow on dilution and shows a green fluorescence.

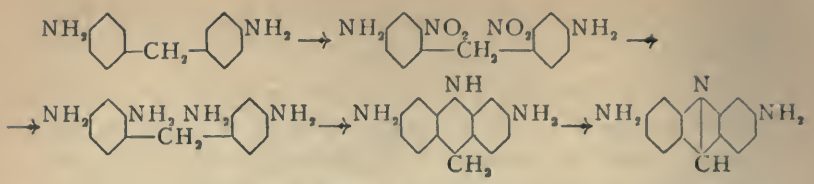
Schöpff mentions that J. Gram (Inaug. Diss., Jena, 1892) had previously obtained the same diaminoacridine by reduction of tetraaminodiphenylmethane.

Duval (*Compt. rend.*, 1905, *141*, 198) found that 2:2'-dinitro-4:4'-diaminodiphenylmethane was reduced by zinc dust in alcoholic potassium hydroxide solution to 4:4'-diamino-2:2'-azodiphenylmethane, m. p. 233°,

$$NH_2 \cdot C_6H_3 \begin{cases} N:N \\ CH_2 \end{cases} C_6H_3 \cdot NH_2$$

This compound gives tetraminodiphenylmethane with stannous chloride in hydrochloric acid, but zinc dust in alkaline solution eventually converts it into 2:8-diaminoacridine (Duval, *Compt. rend.*, 1906, *142*, 341).

Schöpff's method was not of much use technically and Benda, working in the laboratory of L. Cassella & Co., obtained the compound by an easier process (*Ber.*, 1912, *45*, 1787) very similar to that adopted by Gram. *p*, *p*'-Diaminodiphenylmethane was nitrated to *p*, *p*'-diamino-*o*, *o*'-dinitrodiphenylmethane, this reduced to tetraaminodiphenylmethane and the crude reduction product directly condensed at 135—140°, ferric chloride being added afterwards to oxidise any diaminodihydroacridine.



Preparation of Diaminodiphenylmethane. – The following details are taken from D.R.P. 53937/1889 of Meister, Lucius and Brüning. 50 Parts of anhydroformaldehydeaniline (Tollens, *Ber.*, 1885, *18*, 2309) are heated on the water bath with 70 parts of aniline hydrochloride and excess of aniline. After about 12 hours the mixture is rendered alkaline, the excess of aniline driven off by a current of steam and the resultant diaminodiphenylmethane crystallised from benzene. M. p. 87°.

Purification of the technical base may be effected either by preparation of the sulphate and liberation of the base therefrom, or by dissolving 100 grams of the commercial article in 150 grams of 25% hydrochloric acid diluted with twice its volume of water, heating, adding ammonia until opalescent, cooling, pouring off from the separated tar and repeating the operation until bright coloured precipitates are obtained (Schnitzspahn, *J. Pr. Chem.*, 1902, II, *65*, 316; compare Eberhardt and Welter, *Ber.*, 1894, *27*, 1804).

Nitration of Diaminodiphenylmethane. — This operation is described by Schnitzspahn *(loc. cit.)*. Benda employed much the same method and gives the following quantities.

250 grams of diaminodiphenylmethane are added to 5 kilograms of concentrated sulphuric acid (66° Bé.) and the mixture cooled to 0°, well stirred and nitrated at 0° to 5° with 540 grams of a mixture of sulphuric and nitric acid equivalent to 160 grams actual HNO_3. The mixture is left for 2 to 3 hours at 8° to 10°, poured on to 17 kilos of ice and rendered alkaline by addition of 7 kilos of ammonia. (Presumably solution of s. g. 0.880.) The precipitate is collected, well washed with hot water and pressed, the moist paste weighs 900 to 1000 grams.

Reduction to tetraaminodiphenylmethane. — The paste is well stirred with 2 litres of hydrochloric acid (s. g. 1.18), warmed to 50° and 450 grams of granulated tin added. The temperature rises to 110° and reduction is soon complete.

Formation of Diaminoacridine. — The resulting solution, occupying a volume of about $2^1/_2$ litres, is heated in an enamelled autoclave (3 litres capacity) for 4 hours at 135°. After cooling, the crystals are separated from the liquid, boiled with 5 litres of water and ferric chloride added until a reaction for Prussian Blue can be obtained. Caustic soda is added to neutrality, the mixture boiled and filtered and the residue washed with boiling water. The united filtrates give a mixture of diaminoacridine and its hydrochloride on cooling which is dissolved in 2 N sulphuric acid and the sulphate precipitated in red matted needles by adding a slight excess of 2 N sulphuric acid. By one recrystallisation, the sulphate, $C_{13}H_{11}N_3$, H_2SO_4, is obtained.

To isolate the free base, the sulphate is dissolved in water and the solution poured into excess of dilute ammonia, the crystalline precipitate being recrystallised from a large quantity of boiling water.

2:8-Diaminoacridine, thus prepared, forms long brownish needles, melting at 283° after incipient decomposition at 260° and becoming very dark by 279°.

The process was patented by Cassella & Co. (Brit. P. 24652/1910; D. R. P. 230412/1910; U. S. P. of Ehrlich and Benda, 1 205 176/1911; F. P. 433 079/1910), the claim being for the process of heating *o*, *p*, *o'*, *p'*, tetraaminodiphenylmethane in acid solution. Quantities are generally in the same proportion as given in Benda's paper, but it should be noted that the strength of the sulphuric acid in which the diaminodiphenylmethane is dissolved is given in the German patent as 66 per cent and not as 66° Bé. The isolation of the base from the tin double salt of the diaminoacridine is carried out directly by solution in hot water (2 litres per kilo of diaminodiphenylmethane originally taken) neutralisation by caustic soda and further addition of sodium carbonate. From

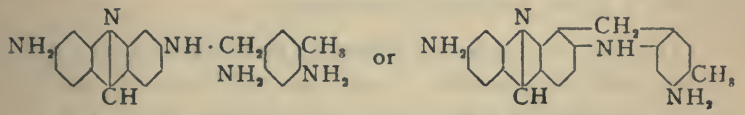
the precipitate, the diaminoacridine is extracted by boiling water, it crysallises out on cooling.

A later patent (Poulenc Frères and Meyer, Brit. P. 137 214/1919) describes the direct production of diaminoacridine from *m*-phenylenediamine. 6 Kilos of *m*-phenylenediamine, 7 kilos of crude oxalic acid, 10 kilos of fused zinc chloride and 10 kilos of industrial glycerine of 25° Bé. are heated to approximately 130°, when the evolution of carbon dioxide has ceased, the temperature is increased to 150–170° and kept there for 2 hours. The resultant, nearly solid mass is heated with water and ammonia and the resultant diaminoacridine filtered off, it may be purified by means of its sulphate. The specification describes the compound as 3:6-diaminoacridine.

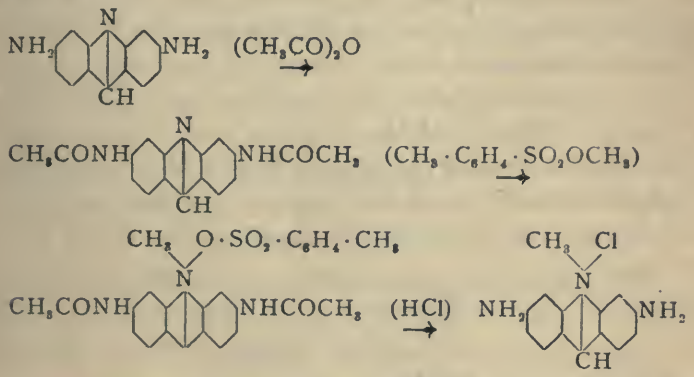
2:8-Diaminoacridine resembles the homologous base of acridine yellow in many respects differing chiefly in the comparatively easy solubility of the base in hot water and of the hydrochloride in cold water. Solutions dye leather and cotton mordanted with tannin a pure yellow. The solution in dilute acid can be diazotised, but on boiling neither aminohydroxyacridine nor dihydroxyacridine could be isolated, only a brown amorphous substance being obtained. But 2:8-dihydroxyacridine may be prepared by heating 12 grams with 50 cc. of water and 40 grams of concentrated sulphuric acid for 8 hours at 195°, after purification the orange matted needles were found to turn red about 275° but not to melt by 300°. Both acid and alkaline solutions are yellow (those in alkalies are darker) and fluoresce feebly green (Benda, *loc. cit.*, 1795). Successive treatment of a concentrated sulphuric acid solution of diaminoacridine with nitrosyl sulphate and alcohol leads to the production of acridine.

By treatment with formaldehyde and aromatic bases, new colouring matters are obtained which have a deeper shade and greater dyeing power than the original material, the shades being egg-yellow, orange or brown and more resembling those given by phosphine dyes. The preparation

is carried out by warming an aqueous solution of one molecule each of diaminoacridine, a monamine hydrochloride (or diamine dihydrochloride) and formaldehyde to water bath temperature, the higher homologues are described in two of Cassella's patents (D. R. PP. 131 365, 132 116). The constitution of the dye is not fully explained, Benda considers the one obtained from diaminoacridine, formaldehyde and *m*-toluylenediamine must be either



Benda *(loc. cit.,* 1796) obtained diaminomethylacridinium chloride by acetylating the amino groups, methylating with methyl *p*-toluenesulphonate and removing the acetyl groups by hydrolysis with hydrochloric acid, the steps are represented by the scheme



500 grams of crude diaminoacridine were mixed with 1250 cc. of acetic anhydride and 125 grams of dehydrated sodium acetate and heated to 80°; the mixture then boiled spontaneously and the reaction was finished in 15 minutes. After dilution with 3.5 litres of water, boiling and filtering, the diacetylaminoacridine acetate was allowed to crystallise, collected, dissolved in hot water and the free acetylated base precipitated by 800 cc. of ammonia.

For methylation, which occurs instantaneously, 400

grams of diacetaminoacridine were dissolved in 4 kilos of nitrobenzene and treated at 175° with 330 grams of methyl *p*-toluenesulphonate. After 12 to 15 hours, the crystals were collected and washed out with ether. 545 grams of the salt thus obtained were heated for several hours with 1750 cc. of water and 1750 cc. of hydrochloric acid (s. g. 1.18), long red prisms of 2:8-diamino-10-methylacridinium chloride separating from the solution on cooling. (The directions in Cassella's patent are much the same.)

The salt is extremely soluble in cold water with yellow colour, green fluorescence is observed only in dilute solution and disappears on addition of hydrochloric acid. On the other hand, the solution in concentrated sulphuric acid is only feebly yellow and shows an intense bluish green fluorescence. In distinction to the parent 2:8-diaminoacridine, an aqueous solution of 1:1000 is not precipitated by N/1 caustic soda or strong ammonia, and 1 per cent solution is only rendered cloudy by strong ammonia the cloudiness almost disappearing when the ammonia is added in excess. By warming a suspension in concentrated alkali for some time on the water bath, a product, difficulty soluble in water, but easily in acids, is obtained. Solutions of the chloride have a bitter taste, dilute sulphuric and nitric acids precipitate the sulphate and nitrate respectively; these salts dissolve however in acid free water.

The amino groups are removed by heating with diluted sulphuric acid at 190—200°, on isolation, the resulting base gave figures on analysis agreeing with the formula $C_{28}H_{24}O_3N_2$ (m. p. 275°).

Action of 2:8-diamino-10-methylacridinium salts on organisms. The chloride is extremely active in killing trypanosomes. Not merely does this compound surpass any other dyestuff examined by Ehrlich up to 1912, but it proved for equally toxic doses to be three times as active as the homologous compound obtained from acridine yellow. Mice weighing 20 grams which had been infected by a very virulent race of trypanosomes were completely cured by in-

jection of 1 cc. of 1 : 5000 solution, whilst 1 cc. of 1 : 1500 to 2000 solution of the homologous compound from acridine yellow was necessary to get rid of the trypanosomes, and, in most cases, the mice. The remedy was tried on human beings suffering from sleeping sickness and considerable effect on the parasites was observed.

The observations of Browning, Gulbransen, Kennaway and Thornton (*Brit. Med. J.*, 1917, 1, 73; see also *Proc. R. S.*, 1918, (B), *90*, 136) on the behaviour of "flavine" towards certain organisms led to a renewal of interest in this compound. [1]) Most antiseptics act more powerfully in water than in blood serum, but it was found that whilst Staphylococcus aureus was killed at a dilution of 1 : 20000 of water containing 0.7 per cent of peptone, the dilution in blood serum was as great as 1 : 200 000. The respective dilutions with respect to Bacillus coli were 1 : 1300 and 1 : 100 000.

The Gesellschaft für chemische Industrie in Basel have taken patents for disinfectants (U. S. P. 1 227 624/1917) obtained by the action of silver salts on acridine dyes, which may be alkylated or not, in presence of a solvent. Special mention is made of the silver derivative of 3 : 6-diamino-2 : 7-dimethyl-10-methylacridinium salts. (Remember older method of numbering the acridine nucleus.) It forms a brownish red powder giving coloured solutions in water, ethyl alcohol and other solvents. It is said to act as a disinfectant at great dilutions, strongly checking the growth of bacteria, especially streptococci and splenitis bacilli.

The same firm have also patented (U. S. P. 1 228 926/1917) the preparation of soluble cadmium salts of acridine dyes, the acridinium salt referred to above being specially mentioned.

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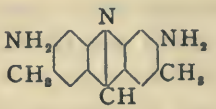
1) Cassella introduced Diaminomethylacridiniumm chloride under the name of "Trypaflavine" (Brit. Trade Mark, 327 437, Class 1). It was called "flavine" in this country, but to avoid confusion, this name was subsequently changed to "Acriflavine". "Proflavine" or Diaminoacridine Sulphate has similar properties but is not so active.

2:8-Diamino-3:7-dimethylacridine (Acridine Yellow).

The synthesis of 2:8-diamino-3:7-dimethyl-5-phenylacridine (K. Öhler, D. R. P. 437201/1887), which soon found technical application under the name of "Benzoflavine", led to experiments on the condensation of other aldehydes than benzaldehyde with *m*-toluylenediamine. Generally, the aliphatic aldehydes were found to be unsuitable, formaldehyde proved however to be exceptional and A. Leonhardt & Co. (Brit. P. 17971/1889; F. P. 201798; D. R. P. 52324/1889) introduced acridine yellow, a dyestuff of the constitution



According to the directions of the patentees, 9 kilos of formaldehyde are brought together with 26 kilos of *m*-toluylenediamine and 10 kilos of sulphuric acid in aqueous solution the whole making a volume of 400 litres. The liquid is filled almost immediately with needles of the condensation product (about 35 kilos) which is filtered off, washed with cold water and heated for several hours with 90 kilos of concentrated hydrochloric acid and 270 litres of water in an autoclave to 150°. After cooling, ferric chloride solution is added as long as crystals of the dyestuff separate, these are filtered off and iron carefully removed by washing with cold dilute hydrochloric acid: the substance is then dried.

Working in this manner, Ullmann and Maric (*Ber.*, 1901, *34*, 4308) obtained 4.5 grams of diaminodimethylacridine from 6 grams of tetraaminoditolylmethane. They purified the base by crystallisation from aniline, and observed that the solution in concentrated sulphuric acid was yellowish and showed a bluish green fluorescence. They also prepared the hydrochloride and platinichloride.

The condensation of the formaldehyde and *m*-toluylenediamine may be effected in other solvents, e. g. methyl

alcohol, and the oxidation can be carried out by bichromate, nitrous acid etc. in place of ferric chloride.

Probably the same compound is produced when *m*-toluylenediamine is condensed with oxalic acid, glycerine and zinc chloride (Ges. f. chem. Ind., Basel, F. P. 203 467/1890, abandoned after one year) and the dyes obtained by the Soc. anon. d. mat. col. de St. Denis (F. P. 188 417/1888) by acting with aldehydes, acetone etc. on meta (? and ortho) diamines may belong to the same class.

Acridine yellow (Marks *G, R, T,* Leonhardt, Savoz and Boasson) in its colouring power bears much the same relationship to Benzoflavine that Succinrhodamine does to Phthalrhodamine (Friedländer, II, 1101).

Aqueous solutions are yellow with green fluorescence. Hydrochloric acid gives a yellow precipitate of the hydrochloride, caustic soda one of the base. The solution in concentrated sulphuric acid is bright yellow, water produces a yellow precipitate. Cotton mordanted with tannin and antimony is dyed yellow, silk greenish yellow with green fluorescence.

2:8-*Diamino*-3:7-*dimethyl*-10-*methylacridinium salts.* — Ullmann and Maric (*Ber.*, 1901, *34*, 4307) found that whilst alkyl halides acted on the diaminoacridines, partly by alkylating the amino groups, alkylation of the cyclic nitrogen atom could be effected if the amino groups were protected by acetylation and the resulting compound then treated with methyl sulphate. On hydrolysis, the methylacridinium compound was obtained and the observation was also made that the same acridinium salts were formed by direct addition of methyl sulphate to the diaminodimethylacridine.

The directions given by Ullmann and Maric are briefly as follows.

Acetylation. 8 grams of acridine yellow, 20 cc. of acetic anhydride and 2 grams of sodium acetate boiled for 1—1½ hours under reflux gave 8 grams of precipitated diacetyl derivative, which, for purposes of analysis, was recrystallised from aniline.

Alkylation. 6 grams of diacetyl compound in 150 cc. of nitrobenzene were treated at 190° with 3 grams of methyl sulphate and yielded 8 grams of the methylacridinium methylsulphate.

This methylsulphate is very soluble in water, the solution tastes bitter and addition of solutions of sodium chloride, nitric acid and potassium dichromate precipitate respectively the chloride, nitrate and dichromate.

Alkalies produce no immediate precipitate in dilute solution, the substance eventually obtained is certainly not unaltered carbinol base since it cannot be completely reconverted into the original salt by acid, probably it contains some of the corresponding acridone (Compare Decker, *J. pr. Chem.*, 1892, II, *45*, 161; Hantzsch, *Ber.*, 1899, *32*, 3124).

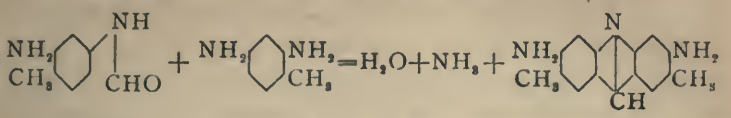
Hydrolysis. 3:7:10-Trimethyl-2:8-diaminoacridinium chloride was obtained as red needles by dissolving the foregoing compound in a little hot water, adding an equal volume of concentrated hydrochloric acid, boiling for one hour under reflux and allowing to cool.

Direct alkylation of acridine yellow was effected by dissolving 2 grams of base in 50—60 cc. of boiling nitrobenzene and adding 2 grams of methyl sulphate. 2.5 grams of methylacridinium methylsulphate were obtained, conversion into chloride, nitrate and dichromate established the identity of these salts with those obtained by the previous method involving acetylation. These acridinium salts dye cotton mordanted with tannin in yellow shades fast to alkali.

Colouring Matters related to Acridine Yellow.

The colouring matters obtained by heating the formyl derivatives of diamines are stated by J. R. Geigy (D. R. P. 149409/1903; F. P. 330487/1903) to be faster than acridine yellow and to have a shade more resembling that of phosphine. Since the process described consists in heating the formyl derivatives of *m*-phenylenediamine or *m*-toluylenediamine either alone or in presence of the *m*-diamines with

ammonium salts, it might be expected that the dyes formed would be identical or homologous with acridine yellow, e. g.,



Example 1. 100 kilos of diformyl-*m*-tolulyenediamine and 25 kilos of ammonium chloride are gradually heated with stirring to 230—240° and kept at this temperature until the mass is viscous and frothing and increase of dye formation is finished. The colouring matter is easily soluble in water and is precipitated by alkalies in bright brown flocks.

Example 2. 68 kilos of monoformyl-*m*-phenylenediamine, 61 kilos of *m*-toluylenediamine and 37 kilos of ammonium chloride are treated as before, the melt taken up in 1000 litres of hot water with addition of hydrochloric acid and salted out with zinc and sodium chlorides.

Example 3. 17.8 kilos of diformyl-*m*-toluylenediamine, 24.4 kilos of *m*-toluylenediamine and 21 kilos of aniline hydrochloride are heated gradually to 220° and kept at this temperature until the completion of the reaction.

In further claims J. R. Geigy describes the production of dyestuffs by heating the formyl derivatives of monamines with *m*-diamines (D. R. P. 149 410/1903; Brit. P. 11 882/1903; U. S. P. of Ris and Mylius 740 463/1903; F. P. 330 487/1903).

Example 1. 24.4 kilos of formanilide, 48 kilos of *m*-toluylenediamine and 42 kilos of aniline hydrochloride are stirred and heated gradually to 210—215°, heating being continued until no further increase of dyestuff formation occurs; the mass is then allowed to cool and ground.

Example 2. 36 kilos of formyl-*o*-toludine, 43.2 kilos of *m*-phenylenediamine and 30 kilos of ammonium chloride are treated as in example 1.

Both colours may be used for tannined cotton or leather, the former dyes a golden yellow, the latter brown. From consideration of the method of manufacture, these dyes might be expected to be monoaminoacridines.

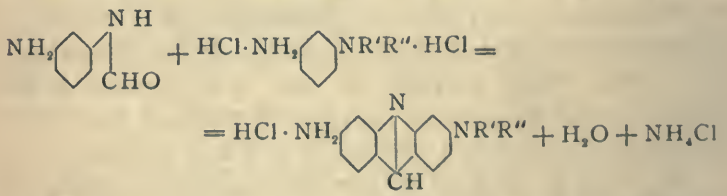
An additional patent (D. R. P. 161 699/1904) extends the reaction to the preparation of orange yellow to orange red dyes by using mono- and dialkyl derivatives of *m*-diamines in place of unsubstituted meta phenylene or toluylene diamines. Analogous results are obtained with mono- or dialkyl-*m*-aminophenols; addition of glycerine as a diluent has been found useful.

Example 1. 30 kilos of monoethyl-*m*-toluylenediamine, 18 kilos of diformyl-*m*-toluylenediamine and 21 kilos of aniline hydrochloride are heated to 200°.

Example 2. 15.7 kilos of monoethyl-*m*-aminophenol, 30 kilos of *m*-toluylenediamine hydrochloride, 26.7 kilos of diformyl-*m*-toluylenediamine and 30 kilos of glycerine at 150—160°.

Example 3. 16.7 kilos of diethyl-*m*-aminophenol, 17.3 kilos of diformyl-*m*-toluylenediamine, 19.5 kilos of *m*-toluylenediamine hydrochloride and 20 kilos of glycerine at 150—160°.

The dyestuffs obtained according to Geigy's patents leave something to be desired both in quality and yield. The A. G. für Anilinfabr. (D. R. P. 292 848/1915) claim that if mono- or di-formyl derivatives of *m*-diamines of the benzene series are melted with mono- or di-alkylated *m*-diamines good yields of yellow to orange red dyestuffs are obtained, which on account of their eveness in dyeing and their isensibility to lime, promise to be valuable if applied to leather goods.



Example 1. 15 parts of monoformyl-*m*-toluylenediamine ($CH_3 : NH_2 : NHCHO = 1 : 2 : 4$) and 21 parts of dimethyl-*m*-aminophenol-hydrochloride are heated gradually to 185 to 190°. About 140°, water vapour is evolved and care is necessary, the reaction is complete in about 6 hours. The melt is run into water (400 parts), allowed to dissolve, filtered

and the solution salted out with sodium and zinc chlorides. Clear orange red shades are produced on leather.

Example 2. Treat 15 parts of monoformyl-*m*-toluylenediamine and 22.5 parts of dimethyl-*m*-toluylenediamine ($CH_3 : N(CH_3)_2 : NH_2 = 1:2:4$) as in example 1. Gives a pure yellow on leather.

Example 3. The dyestuff made from 17.8 parts of diformyl-*m*-toluylenediamine and 21 parts of dimethyl-*m*-aminophenol hydrochloride gives shades resembling those produced by the dyestuff of example 1.

Example 4. 15 parts of formyl-*m*-toluylenediamine and 21 parts of monomethyl-*m*-toluylenediamine are used. The dye gives a pure yellow on leather.

Example 5. The product from 13.6 parts of monoformyl-*m*-phenylenediamine and 22.3 parts of monoethyl-*m*-toluylenediamine dyes in yellowish brown shades.

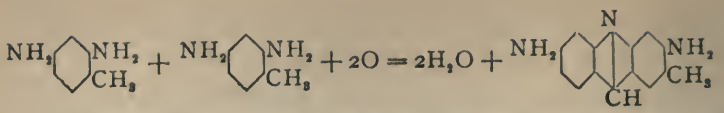
Example 6. 16.4 parts of diformyl-*m*-phenylenediamine and 22.3 parts of monoethyl-toluylenediamine are employed. The product is said to resemble that obtained in example 5, but to dye in clearer and redder shades.

Example 7. The product from 17 parts of 4-chloro-1-amino-3-formylaminobenzene and 21 parts of dimethyl-*m*-phenylenediamine dyes leather reddish yellow.

The patentees state that their products differ from those produced according to D. R. P. 161 699.

U. S. P. 1 255 739/1918 of the same firm refers specially to the use of the halogenated derivatives of formyl-*m*-diamines. (Compare example 7 above.)

The brown basic dyestuffs obtained by Cassella & Co. (D. R. P. 258 560/1912; F. P. 453 880/1912) by heating *m*-diamines containing at least one methyl group ortho to an amino group with an aromatic nitro compound in presence of hydrochloric acid probably belong to this class. The nitro compound plays the part of an oxidising agent and carbon atom 5 of the acridine complex is derived from a methyl group.



That the reaction stops at this stage appears improbable for the dyestuff gives a brown solution and dyes leather and tannined cotton in brown shades.

Example 1. 100 parts of neutral *m*-toluylenediamine hydrochloride and 75 parts of the base are heated for 3 hours in an iron pot provided with stirrer. Then 60 parts of nitrobenzene are gradually added, a very energetic reaction takes place and the mass becomes viscous. After cooling, the melt is dissolved in 2000 parts of water and 120 parts of hydrochloric acid (s. g. 1.15). Any remainder of nitrobenzene is removed in a current of steam, the solution filtered and salted out with sodium and zinc chlorides.

Example 2. 100 parts of *m*-toluylenediamine hydrochloride and 75 parts of the base are heated for 3 hours at 160° with stirring. The mixture is diluted with 60 to 70 parts of aniline and 60 parts of nitrobenzene and 1 to 2 parts of dry ferric chloride added. A lively reaction accompanied by water formation ensues, the reaction is completed by several hours heating and the product worked up as before.

Example 3. 100 parts of *m*-xylylenediamine base ($CH_3 : CH_3 : NH_2 : NH_2 = 1 : 3 : 4 : 6$) and 100 parts of dry aniline hydrochloride are melted for 2 or 3 hours at 170°, 40 to 50 parts of nitrobenzene are added, and heating continued for a further 4 hours.

Probably the iron salts act as oxygen carriers as in other cases. An iron pot is specified in example 1, the material of the pot is not specified in example 2 but ferric chloride is added. In example 3, iron is not specified either as material for the pot or as a salt addition.

Patent Phosphine. The alkylation of acridine yellow and benzoflavine may be carried out with an alcohol and an acid or with an alkyl halide (Ges. f. chem. Ind. Basel, D. R. P. 79703/1904). According to the intensity of the alkylation,

orange yellow to orange red dyes are obtained which, like the phosphines, are well suited for leather dyeing.

Example. 10 parts of acridine yellow, 20 parts of methyl alcohol, and 5 parts of fuming hydrochloric acid are heated 3 to 4 hours in autoclaves at 180—190°. After cooling, the excess of alcohol is distilled off, the residue dissolved in water and the solution filtered and evaporated. The dyestuff obtained in this manner is very easily soluble (distinction from acridine yellow), the solutions do nat gelatinise and no precipitates are formed by excess of mineral acid. Replacement of methyl by ethyl alcohol gives a yellower dye.

Alternatively, 10 parts of acridine yellow, 10 parts of alcohol and 5 parts of ethyl bromide are heated for 2 hours at 180°.

Ullmann and Maric compared Patent Phosphine (RGM.), which is put on the market as a zincichloride and used for leather dyeing, with the acridinium salts they had obtained (*Ber.*, 1901, *34*, 4316). After removal of zinc, it was found that the aqueous solution was completely precipitated by ammonia, hence alkylation had not extended further than the amino groups. This is attributed to the presence of free acid during the process. The patentees disclaim knowledge of the constitution of their compounds.

Brilliant Phosphine. Mark 5 G of Leonhardt & Co. and of the Gesellschaft für chemische Industrie in Basel is probably prepared (Friedländer, VI, 486) according to D. R. P. 131 289/1894, an addition to D. R. P. 79 703. The claim made in this patent is for the further alkylation of aminoacridinium salts in place of aminoacridines.

Example 1. 20 parts of 3:7:10-trimethyl-2:8-diaminoacridinium chloride, as obtained by the action of methyl chloride on acridine yellow according to D. R. P. 79 703, are stirred into a cooled mixture of 50 parts of sulphuric acid and 15 parts of methyl alcohol, then heated for 2 or 3 hours to 130—140° in an autoclave, diluted with 100 parts of water, filtered and salted out with sodium and zinc chlorides. Orange shades are obtained on dyeing with this product,

redder ones if the alkylation has been carried out at 170 to 180°.

Example 2. 20 parts of the diaminoacridinium salt are added to a mixture of 60 parts of sulphuric acid and 20 parts of methyl alcohol, then heated for 3 hours with continuous stirring, diluted with 500 parts of water and the dyestuff isolated.

Friedländer remarks on the presence of acridine compounds mixed with the acridinium salts in Brilliant Phosphine.

Patents were obtained for the alkylation of aminoacridine compounds in neutral solution by the Gesellschaft für chemische Industrie in Basel (Brit. P. 8872/1900; U.S. P. of Jedlicka 666 095/1901; F. P. 299 064/1900) but an application for a German patent (P. Anm. 12816, Kl., 22b of 11.4.1912) on the part of Leonhardt & Co. for alkylation of acridine dyestuffs in neutral (e. g. nitrobenzene) solution by means of the esters of *p*-toluenesulphonic acid was refused.

A number of patents relating to the action of formaldehyde on acridine yellow in presence or absence of amines have been taken. When no amine is added, it is likely that the formaldehyde acts in part as a methylating agent; it is well known that methylamines are produced by the action of formaldehyde on ammonia (Plöchl, *Ber.*, 1888, *21*, 2117; Brochet and Cambier, *Compt. rend.*, 1895, *120*, 449, 557; *Bull. soc. chim.*, 1895, III, *13*, 392; Knudsen, *Ber.*, 1914, *47*, 2694; Jones and Wheatley, *J. Amer. Chem. Soc.*, 1918, *40*, 1411). Friedländer (VI, 489) expresses the opinion that the dyestuffs obtained by heating aminoacridines with acid and formaldehyde under pressure belong to the class of the Patent Phosphines.

Cassella & Co. (Brit. P. 15064/1901; D.R.P. 131 365/1901; F.P. 312771/1901) first condensed dyestuffs such as acridine yellow (or their leuco compounds) with formaldehyde and metadiamines; the resulting dyes were stated to be more orange or brown in shade, to be faster to light and alkali, and further, in consequence of their greater basicity,

to give more soluble salts and have a greater affinity for tannined cotton and leather. The dyestuffs are said to be also formed by condensing tetraaminoditolylmethane with formaldehyde in presence of acid and a metadiamine, but the reaction does not lead to such good results.

Example 1. Suspend 27 kilos of acridine yellow in 150 kilos of hydrochloric acid (7.3 kilos HCl), at 40° add 8 kilos of formaldehyde solution (38%) and 12.1 kilos of powdered *m*-toluylenediamine. Boil for 36 hours under reflux, leading through a current of air. Dilute the clear dark brown solution and add sodium, and preferably zinc, chlorides.

Example 2. Dissolve 36.6 kilos of *m*-toluylenediamine in 180 litres of dilute hydrochloric acid (21.9 kilos HCl), then add 17.6 kilos of formaldehyde solution (38%) at 45°. After standing for 6 hours, add $^1/_2$ kilo of ferric chloride, then boil for 36 hours under reflux, passing a current of air through the solution. Precipitate the crude dyestuff and separate from unaltered acridine yellow by solution in dilute hydrochloric acid in which the acridine yellow is much less soluble, and again precipitate.

The operation may be shortened to 5 to 6 hours by heating in an autoclave to 120°.

The dyestuff made from *m*-phenylenediamine dyes brownish yellow, that from dimethyl-*m*-phenylenediamine, orange.

In an additional patent (D. R. P. 132 116/1901) claim is made for the condensation of acridine yellow or its leuco compound with aniline, *o*- and *p*- toluidine, xylidine, mono- and di-alkylanilines and monoalkyl-*o*-toluidine in presence of formaldehyde.

Example 1, Heat 25.6 kilos of tetraaminoditolylmethane, 90 kilos of hydrochloric acid (21° Bé.) and 270 litres of water for 7 hours at 145—150°. Cool, and add 9.3 kilos of aniline and 8 kilos of formaldehyde solution (38%). Close the autoclave and heat for 2 hours at 105—110°. Salt out, any leuco compound accompanying the dyestuff is oxidised spontaneously.

Example 2. The quantities for the leuco-acridine yellow are as before, but add 6.3 kilos of dimethylaniline and 8.2 kilos of formaldehyde solution and heat for 6 hours to 130°.

Cassella and Co. took an independent patent for the action of formaldehyde without an amine (D. R. P. 135771/1901). As an example, the following quantities are given.

Heat 25.6 kilos of tetraaminoditolylmethane with dilute hydrochloric acid as above, cool, add 8.1 kilos of formaldehyde solution (38%) and heat for 6 hours at 125°. Cool to about 80° and blow over the contents of the autoclave into 2000 litres of salt water (concentration not stated). The reddish yellow dyes thus obtained are claimed to be very fast to milling and light; they may be used for leather &c.

Several methods, other than those referred to, have been used for making new dyes from acridine yellow, presumably by alkylation.

In place of the monochloracetic acid mentioned in Meister, Lucius and Brüning's patent (D. R. P. 133788/1901) the alkyl esters of this acid may be employed (D. R. P. 136729/1902), leuco-acridine yellow being heated with ethyl chloracetate for 1 hour at 120°. The resulting dye gives a bright yellow on tannined cotton.

The dyestuff produced by alkylating acridine yellow with alcohol and hydrochloric acid (D. R. P. 135771/1902) may be converted into another dye by solution in 10 times its weight of concentrated sulphuric acid and, at about 50°, adding three-fifths to its own weight of formaldehyde, stirring and heating for one hour, eventually to 170°. By solution in water (30 parts to 1 part of dyestuff taken) and addition of 4 parts of sodium chloride, a by-product is removed, the resulting dye being precipitated from the filtrate by zinc chloride and sufficient alkali to neutralise most of the excess of sulphuric acid.

The dye gives orange yellow shades on tannined cotton and leather; it is not an individual substance but contains a mixture of acridine and acridinium derivatives.

Dyestuffs of unknown constitution, but stated to possess valuable qualities, are obtained by heating acridine yellow or benzoflavine or the hydrochlorides of their leuco compounds with glycerine (Badische Co., U. S. P. 746 981/1903 of C. L. Müller; D. R. P. 151 206/1903). Thus 10 parts of acridine yellow and 20 parts of glycerine are heated for 4 to 6 hours at 170—180°, or 10 parts of benzoflavine with 15 parts of glycerine for 5 hours to 165—170°. The melts are afterwards dissolved, filtered and salted out, both dyes give orange shades on tannined cotton and leather.

In an additional patent (D. R. P. 151 207/1903) the process of heating *m*-aminobenzoflavine (D. R. P. 45 294) with twice its weight of glycerine for 3 hours at 165—170° is described.

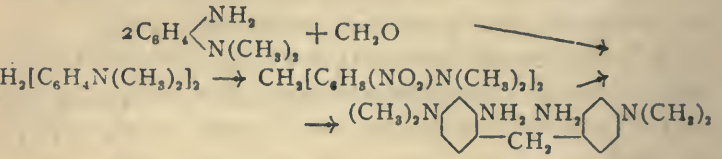
The production of dyestuffs resembling phosphine is claimed in patents taken out by Leonhardt & Co. and the Gesellschaft für chemische Industrie in Basel (U. S. P. 730 771/1902; F. P. 241 916/1902; D. R. P. 144 092/1902; additional patent to D. R. P. 79 203/1894). An example states that 100 kilos of acridine yellow (colour base) is suspended in 1000 litres of water and 90 kilos of 30 per cent hydrochloric acid, 36 kilos of acetaldehyde are added and the mixture stirred and slowly heated by steam to 70—80°. The acridine yellow goes into solution, the liquid is allowed to cool and salted out.

Acridine yellow forms salts with mineral acids which are usually sparingly soluble. To overcome this difficulty, Bayer & Co. (Brit. P. 11 666/1902; U. S. P. of Nastvogel, 716 084/1902; F. P. 321 272/1902; D. R. P. 140 848/1902) introduced salts of monobasic organic acids e. g. formic, acetic, propionic, butyric, valeric, glycollic, lactic etc. The formation of the salts may be effected by direct union of base and acid or by double decomposition.

Benzoflavine forms salts with several organic acids which are more soluble than those with mineral acids; their production is mentioned by Bayer & Co. (D. R. P. 142 453/1902.)

Tetramethyl-2:8-diaminoacridine. (Acridine Orange.)

Whilst the condensation of formaldehyde with *m*-phenylenediamine does not proceed as smoothly as that with *m*-toluylenediamine, dimethyl-*m*-phenylenediamine reacts with formaldehyde giving tetramethyltetraaminodiphenylmethane. The same compound may also be obtained by nitration of 4:4'-tetramethyldiaminodiphenylmethane and subsequent reduction.



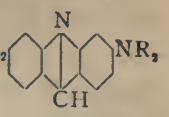
Leonhardt & Co. (Brit. P. 8243/1890; U. S. P. of Bader, 503 305/1803; F. P. 205 459/1890; D. R. P. 59 179/1899) condensed the tetraamine by means of acid and oxdised the resulting dihydroacridine to dyestuff which they introduced under the name of Acridine Orange.

Example 1. 5 kilos of tetramethyltetraaminodiphenylmethane, 10 kilos of 30 per cent hydrochloric acid and 30 litres of water are heated several hours at 140°. The contents of the vessel are extracted with water adding acid if necessary, and the dyestuff precipitated by the addition of ferric and zinc chlorides.

Example 2. 5 kilos of tetraamino base, 50 kilos of concentrated sulphuric acid and 200 litres of water are evaporated in an opeen vessel and finally heated for some time at 130°. Oxidation takes place spontaneously by the action of the air, after cooling, the mass is considerably diluted and salted out with sodium and zinc chlorides.

Leonhardt & Co. took out two additional patents. In D. R. P. 67 609/1890, claim was made for the use of ethyl instead of methyl derivatives; D. R. P. 70 935/1892 deals with tetraalkyltetraaminoditolylmethanes; whilst in D. R. P. 67 126/1890, the same firm describe the condensation of

dialkyl-*m*-diamines with formic acid or substances capable of yielding formic acid such as oxalic acid.

$$2C_6H_4(NH_2)(NR_2) + HCO_2H = 2H_2O + NH_3 +$$ 

Example 1. 12 kilos of dimethyl-*m*-phenyldiamine, 12 kilos of dehydrated oxalic acid, 10 kilos of zinc chloride and 11 kilos of zinc chloride are heated gradually to 150° with continued stirring and kept at that temperature for 3 hours.

Example 2. 12 kilos of dimethyl-*m*-phenylenediamine, 10 kilos of formic acid (s. g. 1.2) and 10 kilos of zinc chloride are caused to react at 150—160°.

Example 3. 12 kilos of diethyl-*m*-phenylenediamine, 12 kilos of dehydrated oxalic acid, 15 kilos of glycerine and 15 kilos of stannic chloride are slowly heated to 170° and kept at that temperature for 2 hours.

Leonhardt & Co. extended the reaction to the case of the condensation products of aromatic aldehydes with dialkyl-*m*-diamines thus obtaining alkylated derivatives of benzoflavine (D. R. PP. 68908/1890, 70065/1891, 71362/1892).

In their patents, Leonhardt & Co. do not describe the preparation of tetraalkyltetraaminodiarylmethanes, having taken over the patent of A. Gerber & Co. of Basel (D. R. P. 60505/1889).

One preparation of tetramethyltetraaminodiphenylmethane is as follows.

1. A mixture of 40 grams of dimethylaniline, 100 cc. of alcohol and 30 cc. of fuming hydrochloric acid is cooled and treated with 125 cc. of 40 per cent formaldehyde solution, allowed to stand for one or two days, warmed and poured into a concentrated solution of sodium acetate. The yield is quantitative, m. p. 90—91°, after crystallisation from alcohol (Biehringer, *J. Pr. Chem.*, 1896, II, *54*, 240; see also Pinnow, *Ber.*, 1894, *27*, 3166).

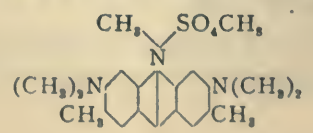
2. 10 kilos of the tetramethyldiaminodiphenylmethane in 200 kilos of concentrated sulphuric acid are nitrated at

0—5° with 9.5 kilos of nitric acid (53%) in 30 kilos of sulphuric acid. After some hours, the mixture is poured into 1000 litres of ice and water and directly reduced with 40 kilos of zinc dust. The isolation of the base is not described in the patent, compare Biehringer, *loc. cit.*

The other preparation of tetramethyltetraaminodiphenylmethane is described by Biehringer (*loc. cit.*, 242). A mixture of 5 grams of dimethyl-*m*-phenylenediamine (2 mols), 10 cc. of alcohol and 0.9 grams of 20 per cent hydrochloric acid 1/8 mol.) is cooled and treated with 1.4 gram 40 per cent formaldehyde solution (1 mol.). The condensation product crystallises out; after some time the mother liquor is poured off, the residue dried and extracted with ligroin from which, on cooling, the base separates as yellowish needles. After several recrystallisations from ligroin and eventually from alcohol, Biehringer obtained the compound with m. p. 139 to 141°.

Acridine Orange NO (Leonhardt, Sévoz and Boasson), *Euchrysin 3R* (Badische) or *Orange pour Cuir* (St. Denis) occurs as the zincichloride, $C_{17}H_{20}N_3ZnCl_3$, an orange coloured powder, soluble in water and alcohol with orange yellow colour and green fluorescence. Hydrochloric acid reddens the solution, caustic soda produces a yellow precipitate, the solution in concentrated sulphuric acid is nearly colourless with green fluorescence, dilution turns the solution first red and further dilution orange yellow. The dye can be used on cotton (antimony-tannin mordant); the fastness to light and soap is moderate.

Reference has already been made to the further methylation of similar compounds (Ullmann and Maric, *Ber.*, 1901, *34*, 4316). A solution of tetramethyldiaminodimethylacridine (3.8 grams) in boiling anhydrous toluene (500 cc.) reacts immediately with methyl sulphate (2 grams) giving a red crystalline precipitate of the acridinium methylsulphate,



The corresponding nitrate was also prepared; cotton mordanted with tannin is dyed a beautiful orange red, fast to alkalies.

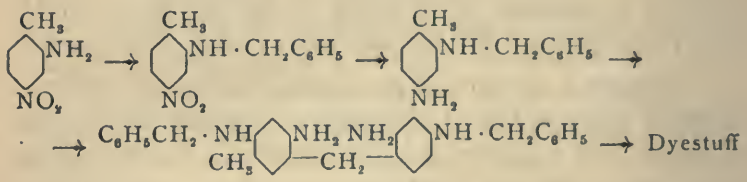
The use of acetaldehyde in place of formaldehyde for the preparation of acridine dyestuffs received the attention of the Gesellschaft für chemische Industrie in Basel, the resulting compounds were found to be far more soluble (Brit.P. 15659/1902; F.P. 241916/1902; D.R.P. 143893/1902).

Example 1. 25 parts of *m*-toluylenediamine are dissolved in 500 of water and 10 of concentrated sulphuric acid, cooled to 5—10° and 4.4 parts of acetaldehyde added with stirring. After some time, the condensation product is precipitated as a resin by the addition of caustic soda solution; the subsequent elimination of ammonia with closing of the acridine ring can be effected in open vessels on the water bath but is better carried out by heating under pressure for 4 hours at 130—150°. For condensing liquid, 6 to 8 times the quantity of 20 per cent sulphuric acid can be used. The sulphate of the dye is fairly soluble in cold and very easily in hot water, thus distinguishing the compound from acridine yellow. Another distinction lies in the lack of precipitation of dilute solutions by weak alkalies such as sodium carbonate and ammonia except under special conditions.

Example 2. 27 parts of dimethyl-*m*-phenylenediamine in 300 of water and 25 of concentrated hydrochloric acid (or 10 of concentrated sulphuric acid) are condensed with 4.4 parts of acetaldehyde. After standing several hours, the tetraamino base is precipitated and ring formation effected by heating from 3 to 4 hours at 140—150° with 15—20 per cent sulphuric acid. This is followed by oxidation and salting out.

Acid Dyestuffs of the acridine series can be obtained by sulphonating the dibenzyl derivative of acridine yellow (Bayer & Co., D. R. P. 141 297/1902). As an intermediate, monobenzyl-*m*-toluylenediamine is necessary. This compound (m. p. 80°) is prepared by benzylating *p*-nitro-*o*-toluidine and reducing the resulting *p*-nitro-*o*-benzyltoluidine (m. p. 124°).

A tetraamino base results from the condensation of the diamine with formaldehyde, it may be sulphonated either before or after the elimination of ammonia. Special oxidation of the leuco compound to dyestuff is stated to be unnecessary as it is effected either by presence of air or by the action of the fuming sulphuric acid during sulphonation.



Example 1. 42.2 kilos of benzyl-*m*-toluylenediamine in 200 litres of 5 per cent sulphuric acid are condensed with 7.5 kilos of 40 per cent formaldehyde at the ordinary temperature. The tetraamino base (m. p. 157° after crystallisation from alcohol) is precipitated by alkali, and 43.6 kilos are heated with 400 kilos of 25 per cent sulphuric acid for 7 hours at 160°. After cooling, the mixture of the acridine and its leuco compound is separated from the mother liquor, dried, powdered and sulphonated with 6 times the quantity of fuming sulphuric acid of 25 per cent anhydride content. When a sample is completely soluble in alkali, the sulphonation mixture is poured on to ice, the dyestuff disulphonic acid separating as a red powder.

Example 2. 43.6 kilos of well dried dibenzyltetraaminoditolylmethane base are stirred with 300 kilos of 25 per cent fuming sulphuric acid, when a sample is soluble in alkali, the sulphonation mixture is poured on to 1200 kilos of ice, and the resulting solution heated for 7 hours at 160° under pressure. On exposure of the reaction mixture to the air for some time, the acridine-disulphonic acid separates as a red crystalline precipitate.

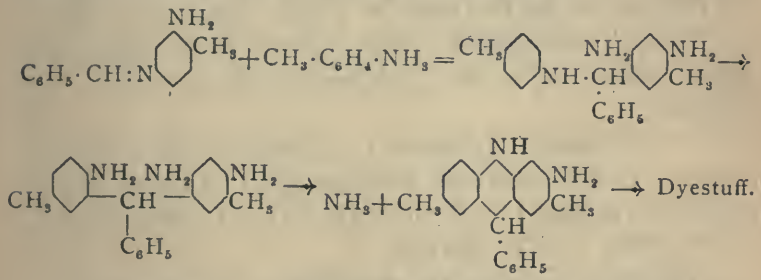
An advantage claimed for these dyestuffs is that they can be used with other acid leather dyes.

CHAPTER VIII.

AMINO-DERIVATIVES OF 5-PHENYLACRIDINE

The monoamino derivatives of phenylacridine are relatively unimportant, but as has been pointed out in the general survey of the acridine dyestuffs, several of the diamino derivatives have attained considerable importance as leather dyes.

2-Amino-3:7-dimethyl-5-phenylacridine formed the subject of a patent of the Badische Co. (D. R. P. 118075/1898). The condensation product of one molecule of an aromatic aldehyde with one molecule of a *m*-diamine if warmed with a parasubstituted amine and its hydrochloride furnishes an "imide" which is further transformed into an acridine, the dihydro-compound undergoing spontaneous oxidation. (Compare Terrisse and Darier, D. R. P. 107517.)



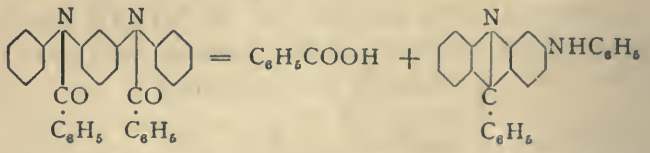
The anhydro- compound from 122 grams of *m*-toluylenediamine and 106 grams of benzaldehyde is dissolved in 6 to 8 times its weight of *p*-toluidine at 100°, 400 grams of *p*-toluidine hydrochloride added and the temperature raised to 120—160°. The operation is finished in about 12 hours, the melt poured into water and the solution filtered and salted out.

The dyestuff forms a brown powder, difficulty soluble in water with brownish yellow colour, alkalies precipitate a yellowish brown base. Excellent dyeing properties were assigned to the material which was recommended for the replacement of phosphine.

In an additional patent (D. R. P. 125697/1898) the pre-

paration of the same dyestuff by heating 100 parts of tetraaminoditolylphenylmethane with 200 parts of *p*-toluidine base and 250 parts of hydrochloride for some hours at 120—140° is described. In this case, one molecule of *m*-toluylenediamine is split off.

2-*Anilino*-5-*phenylacridine* was obtained by E. Besthorn and W. Curtman (*Ber.*, 1891, *24*, 2045) by heating a mixture of 10 grams of dibenzoyldiphenyl-*m*-phenylenediamine with 25 grams of zinc chloride to 250°.



The residue was dissolved in the minimum quantity of hot alcohol, on cooling, a zinc chloride double salt crystallised out from which the free base (m. p. 196—197°) was isolated.

By heating the anilino-compound with 20 per cent hydrochloric acid to 270—280°, 2-hydroxy-5-phenylacridine was obtained.

2:8-*Diamino*-3:7-*dimethyl*-5-*phenylacridine* (*Benzoflavine*). This dyestuff was discovered by C. Rudolph and its production patented by K. Öhler (Brit. P. 9614/1888; D. R. P. 43 714/1887; U. S. P. 382 832).

The following steps are described.

(1.) Preparation of Benzylidene-*m*-toluylenediamine. Grind 12 kilos of *m*-toluylenediamine with water and add 10.6 kilos of benzaldehyde, allow the mixture to harden, powder, wash and dry.

(2.) Preparation of Tetraaminoditolylphenylmethane. Warm 75 kilos of benzylidene-*m*-toluylenediamine with 85 kilos of *m*-toluylenediamine sulphate and 500 kilos of water at 60—70° until all is dissolved, dilute and precipitate by alkali.

Operations 1 and 2 may be combined. Dissolve 61 kilos of *m*-toluylenediamine and 98 kilos of its hydrochloride in 200 kilos of alcohol, add 53 kilos of benzaldehyde and warm

to 70—80° until no further separation of the hydrochloride of the tetraamino-base occurs. Then cool and filter off the salt, $C_{21}H_{24}N_4$, 2HCl (Meyer and R. Gross, describe $C_{21}H_{24}N_4$, 4HCl, $2H_2O$, *Ber.*, 1899, *32*, 2358.)

(3.) Preparation of 2:8-Diamino-3:7-dimethyl-5-phenyldihydroacridine. Heat 1 kilo of tetraaminoditolylphenylmethane and 5 kilos of $13^1/_2$ per cent hydrochloric acid for 5 hours at 160°.

(4.) Preparation of Benzoflavine. Add 350 kilos of 30 per cent ferric chloride solution to a cold solution of 100 kilos of leuco-base in dilute hydrochloric acid containing zinc chloride. Filter off the voluminous yellow precipitate, press and dry.

According to the patentee, benzoflavine and its analogues are difficultly soluble in cold, more easily in hot water, they are precipitated by addition of hydrochloric acid. Concentrated sulphuric acid gives yellowish solutions with green fluorescence; the alcoholic solutions exhibit intense yellowish green fluorescence which disappears on addition of dilute acids. The bases themselves are colourless (compare Meyer and Gross), insoluble in water, soluble in alcohol.

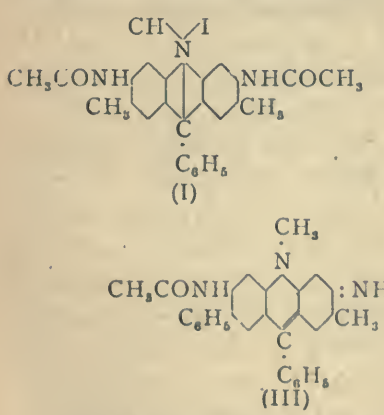
An additional patent (D. R. P. 43720/1887) describes the preparation of tetraaminoditolylphenylmethane sulphate, $C_{21}H_{24}N_4$, $2H_2SO_4$, by boiling a mixture of 100 kilos of *m*-toluylenediamine sulphate, 200 kilos of 50 per cent alcohol and 25 kilos of benzaldehyde for some hours under reflux.

R. Meyer and R. Gross (*Ber.*, 1899, *32*, 2352) examined Benzoflavin No·6B·F·O (K. Öhler) more closely, the free base crystallised from alcohol in short brownish yellow needles of the formula $C_{21}H_{19}N_3$, and salts of the formulae B, 2HCl, B, HBr, B, HI were prepared and analysed. By diazotisation in concentrated sulphuric acid solution with gaseous nitrous acid and decomposition with boiling alcohol (compare O. Fischer and G. Körner, *Ber.*, 1884, *17*, 206) 3:7-dimethyl-5-phenylacridine, m. p. 166—167°, was obtained and compared with a specimen synthesised by heating 10 grams of *p*-ditolylamine, 7 grams of benzoic acid and 20 grams of powdered

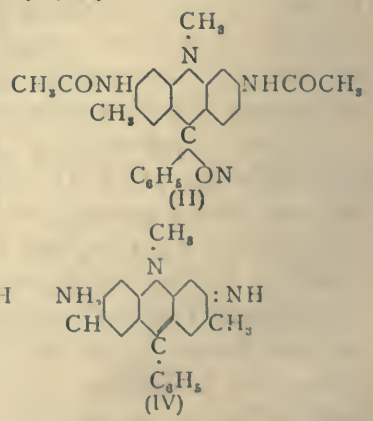
zinc chloride for 10 hours at 260°. (3:7-Dimethyl-5-phenyl-10-methylacridinium iodide forms long red needles, m. p. 186—187°.)

Meyer and Gross (*loc. cit.*, 2365) attempted to prepare 2:8-diamino-5-phenylacridine from benzaldehyde and *m*-phenylenediamine, but although a dyestuff was obtained, they were unable to isolate a pure material. They found that whilst *m*-toluylenediamine condenses with difficulty with a second molecule of benzaldehyde (Schiff, *Annalen*, 1866, *140*, 98), only the dibenzylidene derivative of *m*-phenylenediamine, m. p. 104—105°, could be obtained.

Hewitt and Fox (*Trans. Chem. Soc.*, 1905, *87*, 1058) prepared other derivatives using Mark B. F. 2 (Öhler) as source of the base. Diacetylbenzoflavine does not melt below 280°, the tetraacetyl derivative melts at 264° (273° corr.). The diacetyl compound forms a methiodide (I), the alcoholic solution of which is precipitated by ammonia. This precipitate is at first pale in colour and is probably the carbinol base (II), it darkens considerably on drying in the desiccator after crystallisation from alcohol; and, on analysis, gives figures for the expected carbinol base minus one molecule of water. Its constitution is represented by (III).



(I)



(II)

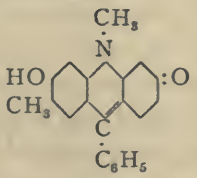
(III)

(IV)

By boiling the last substance (III) with 33 per cent sulphuric acid the other acetyl group is removed, on liberating

the base with ammonia and crystallising from alcohol or chloroform, small needles exhibiting a green reflex are obtained. These soften at about 205° and melt at 226—227° (232—233° corr.). Analysis agrees with the formula $C_{22}H_{21}N_3$, so that the substance probably possesses the constitution represented by (IV).

By heating benzoflavine for 2 days at 180° in acid solution under pressure, Dunstan and Cleaverly (*Trans. Chem. Soc.*, 1907, *91*, 1621) replaced the amino groups by hydroxyl. The free 2:8-dihydrox-3:7-dimethyl-5-phenylacridine (Benzoflavol) crystallises from alcohol in dark brown needles, m. p. 255—260°. The solution in concentrated sulphuric acid shows a strong bluish green fluorescence. The dichromate, platinichloride, and picrate were prepared as well as the diacetyl (m. p. 239—242°) and dibenzoyl derivatives. The diacetyl derivative reacts with methyl iodide or sulphate, when these acridinium salts are completely hydrolysed and precipitated by ammonia, an anhydro-base



is obtained.

Substituted Benzoflavines. Derivatives of Benzoflavine can be obtained by condensing other aldehydes with *m*-toluylenediamine and working up the tetraamino compounds thus produced (Öhler, D. R. P. 45294/1887; U. S. P. of C. Rudolph, 395089). Tolualdehyde gives a homologue of benzoflavine possessing similar properties to the original substance.

More interesting is the use of nitrobenzaldehydes since with the para compound one may arrive at derivatives of 2:8:5-*p*-triaminophenylacridine, the parent base of the rheonines (see p. 179). The preparation is described.

(1.) Prepare the hydrochloride of 2:8-diamino-3:7-dimethyl-5-*p*-nitrophenylacridine by heating 21.5 kilos of *p*-nitrobenzaldehyde, 34.7 kilos of *m*-toluylenediamine, 28 kilos

of hydrochloric acid (22.5° Bé.) and 100 kilos of alcohol (96%) for some hours on the water bath.

(2.) Reduce 26.5 kilos of the product of the last reaction by gradual addition to a warm mixture of 45 kilos of stannous chloride in 120 kilos of hydrochloric acid (22.5° Bé.). Dilute, remove tin with sulphuretted hydrogen and precipitate the crystalline pentaaminoditolylphenylmethane by addition of alkali.

(3.) Heat 10 kilos of the pentaamino-base with 60 kilos of hydrochloric acid (16%) under pressure for some hours at 160°. The hydrochloride of triaminodimethylphenyldihydroacridine separates almost completely on cooling.

(4) Add 150 kilos of 20 per cent ferric chloride solution to a dilute solution containing 30 kilos of the dihydroacridine, 30 kilos of hydrochloric acid (22.5° Bé.) and zinc chloride. Isolate the precipitated dyestuff which is stated to resemble the ordinary benzoflavine.

One nitro group may be introduced into tetraaminoditolylphenylmethane by dissolving 10 kilos of its sulphate in 50 kilos of sulphuric acid (66° Bé.) and nitrating at 5 to 15° with 4.6 kilos of a mixture of 2 parts of sulphuric acid (66° Bé.) and 1 part of nitric acid (44° Bé.). The product is probably identical with that obtained by condensing *p*-nitrobenzaldehyde with *m*-toluylenediamine (Öhler, D. R. P. 45 298/1888).

Alkylation of Benzoflavine. The amino groups of benzoflavine may be alkylated (compare acridine yellow) by heating under pressure with an alcohol and a mineral acid (Ges. f. chem. Ind. Basel, D. R. P. 79 703/1894).

Examples are as follows.

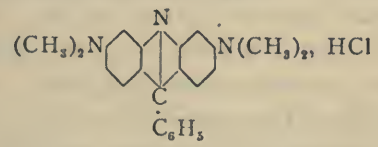
(1) 2 parts of benzoflavine, 4 parts of methyl alcohol and 2 parts of concentrated hydrochloric acid are heated for 4 hours at 150—160°.

(2) 4 parts of benzoflavine, 10 parts of concentrated sulphuric acid and 3 parts of methyl alcohol are heated for 4 to 5 hours at 190—200°. After cooling, dilute with water, filter, precipitate the base with soda, collect, wash, dissolve

in dilute hydrochloric acid, filter from resinous matters and evaporate to dryness.

Cotton mordanted with tannin is dyed a bright reddish orange, by attention to the proportion of sulphuric acid and alcohol, redder or yellower dyes than phosphine may be obtained.

Acridine Orange R extra is the hydrochloride of tetramethyl-2:8-diamino-5-phenylacridine



and was discovered by Bender in 1889 (Leonhardt, Brit. P. 8243/1890; D. R. P. 68908), Benzaldehyde is condensed with dimethyl-*m*-phenylenediamine in alcoholic solution in presence of hydrochloric acid, the elements of ammonia removed from the tetraamino-base by heating with acid and the resulting tetraaminophenyldihydroacridine oxidised to the dyestuff.

The colouring matter forms an orange yellow powder, soluble in water with orange yellow colour, the alcoholic solution exhibits green fluorescence. Caustic soda gives a yellow precipitate, the solution in hydrochloric acid is red, that in concentrated sulphuric acid is yellow with green fluorescence, the colour passes into red on dilution. Orange red shades are produced on cotton mordanted with tannin and antimony.

2-Amino-5-*p*-aminophenylacridine, Chrysaniline or Phosphine,[1]) $C_{19}H_{15}N_3$.

This substance was discovered by Nicholson in the resinous residues left in the manufacture of rosaniline; he obtained the base as a yellow amorphous powder giving

1) Besides being known under the names of Chrysaniline and Phosphine (various marks) essentially the same dye has been known as Patent phosphine GG, G, R, M; Canelle OF; Leather Brown; Philadelphia Yellow; Leather Yellow; Vitolingelb 5 G, R, 2 R; Xanthin; Coréopsine pour cuir &c.

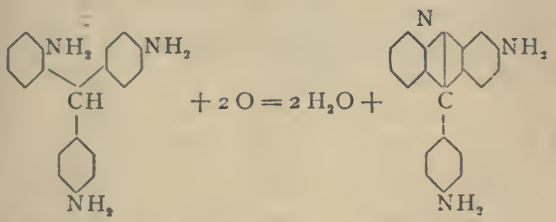
rise to a series of well crystallised salts (*Dingler's J.*, 1863, *168*, 133). Hofmann assigned the formula $C_{20}H_{17}N_3$ to the base (probably the chrysaniline is accompanied by homologues, compare pararosaniline and rosaniline) and described salts with 1 or 2 molecules of hydrochloric or nitric acids (*Compt. rend.*, 1862, *55*, 817; *Jahresb.*, 1862, 346; *Zeitschr. f. Chem.*, 1863, *6*, 33). Other salts such as the picrate, $C_{19}H_{15}N_3, 2\,C_6H_3O_7N_3, H_2O$, and trimethyl and triethyl derivatives formed by the action of alkyl halides, were obtained by Hofmann at a later date (*Ber.*, 1869, *2*, 378). By heating chrysaniline with methyl iodide and methyl alcohol to 100°, red needles of the composition $C_{19}H_{12}(CH_3)_3N_3, 2\,HI$ were produced; from this salt, ammonia removed one molecule of hydriodic acid giving a monacid yellow salt. From this latter compound, the free base was obtained by the action of silver oxide, it was isolated as an amorphous yellow powder, insoluble in water but soluble in alcohol. In the light of our present knowledge, it looks as if the methyl iodide converted one amino into a dimethylamino group and also attached itself to the nitrogen atom of the acridine nucleus.

For the isolation of chrysaniline, advantage may be taken of the sparing solubility of the nitrate in dilute nitric acid. The mother liquor from the preparation of fuchsine is precipitated by sodium chloride and lime, the precipitate dissolved in dilute nitric acid and the nitrate precipitated by the addition of more nitric acid (Graebe and Diehl, *Ber.*, 1879, *12*, 2241).

Impure chrysaniline nitrate was used under the name of phosphine. The free base can be considerably purified by frequent crystallisation from benzene, and is then obtained either as golden yellow needles or leaflets containing one molecule of benzene of crystallisation. O. Fischer and G. Körner completed the purification by boiling the benzene compound with dilute sulphuric acid, precipitating the base by caustic soda and crystallising from dilute (50%) alcohol. It is thus obtained as long golden yellow needles containing two molecules of water.

The anhydrous or benzene free compound melts at 267 to 270°, and may be distilled in small quantities unchanged. The base is scarcely soluble in water and somewhat difficultly in alcohol.

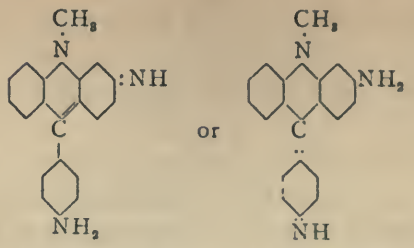
As noted above, chrysaniline usually behaves as a diacid base. That it is a diamino derivative of phenylacridine is evident from the fact that on diazotisation and treatment with alcohol, phenylacridine results (O. Fischer and G. Körner, *Annalen*, 1884, *226*, 184). The last named compound was identified with the product obtained by Bernthsen from diphenylamine and benzoic acid. Additional evidence as to the constitution of chrysaniline is afforded by its formation from *o*, *p*, *p*-triaminotriphenylmethane by heating with arsenic acid to 150—180° (Fischer and Körner, *loc. cit.*, 188).



One amino group in chrysaniline is replaced by hydroxyl when it is heated with hydrochloric acid to 180°.

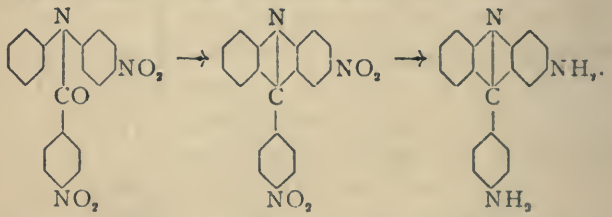
Diacetylchrysaniline. Chrysaniline may be acetylated by heating with $1^1/_2$ times its weight of acetic anhydride for 12 hours to 140—160° (Anschütz, *Ber.*, 1884, *17*, 433). Fischer and Körner found that acetylation could be effected at ordinary pressure, whilst Dunstan and Hewitt (*Trans. Chem. Soc.*, 1906, *89*, 484) by boiling chrysaniline with its own weight of fused sodium acetate and five times its weight of acetic anhydride for four hours under reflux obtained a melt containing both tetraacetyl and diacetyl (m. p. 200°) derivatives.

Diacetylchrysaniline is a monacid base which reacts with one molecule of methyl iodide or sulphate, the resulting acridinium salts on complete hydrolysis furnish an anhydrobase (Dunstan and Hewitt, *loc. cit.*).



Ewer and Pick (D. R. P. 29 142/1884) established a neat synthesis based on the ascertained constitution of the base.

Paranitrobenzoylparanitrodiphenylamine was obtained either by the action of *p*-nitrobenzoyl chloride on *p*-nitrodiphenylamine or by nitrating *p*-nitrobenzoyldiphenylamine. The dinitro-compound was condensed to dinitroacridine and the latter reduced to an isomeride of chrysaniline.



The patent, dated 1st April, 1884, was allowed to lapse in December of the same year, it does not seem to have been of much technical importance.

(1) Preparation of *p*-nitrobenzoyl-*p*-nitrodiphenylamine.

a. Heat equal weights of *p*-nitrodiphenylamine and *p*-nitrobenzoyl chloride to 220° until hydrogen chloride is no longer evolved. Purify by crystallisation from alcohol.

b. Mix 10 parts of *p*-nitrobenzoyldiphenylamine with 5 parts of nitrobenzene, and add $2^1/_2$ parts of nitric acid of s. g. 1.52. The temperature should not rise above 30°. Remove the nitrobenzene in a current of steam.

(2) Condensation to Dinitrophenylacridine.

Heat 10 parts of *p*-nitrobenzoyl-*p*-nitrodiphenylamine with 20 parts of zinc chloride and 3 parts of aluminium chloride for 12 hours in an autoclave at 250—270°. Extract the melt with dilute hydrochloric acid, dissolve the residue

in concentrated sulphuric acid and separate the dinitrophenylacridine by addition of water.

(3) Reduction to Chrysaniline. (Really an isomeride is formed.)

Dinitrophenylacridine is heated for 4 hours in an autoclave at 110° with 10 times its weight of alcoholic ammonium sulphide. Distil off the alcohol and ammonium sulphide, dissolve the residue in dilute hydrochloric acid, pass a strong current of air for 1 hour and filter. Neutralise with lime and salt out with 3 parts of sodium nitrate and sufficient sodium chloride.

Chrysophenol, $C_{19}H_{14}ON_2$, results from the action of 8 parts of concentrated hydrochloric acid on chrysaniline on heating for some hours at 180°. In this case one amino group is replaced by hydroxyl (Claus), the product of the reaction was further examined by O. Fischer and G. Körner (*Annalen,* 1884, *226,* 181). Dunstan and Hewitt (*Trans. Chem. Soc.,* 1906, *89,* 1472) heated for a longer time using, probably, a slightly weaker acid. The crystalline material in the tube, obtained in accordance with the equation

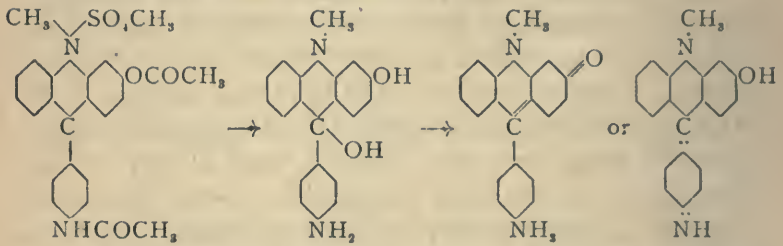
$$C_{19}H_{15}N_3 + H_2O + 2\,HCl = NH_4Cl + C_{19}H_{14}ON_2, HCl,$$

was regarded as a mixture of ammonium chloride and chrysophenol hydrochloride by Claus and Fischer and Körner. On account of the apparent homogeneity of the product, Dunstan and Hewitt consider that it may be a double salt. By solution in water and addition of excess of caustic soda, any residual chrysaniline is precipitated and may be removed by filtration. Chrysophenol is obtained from the filtrate by exact neutralisation with acid and purified by crystallisation from dilute alcohol.

Chrysophenol crystallises in needles (yellowish red, F. & K.; maroon, D. & H.), it melts at 115° (D. & H.). It is difficultly soluble in water, ether and benzene, freely in alcohol and acetone.

Two series of salts may be obtained, viz. with one or two molecules of acid. Chrysophenol dissolves readily in

caustic soda but not in sodium carbonate solution. Diacetyl and dibenzoyl derivatives (the latter was analysed as chromate) may be obtained, the former reacts with methyl sulphate giving an acridinium compound. If the latter be boiled with dilute sulphuric acid, the acetyl groups are removed and on exact neutralisation with alkali, a flocculent precipitate is obtained, soluble both in alkali and acid. On drying, the precipitate becomes very dark, it separates from alcohol as a dark red crystalline deposit, then giving figures agreeing fairly well with the formula $C_{20}H_{16}ON_2$. Probably a carbinol base is first precipitated which furnishes an anhydro-base on drying (Dunstan and Hewitt, *loc. cit.* 1478).



It will be noticed that Dunstan and Hewitt assume that it is the amino group in position 2 and not that in the 5-*p* position which is replaced by hydroxyl when chrysaniline is heated with concentrated hydrochloric acid. This has not been definitely proved, but is rendered extremely probable by the considerable mobility of the amino groups in benzoflavine (L. Cassella and Co., D. R. P. 121 686), and in acridine yellow (Ullmann and Fitzenkam, *Ber.*, 1905, *38*, 3794).

Homologues of Chrysaniline.

The special advantages of chrysaniline (fastness to light and even dyeing of leather) as compared with diaminoacridines containing both amino groups in the acridine nucleus led to attempts to synthesise homologues of chrysaniline in a technical manner. This was accomplished by Meister, Lucius and Brüning (D. R. P. 65 985/1892) by heating *m*-nitraniline and *p*-toluidine with hydrochloric acid and a chloride of iron to a high temperature. The following

directions are given for carrying out the reaction. A mixture of 100 parts of *p*-toluidine, 30 parts of the hydrochloride and 100 parts of ferrous chloride are heated in an iron vessel provided with a stirrer to 190—200°. When the mixture is fused, 30 parts of *m*-nitraniline are gradually added. The reaction then takes place with evolution of heat, care has to be taken not to let the temperature go above 220°. After all the *m*-nitraniline has been added and the temperature fallen somewhat (to about 190—200°), the melt is run into 3000 parts of water and boiled for half-an-hour with addition of 30 parts concentrated hydrochloric acid.

The deep yellow solution is filtered whilst hot from insoluble resin which is again boiled up with 100 parts of water and 3 parts of hydrochloric acid, the solution being filtered and added to that first obtained. The united filtrates are then salted out with 10 parts of zinc chloride and a sufficient amount of sodium chloride.

The crude dyestuff is obtained as a shining resin exhibiting a green metallic lustre, to purify the material it is boiled with 300 parts of water, allowed to cool, filtered from resin and the filtrate fractionally precipitated with dilute sodium carbonate solution, resinous matters coming down first and then fairly pure colouring matter. The correct point is judged by filtering a sample and noting whether a dark resin or a yellow flocculent precipitate is obtained, if the latter point is reached, the resin is separated by filtration and the filtrate precipitated by ammonia.

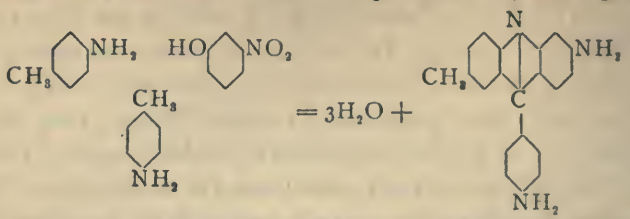
The base is converted into a crystalline salt (large garnet red prisms) by solution in hot 10% nitric acid, the nitrate thus obtained has the composition $C_{20}H_{17}N_3$, HNO_3.

The base (m. p. 230°) is soluble in benzene, alcohol and ether with yellow colour and green fluorescence. Wool, silk and tannined cotton are dyed a reddish yellow.

The chief patent was followed by several subsidiary patents taken out by the same firm, these may be noticed in order.

In D.R.P. 78377/1894, the replacement of the *m*-

nitraniline of the chief patent by *m*-nitrophenol is described, the reaction in this case must be represented by the equation



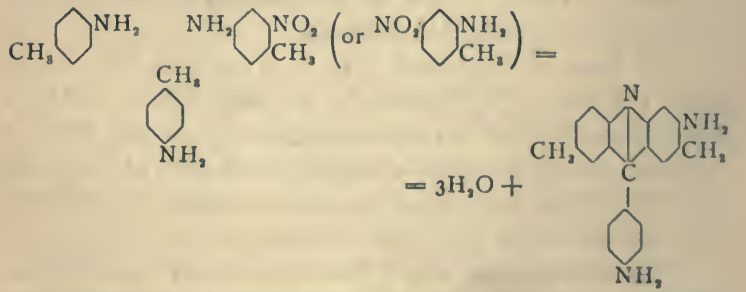
100 parts of *p*-toluidine hydrochloride, 30 parts of *p*-toluidine and 10 parts of ferrous chloride are melted and stirred together. 30 Parts of *m*-nitrophenol are then introduced, care being taken that the temperature of the melt does not much exceed 220°. The further operations are carried out as described in the chief patent.

In D. R. P. 79 263/1894, the use of ethers of *m*-nitrophenol was protected.

$2\,C_7H_9N + C_6H_4(OR)(NO_2) = 2\,H_2O + ROH + C_{20}H_{17}N_3$.

The reaction was carried out exactly as in D. R. P. 78 377, the *m*-nitrophenol being replaced by an equal weight of nitroanisole or nitrophenetole.

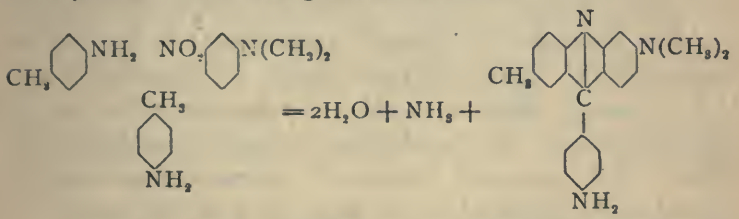
The preparation of a higher homologue, $C_{21}H_{19}N_3$, is described in D. R. P. 79 585/1894, the *m*-nitraniline of the original patent being replaced either by *o*-nitro-*p*-toluidine or by *p*-nitro-*o*-toluidine. Both nitrotoluidines give the same product, the free base melts at 212°.



The quantities of the materials taken and method of carrying out the reaction are as in the preceding patents, but it is considered advantageous to convert the dyestuff eventually into

the sparingly soluble nitrate which crystallises well. The free base shows a magnificent green fluorescence in ethereal solution. The shades on silk, wool and tannined cotton are golden yellow, more on the green side than those obtained with chrysaniline or its first homologue.

D. R. P. 79877/1894 describes the preparation of yellow to orange dyestuffs of the same class, the *m*-nitraniline or analogous compound being replaced by *m*-nitromono- or di-alkylaniline or a homologue. Thus using the quantities and method of preceding patents but replacing the 30 parts of *m*-nitraniline by 30 parts of *m*-nitrodimethylaniline, a colouring matter is obtained, the base of which melts at 230°, is sparingly soluble in water, but readily in alcohol or ether with yellow colour and green fluorescence



Several other dyestuffs prepared by this process correspond to colour bases which are difficultly soluble in water but easily in the usual solvents with yellow colour and green fluorescence. The nitrates are almost insoluble in dilute nitric acid, somewhat difficultly soluble in cold but easily in hot water with yellow or reddish yellow colour. The following table gives the properties of the dyes obtained from *p*-toluidine and various alkylated nitranilines.

Nitro-compound	Colour base, formula	M.P.	Colour on wool, silk or tannined cotton
m-Nitromonomethylaniline . . .	$C_{20}H_{16}N_3(CH_3)$	228°	Reddish yellow.
m-Nitromonoethylaniline	$C_{20}H_{16}N_3(C_2H_5)$	62°	Reddish yellow.
m-Nitrodimethylaniline	$C_{20}H_{15}N_3(CH_3)_2$	230°	Orange.
m-Nitrodiethylaniline	$C_{20}H_{15}N_3(C_2H_5)_2$	82°	Yellowish-red.
p-Nitromonomethyl-*o*-toluidine	$C_{21}H_{18}N_3(CH_3)_2$	83°	Yellow.
p-Nitrodimethyl-*o*-toluidine . .	$C_{21}H_{17}N_3(CH_3)_2$	70°	Reddish-yellow.
o-Nitrodimethyl-*p*-toluidine . .	$C_{21}H_{17}N_3(CH_3)_2$	238°	Yellow (green shade).

According to D. R. P. 81 048/1894, the *m*-nitraniline or *m*-nitrophenol of earlier patents may be replaced by nitro-compounds containing chlorine, bromine or the nitro- or sulphonic-groups in the meta position. For example, a mixture of 100 kilos of *p*-toluidine hydrochloride, 20 kilos of *p*-toluidine, 20 kilos of *p*-nitrotoluenesulphonic acid (CH_3: SO_3H: NO_2 = 1 : 2 : 4) and 10 kilos of ferrous chloride are heated in an iron vessel provided with a stirrer to 180—220°. Formation of colouring matter is finished when no more water distils over. The further working up is carried out as desoribed in the earlier patents.

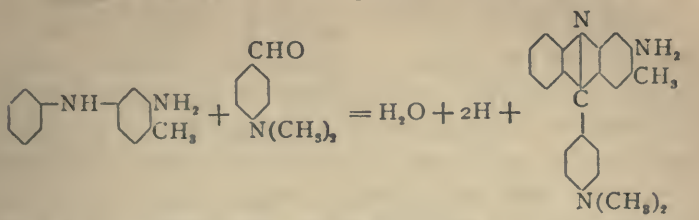
The particular nitro-compounds claimed are *m*-chloro- or bromo-benzene, *m*-nitrobenzenesulphonic acid, *p*-nitrotoluenesulphonic acid, *m*-dinitro-benzene and *m*-dinitroluene.

The Badische Co. (Brit. P. 14 920/1897; U. S. P. of P. Julius and G. Darier 617 340/1897; F. P. 267 848/1897; D. R. P. 94 951/1897) obtained 2 : 5-*p*-diaminoderivatives of 5-phenylacridine by condensing dimethyl-*p*-aminobenzaldehyde with monoaryl derivatives of *m*-toluylenediamine; instead of the expected leuco-bases, the dyestuffs themselves were directly obtained.

Example. Intimately mix 3 kilos of dimethylaminobenzaldehyde and 5 kilos of phenyl-*m*-toluylenediamine hydrochloride and heat in an enamelled vessel to 140—150° until viscous and a sample on cooling solidifies to a brittle mass. Then powder and extract with 200 litres of hot water containing 2.5 kilos of hydrochloric acid (s. g. 1.15), cool, filter, precipitate resinous impurities by a limited amount of saltpeter, separate, cool with ice and salt out. (? as nitrate.) Dry the yellowish red precipitate at 30—40°.

Of the dyestuffs described, that from *p*-aminobenzaldehyde and phenyl-*m*-toluylenediamine is easily soluble and dyes tannined cotton or leather yellow. With *p*-tolyl-*m*-toluylenediamine, a moderately soluble dye giving a reddish yellow is obtained whilst dimethyl-*p*-aminobenzaldehyde condenses with both aryldiamines to give difficultly soluble

dyestuffs producing orange brown shades. The formation of one member of the series is represented by the equation



The nitrates are less soluble than the hydrochlorides, caustic soda gives bright yellow, flocculent precipitates of the bases, soluble in ether with greenish yellow colour and strong green fluorescence.

Resinous impurities are formed in the preceding process and to remedy this defect the reaction may be carried out at a lower temperature using alcohol as a solvent and adding ferric chloride to oxidise the leuco compound formed. (Brit. P. 21 496/1898; U. S. P. of P. Julius and A. Tkatsch 619 577/1898; Addition to F. P. 267 848 dated 5. 8. 1898; D. R. P. 102 072/1898.)

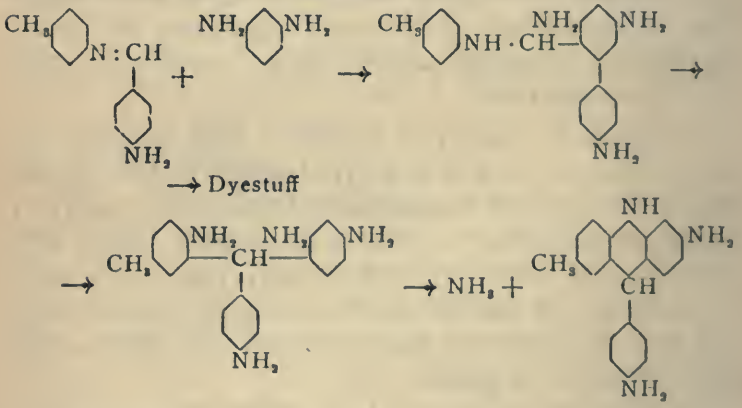
Example 1. Dissolve 5.5 parts of phenyl-*m*-toluylenediamine hydrochloride in 16 parts of alcohol and add a mixture of 2.4 parts of *p*-aminobenzaldehyde and 5 parts of crystallised ferric chloride. Boil 6 hours under reflux, distil off the alcohol, dissolve the residue in 200 parts of hot water and filter. To the still warm filtrate add 5.5 parts of nitric acid (40° Bé.), allow to stand 24 hours and filter off the heavy yellowish red powder.

Example 2. Dissolve 1.5 parts of dimethylaminobenzaldehyde in 4 parts of alcohol, also 2.5 parts of ferric chloride in 4 parts of alcohol, mix the solutions and add gradually to a boiling solution of 2.75 parts of phenyl-*m*-toluylenediamine in 6 parts of alcohol. Boil 5 hours under reflux, distil off the alcohol and take up in 400 parts of boiling water. Cool, allow to stand some hours, filter and precipitate the filtrate by addition of 2.3 parts of hydrochloric acid (19° Bé.) and 54 parts of sodium nitrate solution containing 42.5 parts

of $NaNO_3$ per 100 of solution. Stand 10 hours, filter, press and dry at 40—50°.

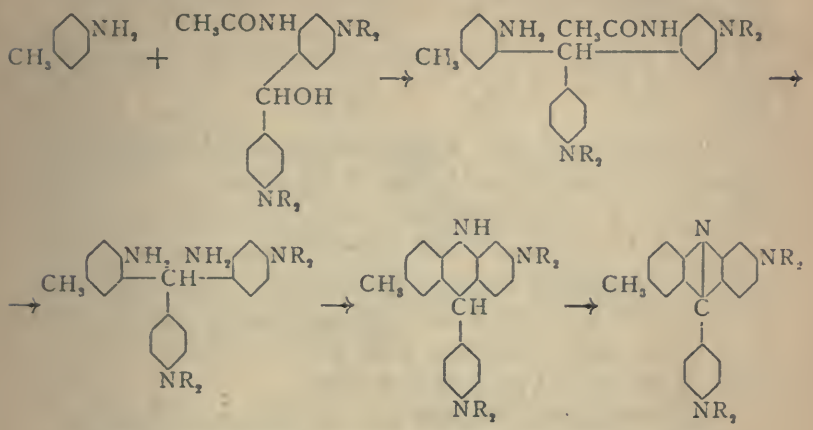
Meister, Lucius and Brüning (D. R. P. 106719/1898) find that the first homologue of chrysaniline, $C_{20}H_{17}N_3$, can be obtained by heating equal weights of *p*-aminobenzylidene-*p*-toluidine, *m*-toluylenediamine hydrochloride and *p*-toluidine slowly to 180° and keeping the melt at this temperature until it becomes thick and shows a metallic reflex. It is then extracted with hot acidified water, the solution filtered and salted out with sodium chloride.

This process, although it leads to the same dyestuffs as those described in earlier patents of the same firm, in some ways more resembles a method described by the Badische Co. considering that the compound of a primary base with an aldehyde is used. The patentees explain the whole reaction as depending on the following intermediate steps.



Bayer & Co. (Brit. P. 16718/1899; F. P. 295142/1899; D. R. P. 114261/1899) obtained alkylated 2:5-*p*-diamino derivatives of phenylacridine by the condensation of *o*-acylamino-*pp*-tetraalkyldiaminobenzhydrols with parasubstituted primary amines, hydrolysis, condensation and final hydrolysis of the leuco-compound. The German Patent was allowed to lapse in November 1902, the interest of the process is sufficient to warrant a slight description. Assuming the Pa-

tentees are right in the way they explain the reactions, the formation of an acridine derivative must be represented by the following scheme. (Compare however D. R. P. 116353.)

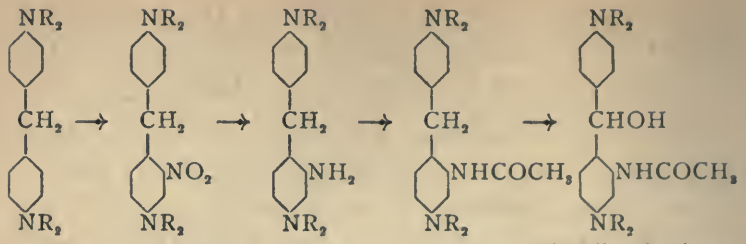


The necessary acylaminotetraalkyldiaminobenzhydrol is obtained by the following steps. (Bayer & Co., Brit. P. 5711/1894; F. P. 239031; D. R. P. 79250/1894.)

I. Tetramethyldiaminodiphenylmethane (25.4 kilos) in sulphuric acid (200 kilos, 66° Bé.) is nitrated below 10° by addition of mixed nitric (10.8 kilos, 40° Bé.) and sulphuric (14.2 kilos, 66° Bé.) acids; the mixture poured on ice and precipitated by alkali.

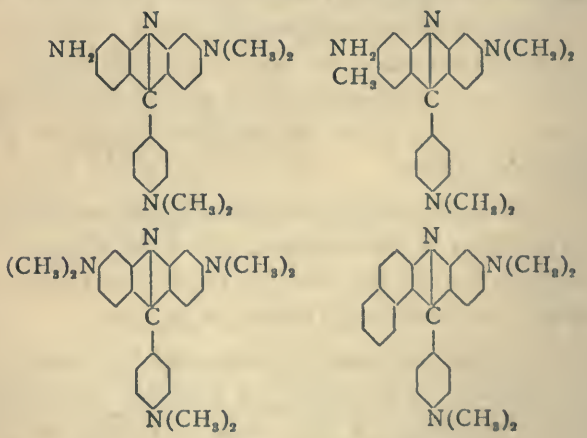
II. *o*-Nitrotetramethyl-*pp*-diaminodiphenylmethane, m. p. 95°, (30 kilos) in hydrochloric acid (100 kilos, 20° Bé.) is treated with ice and zinc dust (20 kilos). The triamino base melts at 96°, its monoacetyl derivative at 136°.

III. Acetylaminotetramethyldiaminodiphenylmethane (31.1 kilos) is dissolved in a mixture of sulphuric (monohydrate, 15 kilos) and acetic (30 per cent, 100 kilos) acids and oxidised by gradual addition of lead peroxide paste (15 per cent, 160 kilos). An intense blue colouration attends the hydrol formation; the lead sulphate is filtered off, the base precipitated by alkali and crystallised from alcohol. M. P. 162°.



In condensing the acetaminotetramethyldiaminobenzhydrol with *p*-toluidine, 32.7 kilos of the former are dissolved in 200 kilos of 10 per cent acetic acid, 11 kilos of *p*-toluidine added and the mixture heated a short time at 50—60°. 100 kilos of hydrochloric acid (36 per cent) are then added and the mixture heated for 5 hours at 135—140°. Finally, oxidation to dyestuff is effected with ferric chloride. The dye gives an orange red on tannined cotton.

The compounds obtained with *m*-phenylenediamine, *m*-toluylenediamine, dimethyl-*m*-phenylenediamine and 2-naphthylamine dye brown, yellowish brown, orange and orange red shades respectively. Their formulae should be



(Compare p. 179) for triaminophenylacridines.)

Very shortly afterwards (Bayer & Co., D. R. P. 116353/1899) claims were made for the preparation of the same dyestuffs directly from the aminotetraalkyldiaminodiphenylmethanes without preparing the acylaminohydrol; thus 27

kilos of aminotetraalkyldiaminodiphenylmethane and 20 kilos of *m*-toluylenediamine hydrochloride are heated to 160°. It is expressly stated that the dyestuff obtained corresponds with the dyestuff of D. R. P. 114261 in all its properties.

This is certainly remarkable, for the product from the hydrol is a leuco base, that from the diphenylmethane compound, a dyestuff.

Friedländer (VI 478) remarks that the dyestuff formation corresponds to the synthesis of a monoaminoacridine derivative from tetraaminoditolylmethane and *p*-toluidine described in D. R. P. 118076.

That the two patents should have been allowed to lapse in 1902 is perhaps significant.

Triamino Derivatives of Phenylacridine. (Rheonine.)

The 2:8:5-*p*-triamino derivatives of phenylacridine contain amino groups both in the chrysaniline and benzoflavine positions, the first compound of the series was discovered by C. Rudolph (Öhler, D. R. P. 45294/1887; U. S. P. 395080). At a later date, 2:8:5-*p*-triaminophenylacridine was prepared by Meister, Lucius and Brüning by the condensation of diaminobenzophenone with *m*-phenylenediamine (D. R. P. 89660/1895), a similar reaction giving rise to alkylated derivatives having been patented by the Badische Co. in the previous year.

Öhler's method (D. R. P. 45294) consisted in condensing *p*-nitrobenzaldehyde with *m*-toluylenediamine, reducing the resulting nitro-tetraamino compound to a penta-amino base, closing the acridine ring with elimination of ammonia and oxidising the leuco base.

I. Heat 21.5 kilos of *p*-nitrobenzaldehyde, 34.7 kilos of *m*-toluylenediamine, 28 kilos of hydrochloric acid (22.5 Bé.) and 100 kilos of 96 per cent alcohol for some hours on the water bath. After cooling, filter off the hydrochloride, wash and dry.

II. Add 26.5 kilos of the nitrophenyltetraaminoditolyl-

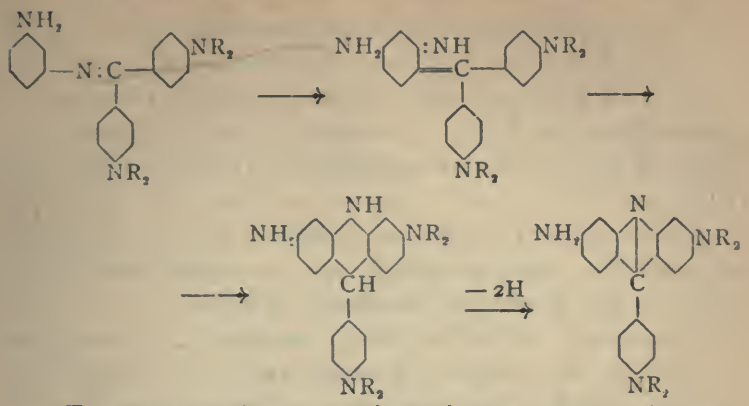
methane hydrochloride gradually to a warm solution of 45 kilos of stannous chloride in 120 kilos of hydrochloric acid (22.5° Bé.). Largely dilute, remove tin with hydrogen sulphide, filter and precipitate the crystalline base by addition of alkali.

III. Heat 10 kilos of pentaaminophenylditolylmethane with 60 kilos of 16 per cent hydrochloric acid for some hours to 160° under pressure. On cooling, the separation from the solution is nearly complete.

IV. To a very dilute aqueous solution of 30 kilos of the dihydro base containing 30 kilos hydrochloric acid and also zinc chloride, add 150 kilos of 20 per cent ferric chloride solution. Filter the precipitate, wash with dilute sodium chloride solution, press and dry. The dyestuff is stated in the patent to completely resemble benzoflavine.

In an additional patent (D. R. P. 45 298/1888), Öhler claims to obtain the same nitrophenyltetraaminoditolylmethane by nitration of the condensation product of benzaldehyde with *m*-toluylenediamine. For this purpose, 10 kilos of the sulphate are dissolved in 50 kilos of sulphuric acid (66° Bé.) and 4.6 kilos of nitrating acid (2 parts sulphuric acid of 66° and 1 part of nitric acid of 44° Bé.) gradually added at 5 to 15°. The reaction mixture is diluted, the nitrotetraamino base precipitated by sodium carbonate solution and purified by solution in dilute acid, filtration and reprecipitation by alkali.

Shortly before the application to protect the condensation of diaminobenzophenone with *m*-diamines, the Badische Co., as mentioned above, patented the production of colouring matters of phosphine type by heating the hydrochlorides of *m*-aminoarylauramines either by themselves or in presence of the hydrochlorides of the corresponding *m*-diamines (Brit. P. 1352/1895; U. S. P. 546 177; F. P. 244 660; D. R. P. 82 989/1894). Compounds of this type were introduced under the name of Rheonine. The reactions involved may possibly be expressed by the scheme



To promote the conversion of the auramine into an acridine derivative, ferric chloride may be added, suitable temperatures lie between 170 and 210°.

To obtain the necessary auramines, several methods may be employed.

I. A tetraalkyldiaminodiphenylmethane is heated with a *m*-diamine in presence of sulphur.

$$CH_2(C_6H_4NR_2)_2 + C_6H_4(NH_2)_2 + 2S$$
$$= 2H_2S + C(:NC_6H_4NH_2)(C_6H_4NR_2)_2.$$

II. Ordinary auramine is heated with a *m*-diamine.

$$C(:NH)(C_6H_4NR_2)_2 + C_6H_4NH_2)_2$$
$$= NH_3 + C(:NC_6H_4NH_2)(C_6H_4NR_2)_2$$

III. The chloride corresponding to a tetraalkyldiaminobenzophenone reacts with a *m*-diamine.

$$CCl_2(C_6H_4NR_2)_2 + C_6H_4(NH_2)_2$$
$$= 2HCl + C(:NC_6H_4NH_2)(C_6H_4NR_2)_2.$$

IV. A tetraalkyldiaminobeenzophenone is heated with the hydrochloride of a *m*-diamine.

$$CO(C_6H_4NR_2)_2 + C_6H_4(NH_2)_2$$
$$= H_2O + C(:NC_6H_4NH_2)(C_6H_4NR_2)_2.$$

The following example for auramine preparation may be taken.

Heat 26 parts of tetrametlyldiaminobenzophenone and 18 parts of *m*-phenylenediamine dihydrochloride for 4 to

6 hours to 130—140° with continuous stirring. After cooling, extract the solidified melt with warm water, filter and precipitate the auramine with sodium chloride. Filter off, press, dry and powder. For other derivatives of benzophenone or other diamines, the corresponding equivalent quantities are taken.

It should be kept in mind that these auramine bases are unstable and easily resolved into the substituted benzophenone and diamine by the action of acids.

In order to convert these auramines into acridine derivatives, their isolation is unnecessary, the reaction mass containing such a compound may be heated for some hours to 180—205°, with or without the addition of more *m*-diamine or its hydrochloride and zinc chloride. The formation of the acridine dyestuff is illustrated in the patent.

Example 1. 100 parts of *m*-aminophenyl- (or tolyl-) auramine hydrochloride is heated in an enamelled vessel in an oil bath to 190—210° for about 5 hours. The melt, originally orange brown in colour, becomes darker and assumes a greenish metallic lustre, setting on cooling to a brittle mass. The melt is dissolved in 2000 parts of hot water acidified with 50 parts of hydrochloric acid (20° Bé.), filtered and precipitated with zinc and sodium chlorides. For further purification, the precipitate is dissolved in 1000 parts of hot water, 200 parts of hydrochloric acid being addeed, allowed to cool, poured off from separated resinous matter, neutralised with caustic soda and precipitated with sodium chloride. Finally, the product is melted on the water bath with 50 parts of hydrochloric acid, evaporated to dryness and powdered.

Example 2. 40 parts of tetramethyldiaminobenzophenone, 27 parts of *m*-phenylenediamine dihydrochloride and 9 parts of *m*-phenylenediamine are heated in a covered enamelled vessel for 4 to 6 hours under continuous stirring, the oil bath surrounding the vessel being maintained at 195 to 210°. An auramine is first formed, this gradually disappears and the completion of formation of the acridine dye-

stuff is found by taking samples of the melt and dissolving in dilute hydrochloric acid. Whilst the auramine is decolourised by this treatment (resolution into ketone and base) the acridine dyestuff is stable, so that if the sample when dissolved in dilute hydrochloric acid and heated shows no diminution in intensity of colour, the formation of the acridine dyestuff may be taken as finished. The solidified melt is dissolved in 400 parts of boiling water with the addition of 20 parts of hydrochloric acid, cooled, filtered and salted out with zinc and sodium chlorides. To obtain an easily soluble salt, the precipitate is treated with 20 parts of hydrochloric acid as in Example 1.

Example 3. 48 parts of tetramethyldiaminobenzophenone, 27 parts of *m*-phenylenediamine hydrochloride, 9 parts of *m*-phenylenediamine and 25 parts of zinc chloride are heated for 4 to 6 hours at 190—205°. The melt is treated in the same way as in Example 2.

The dyestuffs thus obtained form brown or brown black powders with a feeble metallic lustre, they are readily soluble in water with a brownish yellow colour and green fluorescence and dye tannined cotton or leather brownish yellow.

Rheonine (A, AL, N, Badische Co.) is a brown powder; it is the dye obtained from tetramethyldiaminobenzophenone and *m*-phenylenediamine. Both aqueous and alcoholic solutions are brownish yellow and fluoresce green, caustic soda gives a bright brown precipitate. The solution in hydrochloric acid is brownish red and has an orange red fluorescence, that in concentrated sulphuric acid is brown and fluoresces green, on dilution the colour turns brownish red and the fluorescence to orange red.

Besides being used for the production of brownish yellow shades on cotton (tannin and antimony mordant), silk and leather, rheonine is also used in cotton printing. The shades given by this dye are fast to light and washing.

The process of Meister, Lucius and Brüning (D. R. P. 89660/1895) differs from the foregoing in that diaminobenzophenone or its diacetyl (not tetraalkyl) derivative is employed.

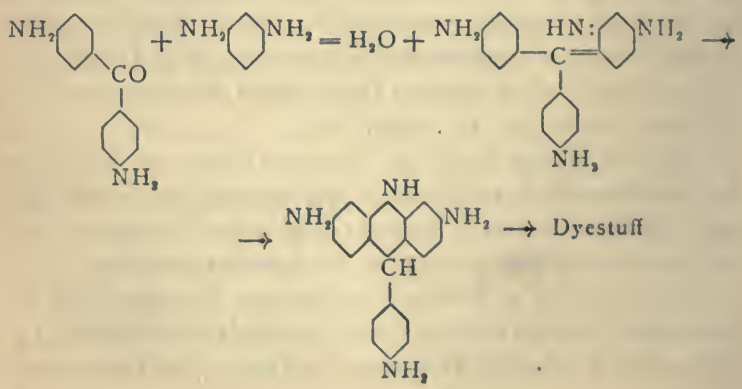
Further, whilst a compound similar to aminobenzoflavine is formed on heating with a *m*-diamine, this is to be considered as an intermediate product, for on further heating, a more brownish yellow dye is produced.

Example. 61 parts of diaminobenzophenone and 54 parts of *m*-phenylenediamine hydrochloride are melted together at 180°. The fusion is facilitated by adding one-seventh of its weight of free base to the *m*-phenylenediamine hydrochloride.

The melt is kept for two hours at 180—190° with continuous stirring, the temperature is then raised for several hours to 220—230°. After cooling, the resulting brittle, brown mass is dissolved in 1000 parts of hot water with addition of hydrochloric acid. The solution is cooled, filtered and salted out with zinc chloride. The resultant mass is dissolved in warm dilute hydrochloric acid, evaporated to dryness and the residue powdered.

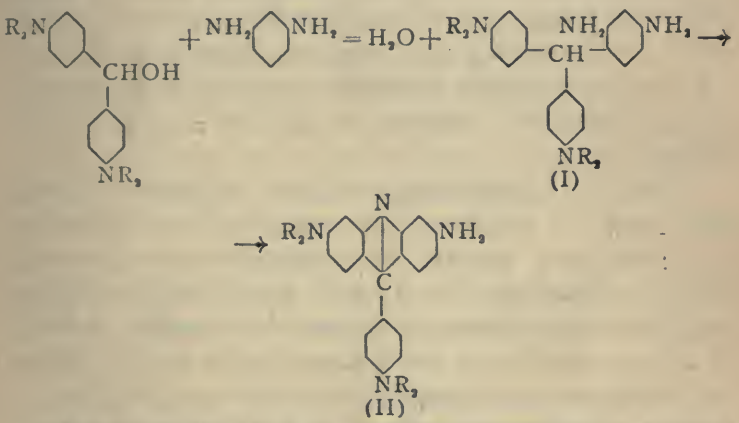
If diacetyldiaminobenzophenone is employed, the acetyl derivative of the dye is obtained, this is hydrolysed by boiling with acid.

The patent mentions that if the heating of the melt be stopped after half-an-hour, a yellow dyestuff having the properties of aminobenzoflavine may be isolated. Evidently the first stages in the process may be represented by the scheme



It is pointed out with some care that the dyestuff differs from that produced by the Badische Co. (D. R. P. 82989) in its greater covering power and yellower shade.

In a further patent of the Badische Co. (D. R. P. 85199/1895) the condensation of tetraalkyldiaminobenzhydrols with *m*-diamines is described, the products obtained being converted on long heating into dyestuffs having the properties of those described in D. R. P. 82989. In this case, the course of the reaction can be expressed by the following scheme, in which it is understood that oxidation somehow takes place.



For example, 18 parts of *m*-phenylenediamine dihydrochloride dissolved in 50 parts of water are added to 27 parts of tetramethyldiaminobenzhydrol dissolved in 25 parts of hydrochloric acid (20° Bé.) and 130 parts of water. After two or three hours on the water bath, the condensation is complete, the liquid is diluted, excess of acid neutralised with sodium carbonate and the base precipitated with sodium acetate, filtered, washed and dried.

The product (formula I above) has the properties of a leuco compound and yields on oxidation a bluish violet colouring matter of the rosaniline series.

To obtain the acridine dye, 10 parts of the condensation product as free base and 10 parts which have been converted into hydrochloride by evaporation with the necessary amount

of hydrochloric acid, are mixed with 5 parts of *m*-phenylenediamine dihydrochloride and heated for 5 to 6 hours to 160—170° with continuous stirring. The melt is dissolved in 100 parts of hot water, 40 parts of hydrochloric acid (20° Bé.) being gradually added, allowed to cool, filtered and the base precipitated with sodium carbonate. By means of excess of hydrochloric acid, the base is converted into its hydrochloride and is then evaporated to dryness.

In a further example, 27 parts of tetramethyldiaminobenzhydrol, 6 parts of *m*-phenylenediamine and 18 parts of its hydrochloride are stirred for one to two hours at 100 to 120°. The temperature is then kept for 5 or 6 hours at 160 to 170°, the resulting melt being dissolved in 250 parts of hot water with gradual addition of 100 parts of hydrochloric acid (20° Bé.). The further working up is as in the last example.

The A. G. f. Anilinfabrikation (D. R. P. 288841/1914) has made use of the thio compounds obtainable from *m*-diamines by the action of sulphur. These thio-derivatives were produced by Kalle and Co. (D. R. P. 86096/1894) by boiling *m*-diamines with alcohol and sulphur. For example, 10.8 kilos of *m*-phenylenediamine are dissolved in 80 kilos of alcohol and boiled for 5 or 6 hours under reflux with 6.4 kilos of sulphur, sulphuretted hydrogen being meanwhile evolved. The alcohol is then distilled off, the residue dissolved in dilute hydrochloric acid, filtered and precipitated with sodium carbonate. After crystallisation from a mixture of alcohol and acetone, greenish yellow, prismatic needles melting at about 73° are obtained. The corresponding compound from *m*-toluylenediamine melts at 145°.

The conversion of such thio-derivatives into acridine dyestuffs is described in D. R. P. 288841.

Example 1. Liquefy the product obtained from 12.5 parts of *m*-toluylenediamine and 6.4 parts of sulphur, add 25.4 parts of tetramethyldiaminodiphenylmethane and 5.5 parts of powdered ammonium chloride and raise the temperature in the course of the reaction from about 120° to about 160 to

180°. Sulphuretted hydrogen and ammonia escape, when the evolution of the latter gas ceases, the formation of the hydrochloride of the acridine dye is taken as complete.

The liquid melt is then stirred with dilute hydrochloric acid, care being taken that the reaction is feebly acid at the end of the operation. Addition of solid sodium chloride and zinc chloride solution salts out a resinous mass which is dissolved in warm water, filtered, salted out with sodium and zinc chlorides and dried. The dyestuff gives strong orange yellow shades on leather.

Example 2. 22.6 parts of *p, p'*-diaminodi-*o*-tolylmethane, 12.5 parts of *m*-toluylenediamine, 6.4 parts of sulphur and 5.5 parts of ammonium chloride are stirred and heated. All evolution of sulphuretted hydrogen is generally finished after 2 to 4 hours at 140°, the temperature is then raised to 170 to 180°, ammonia escapes and when no more is evolved, the temperature raised from 180 to 200° and kept at this for a short time. The melt is worked up as in example 1, the dyestuff gives an even yellow on leather.

Example 3. 25.4 parts of tetramethyldiaminodiphenylmethane, 13.6 parts of dimethyl-*m*-phenylenediamine, 6.4 parts of sulphur and 5.5 parts of ammonium chloride are treated as in example 2, the resulting dyestuff gives brownish red shades on leather.

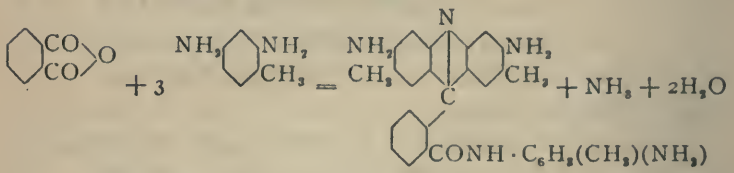
p, p'-Diaminodi-*m*-methoxydiphenylmethane is also mentioned as a component, whilst it is stated that good olive shades are obtained in condensing *p,p'*-diaminodi-*o*-tolylmethane with 2:4-diamino-1-methoxybenzene.

Derivatives of 5-o-carboxyphenylacridine.

Comparatively little has been done with these substances. The Badische Co. (D. R. P. 73 334/1893) converted the 2:8-diamino-5-*o*-carboxyphenylacridine of R. Meyer and O. Oppelt (*Ber.*, 1888, *21*, 3576) into esters, Friedländer (III, 297) describes the operation as being of no especial technical interest. The methods described in the patent consist in heating with an alcohol and a mineral acid, or by heating the

compound directly with an alkyl halide. Compare D. R. PP. 49850, 61867; also Friedländer II, 110.

By the direct condensation of phthalic anhydride and *m*-diamines, one molecule of the former reacts with three molecules of the latter, the product being a derivative of an amide of 5-*o*-carboxyphenylacridine.



The Badische Co. (Brit. P. 11711/1902; U.S.P. of Müller and Schmid, 716264/1902; F. P. 321393/1902; D.R.P. 141356/1902) utilise the reaction, subsequently removing the third molecule of *m*-diamine by acid hydrolysis; in this way homologues of the diaminocarboxyphenylacridine of Meyer and Oppelt are produced.

Example 1. 25 parts of monophthalyltoluylenediamine (m. p. 192°), 18 parts of *m*-toluylenediamine base, 10 parts of its hydrochloride and 14 parts of zinc chloride are heated 4 to 6 hours at 200—210°. After cooling, the mass is powdered, zinc chloride dissolved out at 50—60° by 400 parts of water feebly acidified with hydrochloric acid; the residue is brought into solution by boiling with 1000 parts of water and 30 parts of hydrochloric acid (20° Bé.), the solution filtered and salted out.

At this stage, one is dealing with the aminotoluidide whose formula is given in the above equation, hydrolysis with formation of diaminodimethylphenylacridinecarboxylic acid can be effected by boiling for many hours with five times the weight of concentrated hydrochloric acid.

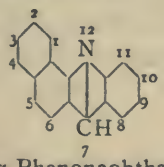
Example 2. A dyestuff, identical with that of the first example, is obtained by heating 30 parts of phthalic anhydride, 48 parts of *m*-toluylenediamine and 47 parts of its hydrochloride with continual stirring. Steam begins to come off at 145°, the temperature is raised to 200—210° and after

four or five hours the formation of dyestuff is finished. The cooled melt is powdered, dissolved in 2000 parts of boiling water and 60 parts of hydrochloric acid, filtered and salted out.

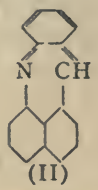
CHAPTER IX

PHENONAPHTHACRIDINES

In these compounds, the central ring containing the nitrogen atom is situated between a benzene nucleus on the one hand and a naphthalene nucleus on the other. Derived from 1-naphthylamine we have only one possibility of a true naphthacridine (I), though it is conceivable that the nitrogen containing ring might be attached to the naphthalene nucleus in the peri position (II)



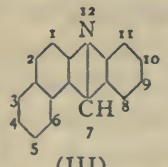
2:1 or α-Phenonaphthacridine
(I)



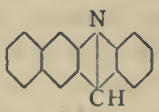
(II)

The latter would, however, involve a seven-membered ring and such a compound and its derivatives could not be looked on as true acridines.

From 2-naphthylamine, two true naphthacridines (III and IV) are derivable, most of the compounds which have been described are derived from structure III.

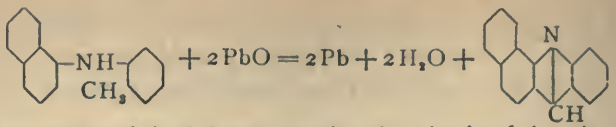


(III)
2:1 or α-Phenonaphthacridine.

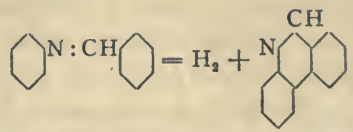


(IV)

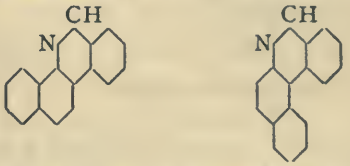
α-Phenonaphthacridine is obtained by the action of lead oxide on *o*-tolyl-α-naphthylamine (Ullmann and A. La Torre, *Ber.*, 1904, *37*, 2924).



The compound had been previously obtained by A. Pictet and S. Ehrlich (*Annalen*, 1891, *266*, 155) who described it as α-chrysidine (m. p. 108°). Pictet and Ankersmit (*Bull. soc. chim.*, 1891, III, *5*, 138) had found that when benzylideneaniline vapour was passed through a red hot tube, hydrogen was eliminated and phenanthridine (m. p. 104°), an isomeride of acridine, was produced.



On extending the reaction to naphthylamine compounds, similar elimination of a molecule of hydrogen occured, and, not unnaturally, Pictet and Ehrlich concluded that the resulting α- and β-"chrysidines" possessed the respective structures



Ullmann and La Torre identified the compounds as α- and β-phenonaphthacridines and gave methods for their preparation.

In preparing α-phenonaphthacridine, *o*-tolyl-1-naphthylamine is required, this was obtained by Friedländer (*Ber.*, 1883, *16*, 2082) by heating 1-naphthol with *o*-toluidine and calcium chloride under pressure. Ullmann and La Torre describe a simpler preparation, heating the components, viz, 25 grams of molten 1-naphthol and 22 grams of *o*-toluidine hydrochloride, in an open vessel for 4 to 5 hours at 240°. Steam is evolved, when the evolution of hydrochloric acid ceases, the brown mass is cooled, caustic soda added and excess of toluidine removed in a current of steam. The remaining oily mass is extracted by ether, on distillation of

the ethereal solution the oily fraction boiling between 395 and 405° is taken as tolylnaphthylamine.

3 grams of the secondary base and 30 grams of lead oxide are heated in a small distilling flask by a metal bath for an hour and then distilled. Without separating water and oil, the distillate is dissolved in alcohol and alcoholic picric acid added. Naphthacridine picrate separates as a yellow crystalline powder, by recrystallisation from alcohol it is obtained with an unchanged melting point, 226—229° (decomp.).

By decomposition of the picrate with dilute caustic soda, an oil is obtained which soon sets to a crystalline mass, on recrystallisation from a mixture of benzene and ligroin it forms long shining needles, m. p. 108°.

The solution in glacial acetic acid is yellow and exhibits a green fluorescence, dilution with water precipitates the base. The solutions in ether and benzene are colourless and show a feeble blue fluorescence, whilst the solution in concentrated sulphuric acid is intensely yellow and fluoresces green.

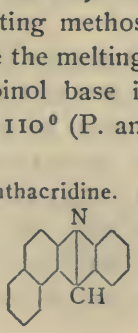
Hydrochloride, m. p. 244° (U. and La T.), about 210° (P. and E.).

Nitrate. m. p. 188—189° (U. and La T.), 155° (P. and E.).

The *platinichloride* and other salts have also been described.

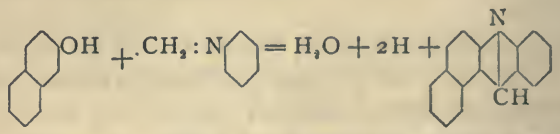
The *methiodide,* $C_{17}H_{11}N \cdot CH_3I$, is stated by Pictet and Ehrlich to melt at 108°; Ullmann and La Torre acted on phenonaphthacridine with methyl sulphate and precipitated the solution of the resulting methosulphate with potassium iodide solution. They give the melting point of the methiodide as 262—263°. The carbinol base is described as forming colourless needles, m. p. 110° (P. and E., no m. p. recorded by U. and La T.).

(1 : 2) or *β*-Phenonnaphthacridine.



This compound was first obtained by Pictet and Ehrlich *(loc. cit.)* and described as β-"chrysidine"; its true constitution was recognised by Ullmann and La Torre in 1904. Meanwhile-Ullmann and co-workers had already synthesised this compound or homologues by various methods; of these, several may be mentioned.

1. From formaldehyde, 2-naphthol and aniline (Ullmann and Nalband, *Ber.*, 1900, *33*, 910; see also Ullmann and La Torre, *Ber.*, 1904, *37*, 2922).

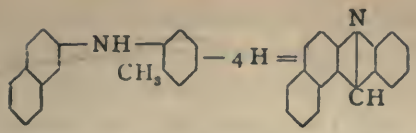


In Ullmann's patent (D. R. P. 123 260/1898, lapsed in 1901) the following directions are given for the preparation of β-phenonaphthacridine (m. p. 129.5°). 10 kilos of 2-naphthol, 8 kilos of aniline and 1 kilo of trioxymethylene are heated to 160°, steam is evolved and the mass becomes yellowish red. On distillation, aniline and the naphthol first pass over, then the β-phenonaphthacridine above 400°. The naphthol is removed by dilute caustic soda and the residue crystallised from a mixture of benzene and ligroin.

o-Toluidine gives a mono- (m. p. 143°) and *m*-xylidine a di-methyl (m. p. 152°) phenonaphthacridine. One of the few aminoacridines containing the amino group in the para position to the *meso*-nitrogen atom was obtained by fusing 5 kilos of monoacetyl-anhydroformaldehyde-*p*-phenylenediamine with 12 kilos of 2-naphthol at 150—180° and subsequently hydrolysing.

2. By heating *o*-aminobenzyl alcohol with $1^1/_2$ molecular proportions of 2-naphthol. About 185° steam is evolved briskly, after about an hour at 200—210° the reaction is finished. The product is isolated from its alcoholic solution as the picrate, liberated by alkali and crystallised from alcohol (Ullmann and C. Bäzner, *Ber.*, 1902, *35*, 2670).

3. By the action of sulphur or lead oxide on *o*-tolyl-2-naphthylamine (Ullmann and La Torre, *Ber.*, 1904, *37*, 2926).



The requisite *o*-tolyl-2-naphthylamine can be prepared by the condensation of 15 grams of *o*-toluidine hydrochloride with 14 grams of 2-naphthol, following the method described in preparing *o*-tolyl-1-naphthylamine. 15.7 grams distilled at 400—405°.

The condensation to *β*-phenonaphthacridine may be effected in two ways

(a) 4 grams of the *o*-tolyl-2-naphthylamine and 1.14 grams of sulphur are heated to 220°, sulphuretted hydrogen is evolved and the reaction finished in four hours. Extraction with dilute acetic and hydrochloric acids gives a solution from which the hydrochloride crystallises; this is decomposed by alkali and the base crystallised from a mixture of benzene and ligroin. M. p. 131°; the compound is identical with the *β*-chrysidine of Pictet and Ehrlich; yield about 25 per cent of the theory.

(b) 45 per cent of the theoretical amount is obtained by heating with lead oxide (4 and 40 grams respectively) as in the case of *α*-phenonaphthacridine, and purifying by means of the picrate (m. p. 260°, sinters at 255°) which is crystallised from nitrobenzene.

Hydrochloride, m. p. about 220° (P. and E.).

Nitrate, m. p. 187° (P. and E.), 210° (U. and La T.).

Methiodide, m. p. 237° (P. and E.), 264° (U. and La T.).

The corresponding carbinol base crystallises in colourless needles and melts at 133° according to Pictet and Ehrlich; Ullmann and La Torre describe it as small, pink, glittering crystals which darken on heating, sinter at 195° and melt at 206—207°.

Homologues of 1:2-Phenonaphthacridine.

Of the various methods given for the preparation of *β*-phenonaphthacridine, the first one using aniline, formal-

dehyde and 2-naphthol is apparently not as satisfactory in preparing the phenonaphthacridine itself, though when aniline is replaced by *p*-toluidine, good yields of its methyl derivative (m. p. 158°, b. p. 460°) may be obtained (Ullmann and Naef, *Ber.*, 1900, *33*, 905).

The reaction between *p*-toluidine, 2-naphthol and formaldehyde may be carried out in either of four ways.

(a) Formaldehyde and 2-naphthol are condensed and the product caused to react with *p*-toluidine.

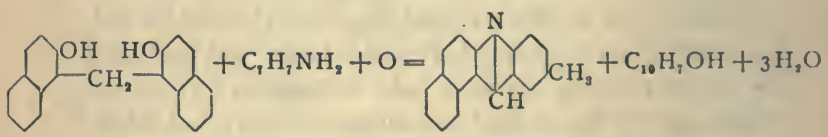
(b) A mixture of 2-naphthol, *p*-toluidine and formaldehyde (as trioxymethylene) is employed.

(c) Methylenedi-*p*-tolyldimide (Eberhardt and Welter, *Ber.*, 1894, *27*, 1808) reacts with 2-naphthol.

(d) Anhydroformaldehyde-*p*-toluidine and 2-naphthol are heated together.

In all these cases, dihydromethylphenonaphthacridine should be produced; in practice, this is accompanied by the acridine itself which may form the chief product if the oxidation has proceeded to any considerable extent.

(a) Formaldehyde is first condensed with 2-naphthol to 2:2'-dihydroxy-1:1'-dinaphthylmethane, and 5 parts of the product are gradually added to a melt of 3.5 parts of *p*-toluidine hydrochloride and 1 part of *p*-toluidine at 120°. On heating gradually, steam is evolved at 150—160°; to complete the reaction



the mixture is heated for a further half hour at 200—220°.

In Ullmann's patent (D. R. P. 119573/1898, lapsed in 1901) 30 parts of dihydroxydinaphthylmethane and 10 parts each of *p*-toluidine and its hydrochloride are heated to about 200°, the melt made alkaline, *p*-toluidine removed in a current of steam and the methylphenonaphthacridine (m. p. 158°) purified through the sparingly soluble nitrate.

(b) Heat 14.4 parts of 2-naphthol and 10.7 parts of *p*-toluidine to 150° and gradually add 4 parts of trioxymethylene. When the chief reaction is over, heat slowly to 200° and finally for 20 minutes to 220—230°. Distil the product and purify the fraction of b. p. 300—460° (17.5 grams) by washing with caustic soda and crystallisation (12.5 grams) (*Ber.*, 1900, *33*, 908).

In D. R. P. 117472/1898 (lapsed in 1901) the quantities given are 16 kilos of the naphthol, 11 kilos of *p*-toluidine and 2 kilos of trioxymethylene.

(c) In this case, methylenedi-*p*-tolyldiimide is added to an equal weight of 2-naphthol at 120° (or 150°) and the temperature raised to 180—200° (*loc. cit.*, 909; D. R. P. 117472).

$$C_{10}H_7OH + CH_2(NHC_6H_4CH_3)_2 + O = 2H_2O + CH_3C_6H_4NH_2 + C_{13}H_{13}N.$$

Eberhardt and Welter (*Ber.*, 1894, *27*, 1808) obtained methylenedi-*p*-tolyldiimide (m. p. 86°) by slowly adding 77 parts of 39 per cent formaldehyde to a warm clear solution of *p*-toluidine (214 parts), alcohol (50 parts) and caustic potash (30 to 50 parts). After some hours warming, the solution was cooled, the product collected and crystallised from alcohol.

(d) Heat 2-naphthol with half its weight (*loc. cit*, 909; D. R. P. 117472 specifies its own weight) of anhydroformaldehyde-*p*-toluidine and finally distil the product. The yield is described as poor (*loc. cit.*) whilst the description in the patent is very meagre.

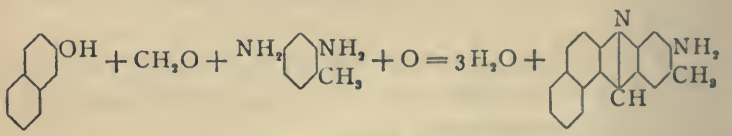
Well crystallised hydrochloride, nitrate and picrate as well as a monosulphonic acid are described.

Amino-derivatives of 1:2-Phenonaphthacridine.

10-*Amino*-1:2-*Phenonaphthacridine.* Comparatively little is known of this compound, Friedländer (VI, 483) states that it may be obtained according to D. R. P. 130943 if *m*-phenylenediamine is used in place of *m*-toluylenediamine.

9-Methyl-10-amino-1 : 2-phenonaphthacridine.

Various syntheses of this compound are described by Ullmann and Näf (*Ber.*, 1900, *33*, 912), the net result in each case being the condensation of equimolecular quantities of *m*-toluylenediamine, formaldehyde and 2-naphthol.



(a) Heat 2 parts of dihydroxydinaphthylmethane and 1 part each of *m*-toluylenediamine and its hydrochloride slowly to 160° and for a short time to 200°. (Time of operation, 45 minutes.) From the hot alcoholic solution of the melt, the dihydro-base (m. p. about 195°) separates on cooling, some of the colour base (m. p. 245° corr.) may be obtained from the mother liquor. In D. R. P. 104748/1898, the proportions given are 3 : 1 : 1, or otherwise, *m*-toluylenediamine itself with double its weight of dihydroxydinaphthylmethane.

(b) 5 parts each of 2-naphthol and *m*-toluylenediamine are heated to 150° and 1 part of trioxymethylene added.

(c) Heat 2.8 parts of 2-naphthol, 0.8 part of sodium acetate and 1.4 part of anhydroformaldehyde-*m*-toluylenediamine slowly to 160—180°. Ullmann's patent (D. R. P. 130943/1898) for this variation of the process lapsed in 1902.

P. Julius and W. Reess (U. S. P. 644324/1899 transferred to the Badische Co.), describe the reaction between 2-naphthol and anhydroformaldehyde-*m*-toluylenediamine in presence of ferric chloride. The anhydroformaldehyde-toluylenediamine was regarded as diaminotolyl alcohol; this view was erroneous for Ullmann and Näf showed by analysis that the compound had the formula $C_8H_{10}N_2$ (*loc. cit.*).

(d) 80 to 85 per cent of the theoretical yield of 9-methyl-10-amino-1 : 2-phenonaphthacridine may be obtained by the action of 2-naphthol on tetraaminoditolylmethane

$$C_{10}H_7OH + CH_2[C_6H_2(CH_3)(NH_2)_2]_2 + O$$
$$= 2H_2O + C_6H_3(CH_3)(NH_2)_2 + C_{18}H_{16}N_2$$

(Ullmann, *loc. cit.*, 916; D. R. P. 104667/1898; see also A.-G. f. Anilinfabr., Brit. PP. 16474, 16475/1898; F. PP. 280164, 280372/1898; 292151/1899).

The following method is described in D. R. P. 104667.

25 parts of tetraaminoditolylmethane are added in portions to 20 parts of 2-naphthol at 150°. Steam is evolved; when the melt is quiet, the temperature is raised for a short time to 200°. After cooling, the mass is treated with alcohol, this leaves the leuco-compound undissolved, whilst if the alcoholic solution is strongly concentrated and treated with caustic soda, the colour base is precipitated. The leuco compound can be oxidised to colouring matter by passage of air through a solution in acetic acid, or by grinding with hydrochloric acid, adding ferric chloride and salting out.

The isolation of the leuco base may be avoided by extracting the melt several times with boiling, very dilute, caustic soda solution, dissolving the residue in hydrochloric acid, adding ferric chloride, filtering and salting out.

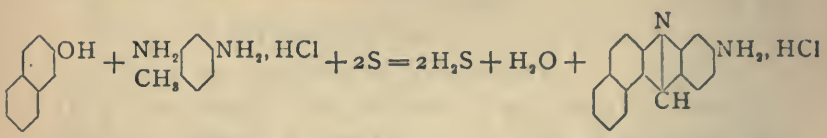
(e) The condensation of methylenediaminoditolyldiimide with 2-naphthol is also described by Ullmann (D. R. P. 130721).

9-Methyl-10-amino-1:2-phenonaphthacridine is easily soluble in hot alcohol with orange yellow colour and yellowish green fluorescence, it dissolves with difficulty in ether, benzene and toluene with yellow colour and bluish green fluorescence. Concentrated sulphuric acid gives a yellowish green solution with a very beautiful green fluorescence, the colour becomes yellow on dilution.

The salts with mineral acids are red, the hydrochloride is easily soluble and dyes tannined cotton orange yellow.

The *acetyl derivative*, obtained by boiling the dye (1 part) with acetic anhydride (2.3 parts) and anhydrous sodium acetate (0.5 part) for 2 to 3 hours, is almost insoluble in the ordinary solvents; it crystallises from nitrobenzene in almost colourless prisms melting at 320—321° (*corr.*).

J. R. Geigy (D. R. P. 130360/1901) uses the methyl group of the toluylenediamine to furnish the extra carbon atom of the pyridine ring; as a result, the lower homologue, aminophenonaphthacridine, is formed.



Example 1. Heat 31 kilos of *m*-toluylenediamine, 36 kilos of 2-naphthol, 16 kilos of sulphur and 20 kilos of zinc chloride with continual stirring, keeping the oil bath at 180 to 190° as long as sulphuretted hydrogen is evolved. After cooling, grind up the melt and boil with 1000 litres of water and 30 kilos of hydrochloric acid, filter, precipitate with caustic soda, collect and wash the precipitate, dissolve in hydrochloric acid and evaporate.

Example 2. Use 40 kilos of *m*-toluylenediamine hydrochloride, 100 kilos of 2-naphthol and 16 kilos of sulphur.

The patent states that 2-naphthylamine can be used in place of 2-naphthol and further, that the isomeride of the *α*-series (from 1-naphthol or 1-naphthylamine) is extremely similar and scarcely differs in shade.

Friedländer (VI, 483) states that the yields obtained by this process are small.

Alkylamino-derivatives of Phenonaphthacridine

If 9-methyl-10-amino-1 : 2-phenonaphthacridine is heated under pressure with an alcohol and a mineral acid, hydrogen of the amino group is replaced by alkyl. The A.-G. für Anilinfabrikation applied this method to the dyestuffs described in D. R. PP. 104667, 104748 and 108273, patenting the process (Brit. P. 1820/1900; D. R. P. 117065/1899; F. P. 296628/1900).

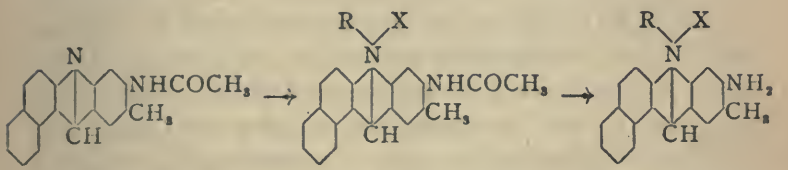
Example 1. Heat 10 kilos of methylaminophenonaphthacridine, 24 kilos of methyl alcohol and 12 kilos of concentrated (crude) hydrochloric acid for several hours to 160

to 170° under pressure. After cooling, distil off the alcohol, dissolve in water and salt out with sodium chloride.

Example 2. Heat 10 kilos of methylaminophenonaphthacridine, 10 kilos of ethyl bromide and 20 litres of alcohol for some hours to about 180° and work up the product as described in example 1.

Acridinium Compounds from aminophenonaphthacridine

Since the fastness to alkali of many acridine dyestuffs leaves much to be desired, Ullmann and Näf (*Ber.*, 1900, *33*, 2470) prepared acridinium compounds from 9-methyl-10-amino-1:2-phenonaphthacridine. The amino group was protected by acetylation, an alkyl ester of a mineral acid added at the *meso*-nitrogen atom and the resulting compound hydrolysed.



In the first experiment (*loc. cit.*, 2472) the acetyl derivative (1.5 gram), methyl iodide (2 cc.) and chloroform (8 cc.) were heated for 8 hours at 140—150°. More satisfactory results were obtained by adding 1 gram of methyl sulphate to 2 grams of the acetyl derivative in 20 cc. of nitrobenzene at 160°. A nearly quantitative yield (2.9 grams) of the acridinium methylsulphate was obtained, which after washing with ether to remove nitrobenzene, was readily converted into the other salts by adding a solution of the chloride, iodide or nitrate of an alkali metal.

Hydrolysis of the acetyl compound was effected by boiling 3 grams with 50 cc. of water and 15 cc. of concentrated hydrochloric acid for about 15 minutes, the amino-acridinium compound was then isolated as nitrate by salting out with saltpeter.

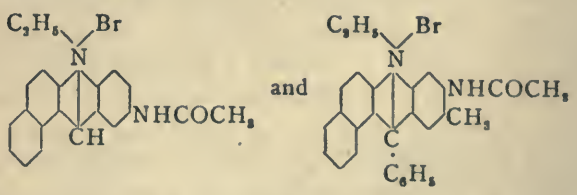
The same amino-acridinium compounds can be obtained

by the direct action of methyl sulphate (0.5 gram) on methyl-aminophenonaphthacridine (1 gram) dissolved in nitrobenzene (10 cc.) .It is interesting that the alkyl sulphate should thus attach itself to the tertiary nitrogen atom of the ring rather than to the primary amino group.

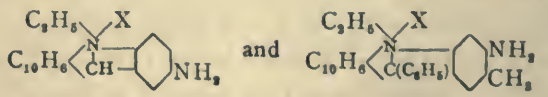
9-Methyl-12-ethyl-10-acetamino-1 : 2-phenonaphthacridinium bromide was also obtained by heating the acetyl derivative with ethyl bromide in chloroform solution for 8 hours at 150°; it melts at 265—269°.

Ullmann obtained patents for the action of alkyl halides on acetaminophenonaphthacridine compounds (Brit. P. 17426/1899; D. R. PP. 118439/1899; F. P. 292151/1899); protection of the use of methyl sulphate was granted in the United Kingdom (17427/1899), the United States (643569), and France (292152) but refused in Germany.

In D. R. P. 118439, the products described by Ullmann and Näf are mentioned as well as the salts obtained by the action of ethyl bromide on the acetaminophenonaphthacridine (m. p. 255°) made from 2-naphthol and anhydroformaldehyde-acetyl-*p*-phenylenediamine and on 9-methyl-10-acetamino-7-phenyl-1 : 2-phenonaphthacridine. These two compounds have the constitutions



respectively; they both dye tannined cotton yellow. By hydrolysis, the acetyl groups may be removed and amino-acridinium salts

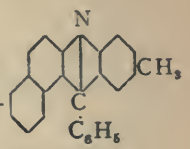


obtained, the former dyes tannined cotton a brick red shade, the latter colours it yellow.

7-Phenyl-9-ehtmyl-1:2-phenonaphthacridine.

Compounds derived from phenonaphthacridine, containing a phenyl group in position 7, may be obtained by using benzaldehyde in place of formaldehyde (Ullmann, Racovitza and Rozenband, *Ber.*, 1902, *35*, 316).

$$C_{10}H_7OH + C_6H_5OH + CH_3 \cdot C_6H_4 \cdot NH_2 + O = 3\,H_2O +$$



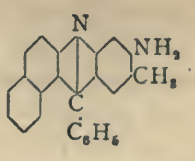
Paranitrobenzaldehyde furnishes but small amounts of an acridine derivative, the chief product being the nitrophenyldinaphthoxanthene described by Zenoni (*Gazzetta*, 1893, *23*, II, 218).

7-Phenyl-9-methyl-1:2-phenonaphthacridine is prepared by adding 3 parts of 2-naphthol to 4 parts of benzylidene-*p*-toluidine at 110° and gradually raising to 250°, the temperature is kept at this level for 1 to 1½ hours after the evolution of steam is apparently over. When sufficiently cool, the dark melt is dissolved in ether, on complete cooling the phenylmethylphenonaphthacridine separates in pale yellow leaflets, m. p. 213°; yield 39 per cent of the theory.

In D. R. P. 117472/1898, Ullmann recommends heating 20 kilos of 2-naphthol to 180° and adding the product made from 10 kilos of *p*-toluidine and 10 kilos of benzaldehyde, the reaction being finished by heating for a short time to 200°. The melt, when cool, is treated with caustic soda and steam blown, and the residue dissolved in warm dilute nitric acid. From this solution, the nitrate of the acridine separates on cooling.

Whilst *m*-nitrobenzylidene-*p*-toluidine reacts with 2-naphthol (equal weights at 195—200°) furnishing eventually a nitrophenylmethylphenonaphthacridine (m. p. 275°, D.R.P. 117472), the isomeride from *p*-nitrobenzylidene-*p*-toluidine was only formed in sufficient quantity for qualitative detection (*Ber.*, 1902, *35*, 318).

7-Phenyl-10-amino-9-methyl-1 : 2-phenonaphthacridine,



is obtained by the action of 2-naphthol on benzylidene-*m*-toluylenediamine (loc. cit., 319; D. R. P. 127 586/1899, lapsed 1902) or on tetraaminoditolylphenylmethane (loc. cit., 321; D. R. P. 108 273/1898).

Isolation of the benzylidene compound is not necessary. 5.3 grams of benzaldehyde (1 mol.) are heated with 6.1 grams of *m*-toluylenediamine (1 mol.) to 110°. 10.8 grams of 2-naphthol ($1^1/_2$ mols.) are added and the temperature gradually raised to 200—205°. At this point the contents of the flask solidify to a yellow crystalline mass and the temperature rises spontaneously to 215—220°. Whilst still warm, the mass is treated with alcohol and boiled up, the process being repeated until the contents are only feebly coloured. The residue of phenylaminomethyldihydrophenonaphthacridine (15.7 grams, 93.5 per cent of the theory) separates from aniline in colourless crystals, m. p. 271°, not sharp.

The substance is almost insoluble in alcohol and ether but dissolves in boiling acetone, benzene, toluene and aniline. The acetone solution is yellow but not fluorescent.

The dihydro-compound is oxidised to the hydrochloride of the colour base by boiling with alcohol and ferric chloride. In the patent mentioned, D. R. P. 127 586, the condensation is somewhat differently described, 10 parts of benzylidene-*m*-toluylenediamine being added to 8 parts of molten 2-naphthol and the temperature gradually raised to 180—190°. This patent also mentions the condensation of *p*-hydroxybenzaldehyde, *p*-chlorobenzaldehyde and *β*-hydroxy-*α*-naphthaldehyde with *m*-toluylenediamine and treatment of the products obtained with 2-naphthol. The aminoacridines obtained by these last three condensations dye tannined cot-

ton in yellowish orange, orange and yellow shades respectively.

The condensation of tetraaminoditolylmethane (7 grams) with 2-naphthol (6 grams) by gradually heating the mixture to 190° does not proceed so smoothly, yielding only 6 grams of the leuco base (loc. cit., 321). According to D. R. P. 108273, 15 kilos of 2-naphthol are heated to 150° and 20 kilos of tetraaminoditolylmethane gradually added, the temperature being finally raised to 200°.[1])

7-Phenyl-9-methyl-10-amino-1 : 2-phenonaphthacridine crystallises from aniline in lemon yellow needles, m. p. 276°. It dissolves sparingly in alcohol with yellow colour and green fluorescence, a few drops of hydrochloric acid turn the colour to orange red and intensify the fluorescence. On suitable dilution of this acid-alcoholic solution with water, the red hydrochloride separates. The solutions in benzene and toluene have a feeble yellow colour and greenish blue fluorescence; the solution in concentrated sulphuric acid is yellow and fluoresces green.

The *acetyl derivative* (10 grams hydrochloride, 4 grams anhydrous sodium acetate and sufficient acetic anhydride to form a stiff paste, reaction spontaneous) forms pale yellow needles, m. p. 265°.

If this compound (14 grams) be dissolved in nitrobenzene (100 cc.), heated to boiling, then cooled to 150° and treated with methyl sulphate (7 cc.), a nearly quantitative yield (19 grams) of phenylacetaminodimethylphenonaphthacridinium methylsulphate is obtained. The corresponding chloride is readily obtained from solutions of this salt and of sodium chloride; the acridol (m. p. 210°, not sharp) is also known.

Phenylaminodimethylphenonaphthacridinium chloride is obtained from the foregoing salts by hydrolysis with hydrochloric acid, the corresponding methylsulphate is formed by

1) Diaminophenylmethylphenonaphthacridine dyes may be produced by adding 20 parts of one of the pentaaminoditolylphenylmethanes of D. R. P. 45294 to 15 parts of 2-naphthol at 150° and then raising the temperature to 200°.

the direct action of methyl sulphate on a nitrobenzene solution of the non-acetylated aminoacridine (loc. cit., 324).

Alkylated derivatives of phenylmethylaminophenonaphthacridine have been described by Ullmann (D. R. P. 128754/1901, lapsed in 1902) and also jointly with M. Rozenband, B. Mühlhauser and E. Grether (*Ber.*, 1902, *35*, 326). The general method of preparation was to condense an alkylated *m*-diamine possessing one primary amino group with benzaldehyde and cause the resulting product to react with 2-naphthol. In the following table, the properties are as stated in the patent with the exception of the melting points, the latter are taken from the paper referred to. The appearances of the dyes as described in the patent probably refer to the hydrochlorides, for in the paper, phenylmethylethylaminophenonaphthacridine is described as being yellow whilst its hydrochloride is red.

Alkylated *m*-diamine	Dyestuff				
	Appearance	M. P.	Solution in dilute acetic acid	Solution in alcohol	Colour on tannined cotton
2-Methyltoluylenediamine	Orange red needles	270°	Orange yellow	Yellow	Orange
2-Ethylphenylenediamine	Yellow brown crystals	220—221°		Orange	
2-Ethyltoluylenediamine	Red crystals	258°	Orange	Yellow	Orange
2-Dimethylphenylenediamine	Brick red needles	216°	Red	Orange red	Red
2-Dimethyltoluylenediamine	Bordeaux red crystals	210°	Orange red	Red	Orange red
2-Diethylphenylenediamine	Bordeaux red crystals	200—201°	Orange red	Red	Orange red
2-Benzyltoluylenediamine	Orange needles	302°	Yellow	Yellow	Orange red

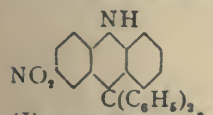
The alcoholic solutions of all these dyestuffs exhibit green fluorescence.

Example. A mixture of 15 parts of 2-ethyl-*m*-toluylenediamine, 11 parts of benzaldehyde and 20 parts of 2-naphthol is heated slowly to 180—200°; steam is evolved and the mass becomes orange red and liquefies. On cooling, the melt solidifies to a vitreous mass and crystallises after removal of the excess of naphthol. It is oxidised to dye by ferric chloride.

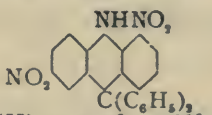
Carbazines.

Brief mention may be made of a group of compounds which contain the same ring system as acridine but possess very dissimilar properties; these are the carbazines discovered by F. Kehrmann, H. Goldstein and P. Tschudi (*Helv. Chim. Acta*, 1919, *2*, 379).

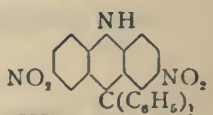
The authors named (*ibid.*, 315), find that 5-diphenyldihydroacridine can give rise to six different products on nitration, these are represented by the formulae



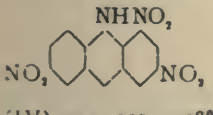
(I) m. p. 300–301°



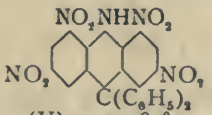
(II) m. p. 287—288°



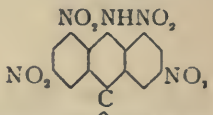
(III) m. p. 322 5°



(IV) m. p. 257—258°

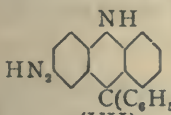


(V) m. p. 180°

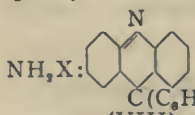


$NO_2 \cdot C_6H_4 \diagdown \diagup C_6H_4 \cdot NO_2$
(VI) m. p. 317—318°.

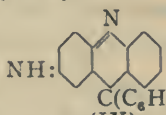
By reducing the nitro compounds, amines are obtained which behave as the leuco compounds of colouring matters. Taking, for example, the nitro compound (I), reduction gives 3-amino-5-diphenylacridine (VII) which, when oxidised, furnishes the aminodiphenylacridine salt (VIII)



(VII)



(VIII)



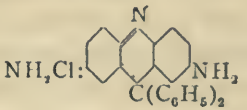
(IX)

The constitution of such a salt more resembles that of an oxazine (or thiazine or azine) than that of the acridine dyes we have considered hitherto.

The mono-acid salts of type VIII are bluish green, ammonium carbonate solution separates the base (IX) which is yellowish-red in ethereal solution and shows a pronounced yellow fluorescence.

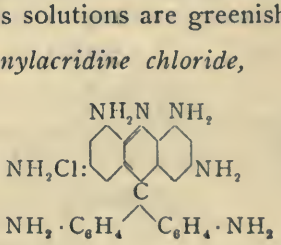
The poly-nitro compounds mentioned were also reduced to polyamines and the latter oxidised to dyestuffs with which dye trials were made.

3:7-*Diaminodiphenylacridine chloride,*



is interesting on account of the formal relationship to many of the azine, thiazine (methylene blue, Lauth's violet) and oxazine dyes; aqueous solutions are greenish blue in colour.

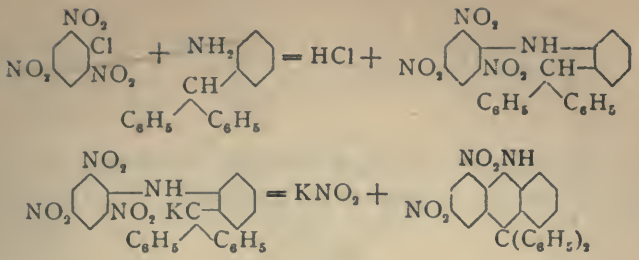
Hexa-aminodiphenylacridine chloride,



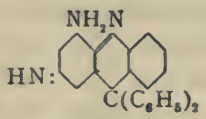
forms almost black prisms with a slight metallic lustre, the base was not isolated on account of its highly basic properties; even an ethereal solution absorbs carbon dioxide from the air.

The property of picryl derivatives of readily losing the elements of nitrous acid (Turpin, *Trans. Chem. Soc.*, 1891, *59*, 714), has been utilised by F. Kehrmann, M. Ramm and Ch. Schmajewski for the further synthesis of carbazine compounds (*Helv. chim. acta.*, 1921, *4*, 538).

Thus picryl chloride condenses with *o*-aminotriphenylmethane and the potassium dervative of the condensation product, when heated with quinoline to the boiling point, splits off potassium nitrite.



2 : 4 - *Dinitro* - 5 - *diphenyldihydroacridine* forms orange yellow, prismatic crystals, m. p. 232°. When this compound is reduced by stannous chloride, the tin double salt of the corresponding diamino compound is obtained; oxidation of the latter with ferric chloride furnishes salts of 1 : 3-diamino-5-diphenylacridine (4-amino-diphenylcarbazimonium-2, Kehrmann).

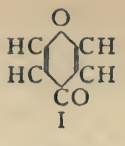


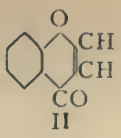
Solutions in concentrated sulphuric acid are dark blue in colour; the shade alters to reddish violet on dilution with water.

CHAPTER X.

THE PYRONE RING

Six membered rings made up of one oxygen and five carbon atoms occur in a number of compounds, many of which are natural vegetable products. These rings may either be isolated, with or without substitution of hydrogen atoms by alkyl, carboxyl etc., or they may be joined on one or both sides to other ring (e. g. aromatic) systems. Thus pyrone (I), chromone (II) and xanthone (III) possess the respective constitutions.


I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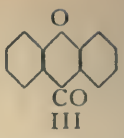
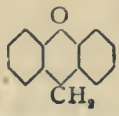

III

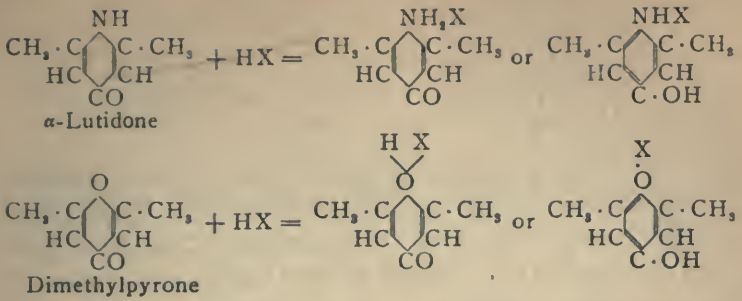
Although the artificial dyestuffs containing the pyrone ring are nearly all related to xanthene



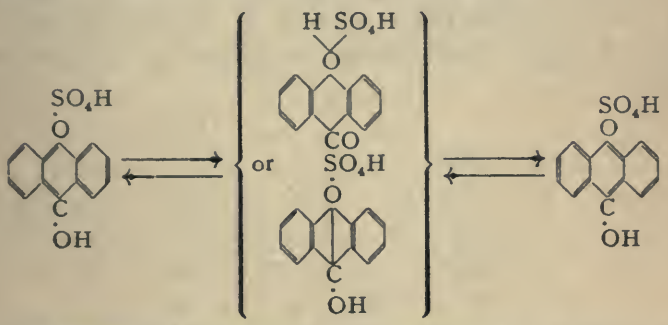
many derivatives of the simpler complexes are coloured and some knowledge of their properties and relationships is essential.

Pyrone is the analogue of 4-pyridone which, as we have previously seen, is tautomeric with 4-hydropyridine. Since pyrone cannot exhibit tautomerism, it is better to compare it with methyl-4-pyridone. The pyridones show distinctly basic properties, and in 1899 J. N. Collie and T. Tickle (*Trans. Chem. Soc.*, 1899, *75*, 710) found that dimethylpyrone, the analogue of lutidone, was capable of forming a series of salts with acids. "Addition compounds" of acids with organic compounds containing oxygen had been previously described; e. g. $(CH_3)_2O, HCl$ (Friedel, *Bull. soc. chim.*, 1875, II, *24*, 166, 241) and the comparatively stable solid compounds of the phthaleins (Baeyer, *Annalen*, 1876, *183*, 27; Fischer, *ibid.*, 68) and many natural yellow colouring matters (A. G. Perkin, *Trans. Chem. Soc.*, 1896, *69*, 1439) with acids (See also, Friedländer and Rudt, *Ber.*, 1896, *29*, 878).

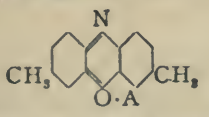
To Collie and Tickle must, however, be awarded the credit of having first recognized that the oxygen in the pyrones had a similar salt forming capacity to the NH group of the pyridones. Thus we may compare the production of salts from pyrones and pyridones in an analogous manner; it will be noted that whilst the acid radicle X is attached in both cases to nitrogen or oxygen as the case may be, the arrangement of the other linkages in the molecule is not necessarily fixed by the structure of the original base.



In Collie and Tickle's original paper, the first of the two formulae given was assigned to the salts of dimethylpyrone. The second formula corresponds to a structure suggested by J. T. Hewitt (*Zeitschr. physikal. Chem.*, 1900, *34*, 12) in the case of the salt produced when xanthone is dissolved in concentrated sulphuric acid, the molecules showing a double symmetrical tautomerism.

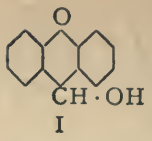


Meanwhile, Kehrmann had suggested oxonium salt structure for certain oxazines (*Ber.*, 1899, *32*, 2601) and isolated salts of dimethylphenoxazonium (*Ber.*, 1901, *34*, 1624) to which he assigned the formula

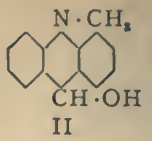


(A = Br or picrate ion)

The constitutional resemblance between xanthydrol (Formula I, the reduction product of xanthone, Meyer and E. Saul, *Ber.*, 1893, *26*, 1276) and the pseudo-bases derived from quaternary acridinium salts

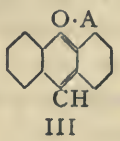


I

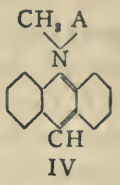


II

pointed to the possibility of the existence of comparatively stable xanthoxonium salts (III) containing quadrivalent oxygen, the analogues of the quaternary ammonium salts (IV) obtained by the addition of alkyl halides to acridine and its derivatives.

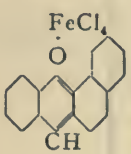


III

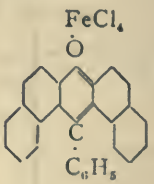


IV

A. Werner (*Ber.*, 1901, *34*, 3300) described salts of type III in which A = Br_8, $FeCl_4$, as well as the ferrichlorides of pheno-*α*-naphthoxanthoxonium and phenyldi-*β*-xanthoxonium (VI)



V

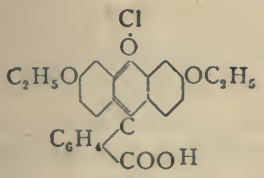


VI

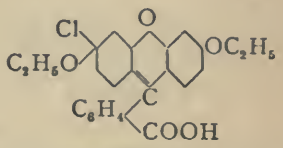
Werner drew attention to the product obtained by the action of bromine on dinaphthoxanthene (Fosse, *Compt. rend.*, 1901, *133*, 100) then regarded as having a constitution represented by $CHBr\langle {}^{C_{10}H_6}_{C_{10}H_6}\rangle O$ but which he considered to be an oxonium salt.

Hewitt had also been engaged in the preparation of oxonium salts from xanthydrol and fluoran with the object of collecting material to support his views on the relation between the constitution and fluorescence of organic compounds, and obtained xanthonium picrate (J. T. Hewitt and A. J. Turner, *Ber.*, 1901, *34*, 3821) as well as a series of salts

of fluoran, dimethylfluoran (*p*-cresolphthalein) and fluorescein with mineral acids (Hewitt and J. N. Tervet, *Trans. Chem. Soc.*, 1902, 81, 663). The compound of lactonoid dimethylfluorescein with hydrochloric acid (Nietzki and Schröter, *Ber.*, 1895, *28*, 56) was recognised as an oxonium salt (VII) and not as having the constitution previously assigned to it (VIII).



VII



VIII

The basic properties of quadrivalent oxygen were soon acknowledged and much work on the subject was published. Some of the more important papers are given in the following list which, however, is by no means complete.

Baeyer and Villiger; *Ber.*, 1901, *34*, 1189, 2679, 3612; 1902, *35*, 1201; 1903, *36*, 2774; 1904, *37*, 597, 2848, 3191.

A. Cohen; *Ber.*, 1902, *35*, 2672.

R. Fosse; *Compt. rend.*, 1901, *133*, 880, 1218; *134*, 177, 663; 1902, *135*, 39, 530; 1903, *136*, 379, 1006, 1566; *137*, 858; 1904, *138*, 282, 575, 1051; *Ann. chim. phys.*, 1904, VIII, *2*, 233, 289; *Compt. rend.*, 1904, *139*, 600; 1906, *142*, 1545; *143*, 59, 239; *Bull. soc. chim.*, 1906, III, *35*, 1005.

A. Hantzsch; *Ber.*, 1905, *38*, 2143.

F. Kehrmann; *Ber.*, 1899, *32*, 2610; 1901, *34*, 1623; 1905, *38*, 2574, 2952.

F. Strauss; *Ber.*, 1904, *37*, 3277; 1906, *39*, 2977.

D. Vorländer; *Ber.*, 1903, *36*, 1470, 3528; 1904, *37*, 1644, 3364; *Annalen*, 1901, *320*, 117.

P. Walden; *Ber.*, 1901, *34*, 4185; 1902, *35*, 1764.

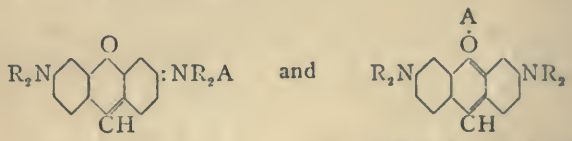
J. Walker; *Ber.*, 1901, *34*, 4115.

A. Werner; *Annalen*, 1902, *322*, 296.

R. Willstätter; *Ber.*, 1900, *33*, 1636. [1])

1) Before the recognition of oxonium salts, a higher valency than two had been suggested by several chemists in order to explain

Whilst the recognition of oxonium structure has been a very important step in explaining the existence of salt forming organic compounds from which nitrogen, sulphur etc. are absent, the extension to the formulation of salts containing amino groups as well as a cyclic oxygen atom must be taken with caution. Thus the pyronines have been written with the formulae



(R = alkyl, A = acid radicle)

and whilst certain chemists use the latter constitution which expresses these compounds as diamino-derivatives of the parent xanthoxonium salt, the stable character of the pyronine salts and the knowledge one possesses with regard to the pronounced basic properties associated with quinonoid quaternary nitrogen atoms (e. g. in the dyestuffs of the pararosaniline and methyl violet series) lead one to the paraquinonoid ammonium formula as more probable (Hantzsch, *Ber.*, 1905, *38*, 2143).

Pyrolium Compounds

As previously mentioned, the basic properties of oxygen in cyclic combination were first definitely identified in the case of dimethylpyrone;

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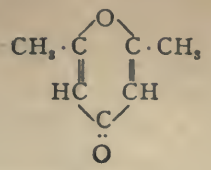
the behaviour of oxygen in many of its compounds. Reference may be made to the following publications.

Naquet; *Compt. rend.*, 1864, *58*, 381, 675.
Williamson; *J. Chem. Soc.*, 1869, *22*, 360.
Friedel; *Bull. soc. chim.*, 1875, II, *24*, 166, 241.
J. F. Heyes; *Phil. Mag.*, 1888, v, *25*, 221, 297.
R. Meldola; *Phil. Mag.*, 1888, v, *26*, 403.
E. Bamberger; *Ber.*, 1891, *24*, 1761.
N. S. Kurnakoff; *J. Russ. phys. chem. Soc.*, 1893, *25*, 726.
J. v. Schroeder; *J. Russ. phys. chem. Soc.*, 1894, *26*, 50.
J. W. Brühl; *Ber.*, 1895, *28*, 2847; 1897, *30*, 163; 1900, *33*, 710; *Zeitsch. physikal. Chem.*, 1895, *18*, 514.



the salts of this compound will consequently be treated in some detail.

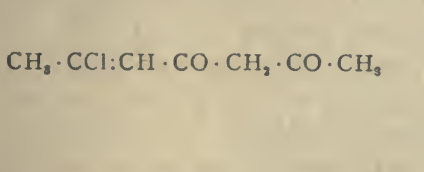
Although Oppenheim and Precht (*Ber.*, 1876, *9*, 324) stated that dehydracetic acid resisted the action of mineral acids, Feist (*Annalen*, 1890, *257*, 253) found that it was converted into dimethylpyrone by the action of concentrated hydrochloric acid or sulphuric acid.

Collie (*Trans. Chem. Soc.*, 1891, *59*, 617) observed that when dehydracetic acid was boiled with fuming hydrochloric acid, a compound, $C_7H_{11}O_3Cl$, was produced according to the equation

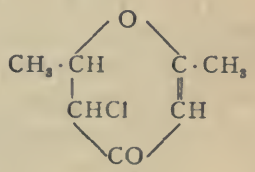
$$C_8H_8O_4 + H_2O + HCl = C_7H_{11}O_3Cl + CO_2.$$

This reaction was further examined by Feist (*Ber.*, 1892, *25*, 1067) who found that whilst the melting point, 83—85°, given by Collie was correct for the fresh crystals, they lost their lustre in a vacuum desiccator, and the resulting hygroscopic substance, which melts at 154°, gave on analysis figures agreeing with the formula $C_7H_9O_2Cl$. The fresh crystals were also found to have the composition $C_7H_9O_2Cl, 2H_2O$.

Feist regarded the substance as having the open chain constitution (I); the ring structure (II) was looked on as less probable.



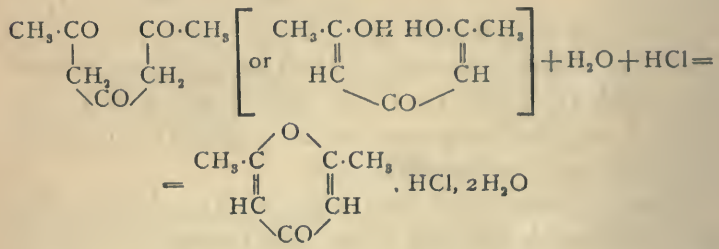
I



II

Collie and Tickle (*Trans. Chem. Soc.*, 1899, *75*, 710) re-examined the product and disagreed with Feist's open chain formula; a derivative of diacetylacetone should, like the

parent substance, give a colouration with ferric chloride, and this reaction was absent. Collie's earlier statement (*loc. cit.*, 620) that dimethylpyrone does not combine with hydrogen chloride was corrected, it now being found that both diacetylacetone and dimethylpyrone when evaporated with hydrochloric acid give the compound $C_7H_8O_2$, HCl, 2 H_2O.



The general behaviour of the substance was that of a salt formed by combination of a weak base with a strong acid; experiments were made with other acids and the following salts prepared (B = Dimethylpyrone).

Hydrobromide	B, HBr
Hydriodide	B, HI
Platinchloride	B_2, H_2PtCl_6
Nitrate	B, HNO_3
Oxalate	B_2, $H_2C_2O_4$
Acid tartrate	B, $C_4H_6O_6$
Chloroacetate	B, $C_2H_3O_2Cl$
Picrate	B, $C_6H_3O_7N_3$

It was further found that the conductivity of hydrochloric acid at moderate dilutions was strongly affected by the addition of dimethylpyrone; thus the equivalent conductivities for hydrochloric acid at dilutions of 2 and 4 litres were found to be 353 and 366 respectively whilst for corresponding solutions of the pyrone hydrochloride they were only 217 and 269. At a dilution of 1024 litres, the figures for the hydrochloric acid and dimethylpyrone hydrochloride were 403 and 376 respectively; that a kation is formed from dimethylpyrone and hydrion is thus rendered evident.

Some caution should be exercised in applying measurements of conductivity of the salts of weak bases, for many organic substances, e. g. cane sugar, added to solutions of mineral acids are able to depress their conductivity. (See Hantzsch, *Ber.*, 1905, *38*, 2145.)

Baeyer and Villiger (*Ber.*, 1901, *34*, 3614) made cryoscopic measurements on aqueous solutions of dimethylpyrone hydrochloride and concluded that in 0.08 N solution the hydrolysis was complete. J. Walker (*Ber.*, 1901, 34, 4115, experiments by J. K. Wood) measured the catalysis of methyl acetate by hydrochloric acid (N/10) to which an equivalent amount of urea, dimethylpyrone or tetramethylpyrone (prepared from dimethyldiacetylacetone by Collie and Tickle, *Trans. Chem. Soc.*, 1900, *77*, 964) had been added. Dimethylpyrone was slightly stronger, tetramethylpyrone slightly weaker than urea in basic properties.

P. Walden (*Ber.*, 1901, *34*, 4185) examined the basic properties of dimethylpyrone, making various physico-chemical measurements. A weak base, such as aniline, markedly accelerates the mutarotation of glucose. (Osaka, Zeitsch. physikal. Chem., 1900, 35, 691); dimethylpyrone is practically without effect. Despite this, it was found that dimethylpyrone and picric acid combine to some extent in aqueous solution; this was shown by partition coefficient determinations using benzene, as well as by conductivity measurements: it was also confirmed, by freezing point determinations, that diemethylpyrone undoubtedly combines with hydrogen ions when added to dilute hydrochloric acid.

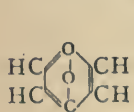
From the various measurements, a dissociation constant for dimethylpyrone as base was calculated and found to be about 3×10^{-14}; it is therefore a stronger base than water (1.2×10^{-14}), weaker however than betaine (7.6×10^{-13}) For purposes of comparison it may be mentioned that aniline and ammonia give values of 5.3×10^{-10} and 2.3×10^{-5} respectively.

Walden considers tetravalent oxygen to possess an amphoteric character; this is based on conductivity measure-

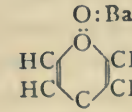
ments made in hydrazine hydrate solution (*Ber.*, 1902, *35*, 1770).

Further salts of dimethylpyrone have been prepared by Plotnikow (*J. Russ. phys. chem. Soc.*, 1904, *36*, 1088; 1905, *37*, 318, 875; 1907, *39*, 1794; 1908, *40*, 64, 1238); Weinland and Reischle (*Ber.*, 1908, *41*, 3671); McIntosh (*J. Amer. Chem. Soc.*, 1910, *32*, 542) and Gomberg and Cone (*Annalen*, 1910, *376*, 183).

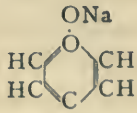
The generally accepted formula for dimethylpyrone, viz. that used above, is due to Lieben and Haitinger (*Monatsh.*, 1883, *4*, 273, 339; 1884, *5*, 339; 1885, *6*, 279: see also J. W. Brühl, *Ber.*, 1891, *24*, 2450). Collie was inclined to assign a different constitution to the pyrones, partly on account of abnormalities in their molecular refractions, partly because their chemical behaviour is that of saturated compounds in so far as they are not attacked by nitric or sulphuric acids, nor hydrogenated by ordinary reducing agents. Further, pyrone gives a yellow barium salt whilst the sodium salt is colourless; both, however, if dissolved in dilute hydrochloric acid, develop a blood red coloration with ferric chloride. The new formulae proposed were



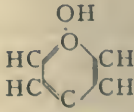
Pyrone.



Yellow Barium Salt.



Colourless Sodium Salt.

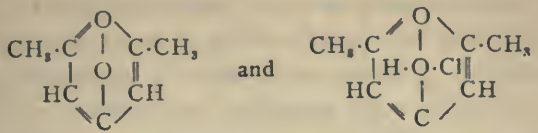


Product of action of acid on sodium Salt.

Dimethylpyrone and its derivatives were represented by corresponding formulae.

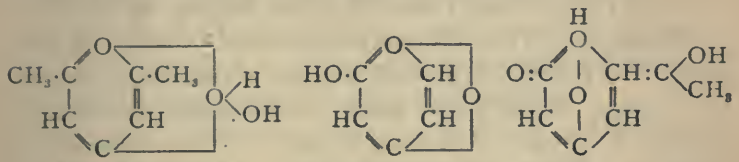
Further attention was drawn to the abnormal refractive powers of the pyrones and nearly related substances by Miss Homfray (*Trans. Chem. Soc.*, 1905, *87*, 1443). The molecular refraction of dimethylpyrone for the D line was found experimentally to be 35·34, whilst the value calculated from the atomic refractions of the elements and correcting for double linkages is only 33·3. To overcome the difficulty the as-

sumption is made that dimethylpyrone already contains quadrivalent oxygen and the structure of the substance and its hydrochloride are represented by the formulae proposed by Collie viz. —



the value 2.65 being taken as the atomic refraction of quadrivalent oxygen.

Alterations were made in the structure of numerous compounds so that they should be represented with at least one oxygen atom in a quadrivalent condition, e. g.



Diacetylacetone Pyromeconic acid Dehydracetic acid

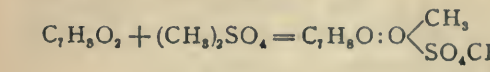
Attention may be drawn to the structure given for dehydracetic acid (taken from the original paper, p. 1460) in which one oxygen and one carbon atom are assigned quinquevalency whilst another carbon atom is sexavalent.

Ternary oxonium salts from dimethylpyrone.

Weak tertiary amines which will not combine with alkyl halides may frequently be converted into quaternary ammonium compounds by the action of methyl sulphate and the methylosulphate radicle subsequently replaced by iodine, the concentrated solution of the ammonium methylosulphate being salted out with potassium iodide.

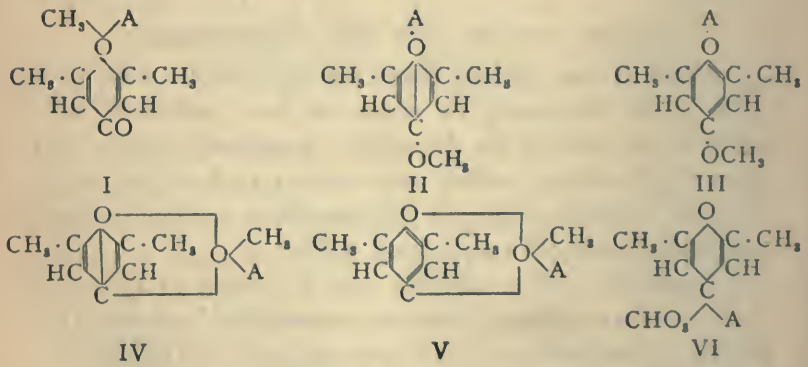
Similarly, methyl sulphate may be added to dimethylpyrone and crystalline iodide and platinichloride obtained by double decomposition (F. Kehrmann and A. Duttenhofer, *Ber.*, 1906, *39*, 1299). 12 grams of dimethylpyrone and 13 grams of methyl sulphate were kept at room temperature

for four weeks with occasional mixing. At the end of this time a few crystals could still be seen in the viscous, fluorescing liquid; a few grams of methyl sulphate were added and after a further eight days the crystals had disappeared. The resulting methylosulphate could not be obtained in a crystalline condition, but by solution in a small quantity of water and addition of twice the volume of saturated potassium iodide solution, the crystalline methiodide was obtained which, after washing successively with very little ice cold water, alcohol, alcohol-ether mixture and finally ether was shown to have the formula



The iodide forms yellowish white, shining leaflets, easily soluble in water; the solution does not taste acid but salt and bitter like potassium iodide; it gives a slight acid reaction with litmus. The dry salt melts, evolving methyl iodide and leaving a residue of dimethylpyrone. The platinichloride, $(C_8H_{11}O_2)_2PtCl_6$, is slightly soluble in cold water and alcohol; heated quickly, it melts at 158° with decomposition.

Kehrmann arrived at no conclusion as to the constitution of the salts, but according to the view taken as to the constitution of dimethylpyrone the following formulae must be considered.

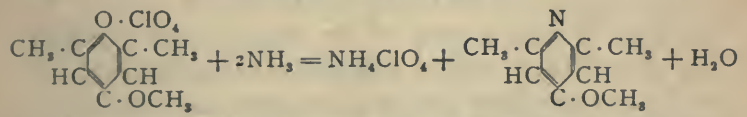


Of these structures Kehrmann considered formula (I) to be the most probable. Von Baeyer took up the matter

four years later (*Ber.*, 1910, *43*, 2337) and showed that formula III (or II) must be adopted. In isolating the ternary salt, the perchlorate was used, the operation being carried out in the following manner. 20 Grams of dimethylpyrone and 25 grams of methyl sulphate were heated to 50°; at the end of 2 or 3 hours the crystals were dissolved and an orange coloured syrup produced. This was cooled with ice and treated with 65 grams of 20 per cent perchloric acid, allowed to stand at 0° for 2 hours and then filtered. The crystals were washed with a little ice cold water and several times with acetone. Yield 24 grams. For purification, the salt was crystallised from methyl alcohol, the operation being repeated if the crystals were not colourless, yield 18 to 20 grams.

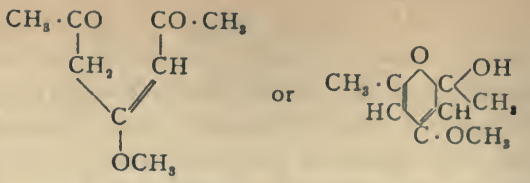
The salt is sparingly soluble in cold water, the aqueous solution tastes salt and bitter; it is neutral when freshly prepared and goes acid on standing: this happens more rapidly on boiling, dimethylpyrone being produced.

The constitution is proved by the following reactions. (a) The perchlorate almost immediately yields 4-methoxylutidine (Conrad, *Ber.*, 1887, *20*, 164; 1889, *22*, 81) when treated with 15 per cent ammonium carbonate solution.

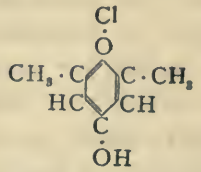


(b) An aqueous solution of the perchlorate if allowed to stand with magnesium carbonate or sodium acetate (to neutralise perchloric acid) yields an oily substance, easily soluble in water. This was not analysed, but it was shown not to contain diacetylacetone by the absence of a colour reaction with ferric chloride and by giving no characteristic copper compound, though after boiling with dilute sulphuric acid, the copper compound of diacetylacetone could be obtained. The substance is, however, converted into 4-methoxylutidine by the action of ammonium carbonate.

These reactions are compatible with the substance being the methyl ether of an enolised diacetylacetone or as having the ring structure of a pseudo-base.



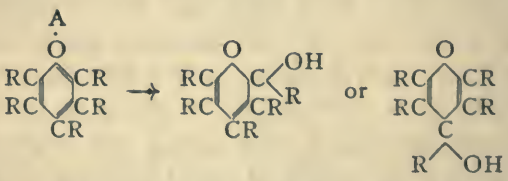
As the result of these experiments, von Baeyer is inclined to put forward a structure for dimethylpyrone hydrochloride corresponding to that of the "dimethyl-methoxyl-pyroxonium" salts, viz. —



a possibility which had been mentioned by Hewitt (*Zeitschr. physikal. Chem.*, 1900, *34*, 3734) respecting the solution of diphenylpyrone (Feist, *Ber.*, 1890, *23*, 3734) in concentrated sulphuric acid.

PYRYLIUM SALTS.

From what is known of the behaviour of xanthydrol (see p. 210) and similar compounds towards acids, the existence of pyrylium salts may be predicted, salts and carbinol bases being related to one another in the following manner. (A = acid radicle, R = aryl or alkyl.)



In fact, Kehrmann and Duttenhofer's salts are of this type, the five R's in the formula being represented by CH_3, H, OCH_3, H, CH_3. The presence of the methoxyl group makes the elimination of alkyl halide easy, and the preparation of pyrylium salts in which alphyl rather than alphoxyl

radicles are the sole substituents is a matter of considerable interest.

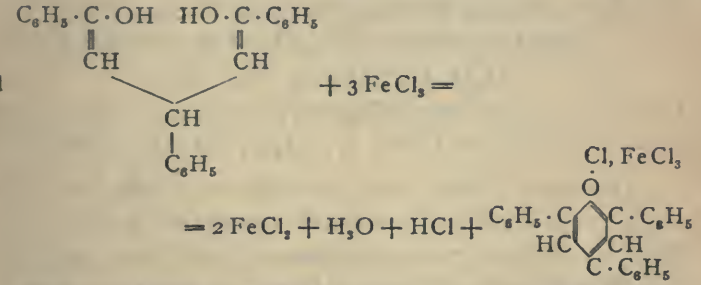
W. Dilthey (*J. pr. Chem.*, 1916, II, *94*, 53) has found that 2:4:6-triphenylpyryl ferrichloride, m. p. 277°, is an easily accesible compound, being produced when two molecules of acetophenone and one of benzaldehyde or one molecule of phenylstyryl ketone and one of acetophenone are boiled with acetic anhydride and ferric chloride. In either case, benzylidene diacetophenone is formed as an intermediate product; the reactions may be represented by the following equations.

$$C_6H_5CHO + 2\,CH_3\cdot CO\cdot C_6H_5 = H_2O + C_6H_5CH(CH_2\cdot CO\cdot C_6H_5)_2$$

or

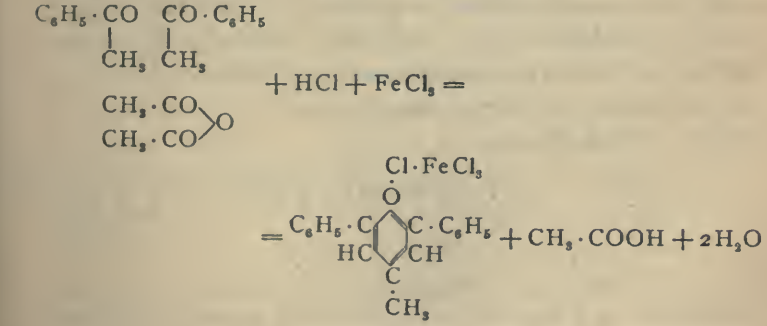
$$C_6H_5CH:CH\cdot CO\cdot C_6H_5 + CH_3\cdot CO\cdot C_6H_5 = C_6H_5CH(CH_2\cdot CO\cdot C_6H_5)_2$$

and



The constitution of the compound is quite definite since it furnishes 2:4:6-triphenylpyridine by the action of ammonia.

In a very similar way, 2:6-diphenyl-4-methylpyryl ferrichloride (m. p. 175° corr.) may be obtained from acetic anhydride, acetophenone and ferric chloride



The pyrylium compound yields 2:6-diphenyl-4-methylpyridine when treated with ammonia.

By the action of alkalies (not amine bases) on triphenylpyrylium salts the pseudo-base, $C_{23}H_{18}O_2$, m. p. 119° (corr.), is obtained; it crystallises in bundles of colourless needles and, of alternative formulae, Dilthey first proposed a cyclic structure but subsequently represented the substance with an open chain constitution (*Ber.*, 1919, *52*, 2040).

The pseudo-base exhibits a faint fluorescence in glacial acetic acid solution and an intense bluish green fluorescence in concentrated sulphuric acid.[1] The *platinichloride* (m. p. 225—226°) and *picrate* (m. p. 224—227°) were also prepared.

When the pyranol is treated with two molecular proportions of semicarbazide in presence of pyridine, $\alpha\gamma\varepsilon$-triphenyl-Δ^{β}-pentene-$\alpha\varepsilon$-dionedisemicarbazone (m. p. 225°),

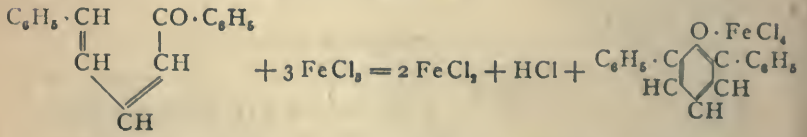
$$NH_2 \cdot CO \cdot NH \cdot N : C(C_6H_5) \cdot CH_2 \cdot C(C_6H_5) : CH \cdot C(C_6H_5) : N \cdot NH \cdot C_6H_5$$

is formed and the pseudo-base is represented by the formula

$$C(OH)(C_6H_5) : CH \cdot C(C_6H_5) : CH \cdot CO \cdot C_6H_5$$

Triphenylpyranol gives yellowish red solutions in alkalies which are unstable; the molecule undergoes fission, benzoic acid and other products being formed (*J. pr. Chem.*, 1917, II, *95*, 107). When treated with methyl iodide and sodium methoxide in methyl alcoholic solution, the hydroxyl group is methylated, the resulting compound of m. p. 142—143° corr. being at first taken for 2-methoxy-2:4:6-triphenylpyran.

Dilthey (*Ber.*, 1917, *50*, 1008) has also obtained pyryl compounds unsubstituted in position 4, thus 2:6-diphenylpyryl ferrichloride, m. p. 185—186°, results on boiling a mixture of phenylcinnamylidenemethyl ketone, acetic acid and anhydride and ferric chloride.

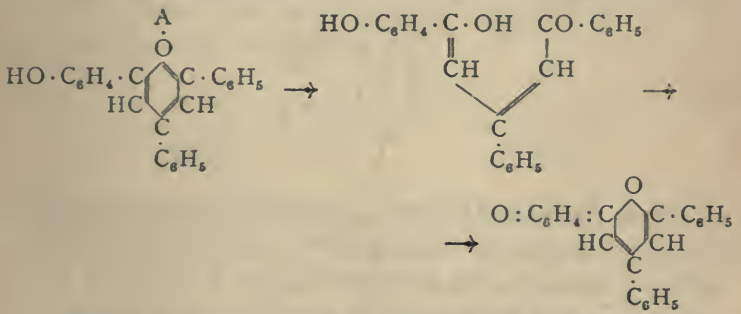


1) It is, perhaps, of interest that 2:6-dianisyl-4-methylpyryl ferrichloride, m. p. 179—180° corr., dissolves in concentrated sulphuric acid with yellow colour and yellowish green fluorescence.

Some very interesting observations were made (*Ber.*, 1919, *52*, 1195) on examining 2:4-diphenyl-6, *p*-hydroxyphenylpyryl salts. The corresponding methoxy ferrichloride was obtained by the condensation of phenylstyryl ketone with *p*-methoxyacetophenone; on treatment with sodium carbonate, α-hydroxy-$\gamma\varepsilon$-diphenyl-α-*p*-anisyl-$\Delta^{\alpha\gamma}$-pentadien-ε-one, m. p. 105—106°,

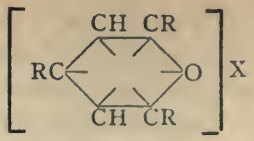
$$CH_3O \cdot C_6H_4 \cdot C(OH) : CH \cdot C(C_6H_5) : CH \cdot CO \cdot C_6H_5$$

was produced. Hydrochloric acid demethylates this compound at 160° giving 2:4-diphenyl-6, *p*-hydroxyphenylpyrylium chloride, from which, by the action of pyridine, alcohol and much water, α-hydroxy-$\gamma\varepsilon$-diphenyl-α-*p*-hydroxyphenyl-$\Delta^{\alpha\gamma}$-pentadien-ε-one is produced (slender yellow needles, m. p. 164°. From this compound, acids regenerate the pyrylium salts, but, on heating, it gives the quinonoid anhydro-base which forms violet blue aggregates.



Similary, *p*-hydroxyphenylstyryl ketone and *p*-hydroxyacetopenone may be made to furnish 4-phenyl-2:6-di-*p*-hydroxyphenylpyryl salts from which the corresponding open chain ketones and anhydro-bases may be obtained.

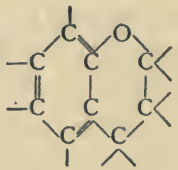
Other pyrylium compounds are described by Dilthey in later papers (*Ber.*, 1919, *52*, 2040; 1920, *53*, 252, 621) and he has been inclined to abandon oxonium structure without adopting a carbonium formulation for pyrylium salts. No individual atom of the complex is regarded as carrying the electron, but the complex is taken as a whole, the negative group being freely mobile in the second "zone" (*Ber.*, 1920, *53*, 261).



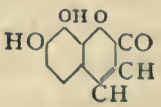
When a pseudo-base is formed, the hydroxyl group attaches itself to either the α- or γ-carbon atom, and the valencies, which are represented more or less free, then rearrange themselves to ordinary double bonds. (See Kauffmann's views on kationic partial valencies, *Ber.*, 1919, *52*, 1422; his views and those of Dilthey have something in common.)

BENZOPYLIUM COMPOUNDS.

Compounds containing the grouping

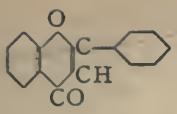


are widely distributed in nature, many of the natural vegetable dyestuffs being derived from them. For the most part, a hydrogen atom of the heterocyclic ring is replaced by an aromatic nucleus though this is not the case with daphnetin or dihydroxycoumarin



which is contained as a glucoside, *daphnin*, in the bark of *Daphnis alpina* and *D. Mezereum*.

Flavone occurs in the "meal" or "farina" found on the flower stalks, leaves and capsules of several varieties of primula (H. Müller, *Trans. Chem. Soc.*, 1915, *107*, 872); its constitution is given by formula (I)



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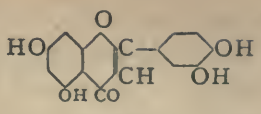
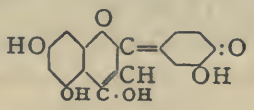


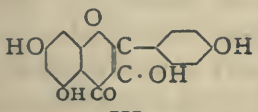
II

Luteolin (II) is the colouring matter of weld, *Reseda luteola;* it forms compounds with mineral acids, e. g. $C_{15}H_{10}O_6, H_2SO_4$; $C_{15}H_{10}O_6, HI$, &c. (A. G. Perkin, *Trans. Chem. Soc.,* 1896, *69,* 216, 799; 1900, *77,* 1315); these are now generally recognized as oxonium salts.

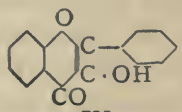
Perkin (*Trans. Chem. Soc.,* 1899, 75, 433) also took into account the possibility of quinonoid structure, thus the lakes formed by luteolin may be derived from the configuration



A number of natural dyestuffs, e. g. kaempferol (III) are derived from flavonol (IV),



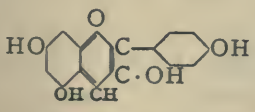
III



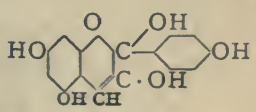
IV

These also give well characterised oxonium salts though their uses in dyeing depend on their power of forming lakes; this they owe to the presence of hydroxyl (and carbonyl) groups.

The colouring matters of flowers are glucosides which yield benzopyranol derivatives on hydrolysis; thus pelargonine, the glucoside in the petals of *Pelargonium zonale,* gives pelargonidine on hydrolysis, the latter compound may be represented as salt and as pseudo-base by the following structures.[1]



and

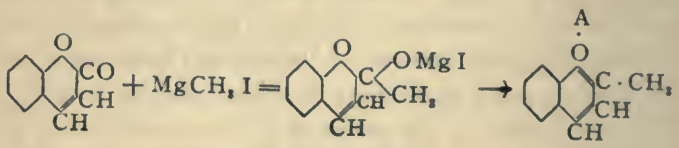


1) Reference may be made to the monograph in this series, *The Natural Organic Colouring Matters,* by A. G. Perkin and A. E. Everest, 1918.

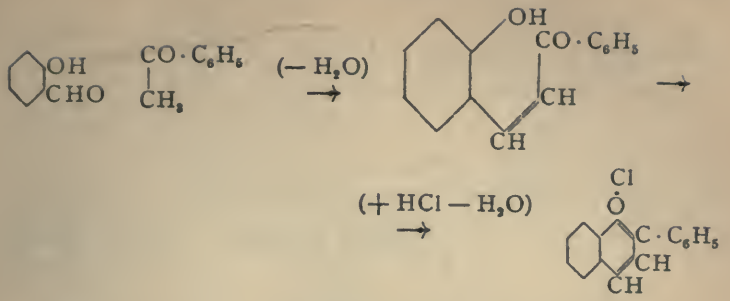
Artificial dyestuffs of the benzopyranol series are scarcely likely to have much application and since the theoretical questions underlying oxonium salt formation have been discussed somewhat fully with regard to the pyrylium compounds, the benzopyrylium (Decker uses the term "phenopyrylium") group will be treated comparatively briefly.

Decker foresaw the existence of benzopyrylium and pyrylium salts which would bear the same relationship to quinolinium and pyridinium salts that the xanthylium and acridinium salts bear to one another, and in conjunction with von Fellenberg (*Ber.*, 1907, *40*, 3815) effected the synthesis of the first members of the series. The method employed was analogous to that used by Bünzly and Decker (*Ber.*, 1904, *37*, 2934) in the synthesis of acridinium and xanthylium compounds.

Coumarin and its derivatives were brought to reaction with alkyl magnesium halides, by treatment of the products with acids, benzopyrylium salts, substituted in position 2 were obtained. In this way salts of 2-methylbenzopyrylium were formed by acting on coumarin with methyl-magnesium iodide, of which only one-half or one-third of the theoretical quantity was used.



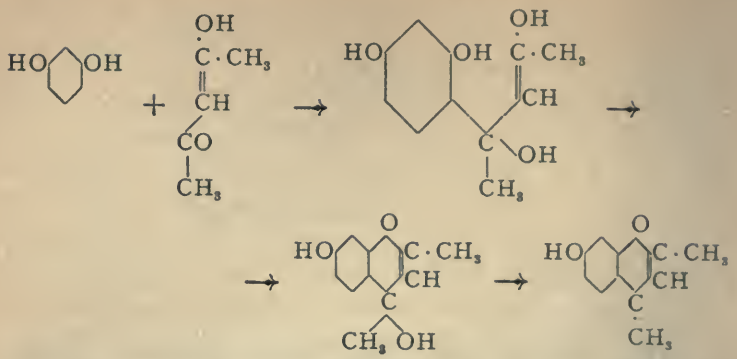
A more general synthesis is effected by condensing salicylaldehyde with aldehydes or ketones and then closing the ring by addition of an acid; thus when equivalent quantities of salicylaldehyde and acetophenone are mixed and treated in the cold with hydrogen chloride, either in presence or absence of a solvent, the two consecutive reactions occur, and by extracting the mass with hydrochloric acid and precipitating with ferric chloride 2-Phenylbenzopyrylium ferrichloride, m. p. 125°, is obtained.



These reactions were subsequently extended to the preparation of a number of compounds not only in the benzopyrylium but also in the xanthylium and coeroxonium series (Decker and von Fellenberg, *Annalen*, 1907, *356*, 281; 1909, *364*, 1).

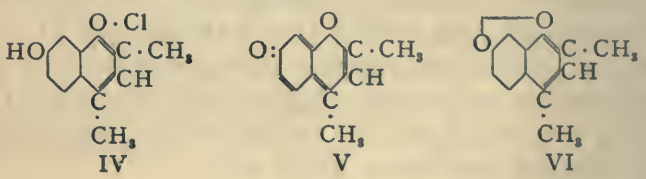
Hydroxylated benzopyranols had been obtained a few years previously by C. Bülow in conjunction with H. Wagner (*Ber.*, 1901, *34*, 1189) and W. von Sicherer (*ibid.*, 2368, 3889) by condensing phenols containing two hydroxyl groups situated in the meta position to one another with 1 : 3-diketones or 1 : 3-aldehyde-ketones. (Compare von Pechmann's synthesis of coumarin, *Ber.*, 1899, *32*, 3681.) Phenols not containing two meta hydroxyls reacted less readily, and those with negative substituents not at all.

As a simple case, we may consider the condensation of resorcin with acetylacetone; this was effected by Bülow and Wagner (*loc. cit.*) by leading dry hydrogen chloride into a solution of the substances in glacial acetic acid at 0°, allowing to stand 12 to 24 hours, adding absolute alcohol and filtering off the hydrochloride which, on crystallisation from a mixture of alcohol and aqueous hydrochloric acid, separated as straw yellow prisms. The base, liberated by means of sodium acetate from the hydrochloride, was orange and amorphous; its analysis agreed with the formula $C_{11}H_{10}O_2$ and not with the expected $C_{11}H_{12}O_3$. Bülow represented the changes by the scheme



The intermediate products (I) and (II) were capable of isolation; the hydrochloride was not recognised as an oxonium salt but the elements of hydrochloric acid were supposed to attach themselves to carbon atoms.[1]

In the light of our present knowledge, the hydrochloride must be represented by formula (IV), whilst the anhydrobase might have the constitution (V). An oxonium betaine formula (VI) is less probable.



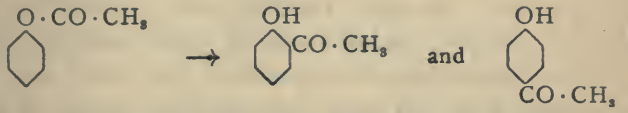
Phenacetein.

By boiling a mixture of 10 grams of phenol with 20 grams each of acetic anhydride and zinc chloride for half-an-hour, Raisinski obtained small amounts of a substance of unknown constitution which was named "phenacetein" (*J. pr. Chem.*, 1882, II, *26*, 54). To isolate the product, the melt was washed with water, the residue dissolved in hot dilute hydrochloric acid (5 per cent), allowed to stand some days, filtered and precipitated with ammonia (not an excess).

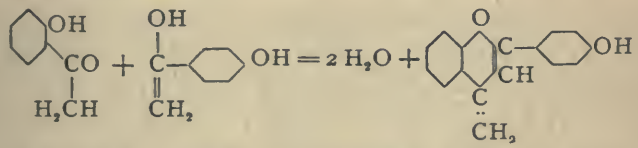
1) Other papers by Bülow dealing with the condensation of 1:3-diketones with phenols, *Ber.*, 1903, *36*, 190; 1904, *37*, 1791.

A crimson amorphous powder was thus obtained, insoluble in water and benzene, but easily soluble in alcohol, ether, glacial acetic acid and alkalies. The acid solution was yellow, the alkaline raspberry red, but became discoloured on standing, owing to decomposition.

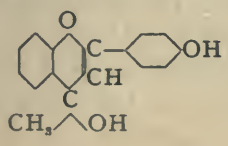
Bülow (*Ber.*, 1903, *36*, 732) explains the formation of the compound in the following manner. The phenyl acetate first produced is isomerised to a mixture of *o*- and *p*-hydroxyacetophenones.



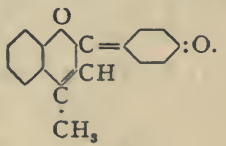
The two ketones then react with one another; the equation given by Bülow represents the para isomeride in the enolic condition.



This is the anhydro-derivative of 2-*p*-hydroxyphenyl-4-methylbenzopyranol (I); the anhydro-compound might be written with an alternative quinonoid formula (II)



I



II

Bülow's representation of the formation of phenacetein is analogous to that which has been given for the preparation of flavaniline from acetanilide by heating with zinc chloride. (See p. 34)

Resacetein.

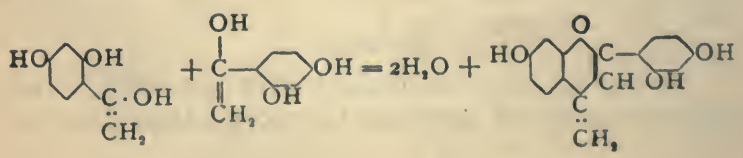
Several products are obtained when resorcin is heated with acetic acid and zinc chloride, amongst these a colour-

ing matter, resacetein, $C_{16}H_{12}O_4$ (Nencki and Sieber, *J. pr. Chem.*, 1881, II, *23*, 54). If comparatively small amounts of zinc chloride are used, resacetophenone ((2:4-dihydroxy-acetophenone) is the chief product (*loc. cit.*, 147) but this undergoes further condensation.

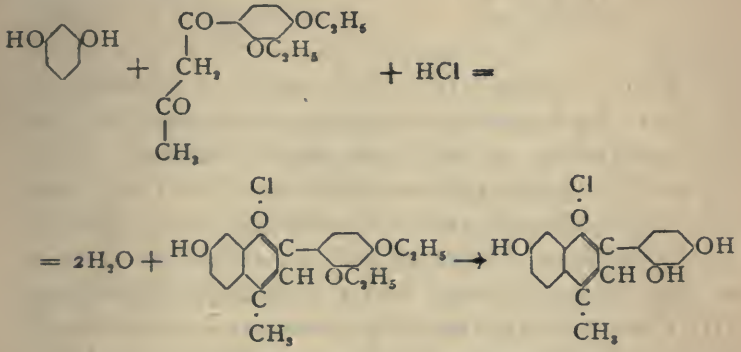
Nencki and Sieber boiled one part of resorcin, 2 parts of glacial acetic acid and 3 parts of zinc chloride for $1^1/_2$ to $2^1/_2$ hours under reflux, poured the melt into water, dissolved the precipitated resin in alcohol and filtered the solution into a large volume of water acidified with hydrochloric acid. Ammonia was then added until the liquid was only faintly acid and the precipitate thus produced was boiled repeatedly with alcohol until the residue dissolved in ammonia with a pink colour and showed no fluorescence. The alcoholic solution contained the acetfluorescein, $C_{24}H_{18}O_5$, which was formed in the reaction; the residual resacetein was then dissolved in warm dilute ammonia. On allowing the ammonia to evaporate by exposure to the air, red needles containing ammonia were deposited, the free resacetein being obtained as an amorphous powder. Bülow (*Ber.*, 1903, *36*, 733) used the same quantities but made a variation in the method of isolation.

Resacetein is soluble in alkalies with red colour; the solution, however, soon decomposes. The compound exhibits basic properties, being readily soluble in hydrochloric and acetic acids; Nencki and Sieber isolated the salts $C_{16}H_{12}O_4$, HCl, $2H_2O$ and $(C_{16}H_{12}O_4)_2H_2SO_4$. A *triacetyl*-derivative, $C_{16}H_9O_4(C_2H_3O)_3$, m. p. 229°, was prepared by Raisinski (*J. pr. Chem.*, 1882, II, *26*, 58).

Bülow (*Ber.*, 1903, *36*, 730) took up the examination of the compound and considered it was produced by the condensation of two molecules of resacetophenone according to the equation



In support of this view, Bülow found that resacetophenone and resorcin were produced on fusion with alkalies. Full confirmation was afforded by Bülow and C. Sautermeister's synthesis of the diethoxy-derivative (*Ber.*, 1904, *37*, 354) from diethoxybenzoylacetone and resorcin which gave resacetein on de-ethylation.



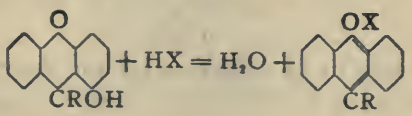
The condensation was effected by passing dry hydrogen chloride into a cooled solution of 9 grams of the diketone and 4 grams of resorcin in 45 parts of glacial acetic acid, the dealkylation by heating 3 grams of the hydrochloride with 25 cc. of concentrated hydrochloric acid to 150—180°.

The resacetein hydrochloride was thus obtained with only half a molecule of water of crystallisation, its identity was established by analysis and by preparation of free resacetein and its triacetyl-derivative.

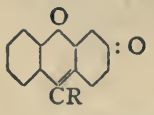
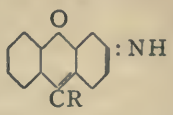
CHAPTER XI.

FLUORONE AND FLUORIM COMPOUNDS

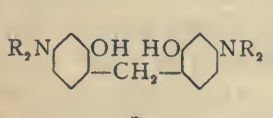
Xanthydrol and its derivatives yield salts with strong mineral acids according to the general reaction



These salts must be regarded as possessing ortho-quinonoid structure; if however positions 3 and/or 6 are occupied by hydroxyl or amino groups, the production of para quinonoid compounds is possible, e g.

Even a dialkylated amino group in position 3 or 6 renders the formation of *p*-quinonoid salts possible, though the constitution of such salts may correspond to an *o*-quinonoid oxinium salt configuration. Thus formaldehyde may be condensed with two molecules of a dialkyl-*m*-aminophenol to a diphenylmethane derivative (I), which by loss of water passes into a tetraalkyldiaminoxanthene (II). Oxidation of the latter compound gives a pyronine (III) to which the alternative oxonium constitutions (IV) and (V) may be assigned. The corresponding pseudo-base is in any case represented by the carbinol formula (VI).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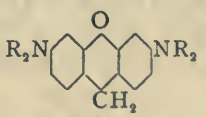
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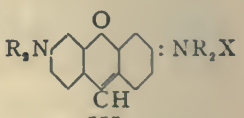
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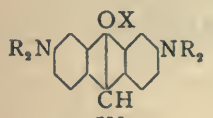
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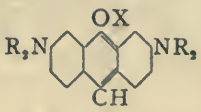
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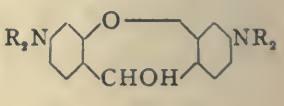
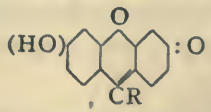

VI

The compound in which R = CH_3 was discovered by Bender in 1899; it forms the dyestuff known as Pyronine G.

Compounds containing groups of the structure



had been known in an impure state for many years, but it was not until after the discovery of the pyronines that their

constitution was recognised, whilst their preparation in a pure condition is of comparatively recent date.

The reactions between aldehydes and phenols were first studied by Baeyer; amongst them, the action of methylene diacetate on gallic acid was examined (*Ber.*, 1872, *5*, 1096). Two crystalline substances were obtained to which the formulae $C_{16}H_{12}O_{10}$ and $C_{16}H_{14}O_{11}$ were assigned.

At a much later date, Kleeberg (*Annalen*, 1891, *263*, 285) condensed formaldehyde with gallic acid; he gave the formula $C_{16}H_{12}O_{10}$ to the amorphous acid he obtained.

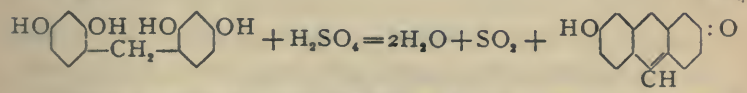
N. Caro (*Ber.*, 1892, *25*, 946) carried out the same reaction by boiling two molecular proportions of gallic acid and one of formaldehyde with 15 times the quantity of dilute (1 : 5) hydrochloric acid; the resulting white powder was crystallised from dilute alcohol. Caro recognised that the reaction took place according to the equation

$$2\,C_6H_2(OH)_3COOH + CH_2O = H_2O + CH_2[C_6H(OH)_3COOH]_2$$

Resorcin and pyrogallol when condensed with formaldehyde gave respectively tetra- and hexa-hydroxydiphenylmethane.

From compounds of this type, Möhlau and Koch (*Ber.*, 1894, *27*, 2887) prepared substances to which they gave the name of fluorones; these resulted by the action of sulphuric acid which removed the elements of water and oxidised the xanthene.

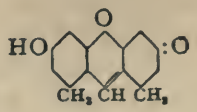
Thus "formaldehydoxyfluoron" was obtained by heating 10 grams of methylenediresorcin (2 : 4 : 2' : 4'-tetrahydroxydiphenylmethane) with 60 grams of concentrated sulphuric acid for 15 minutes to 140—150° and pouring the solution into water.



The analytical figures obtained for the substance agreed very badly with the proposed formula;[1] more satisfactory

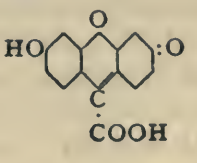
1) At a much later date, Kehrmann and S. M. Jones obtained 3-hydroxyfluorone in a pure condition (See p. 241).

results were obtained when methylenediorcin was condensed to "formaldehydoxytolufluoron",



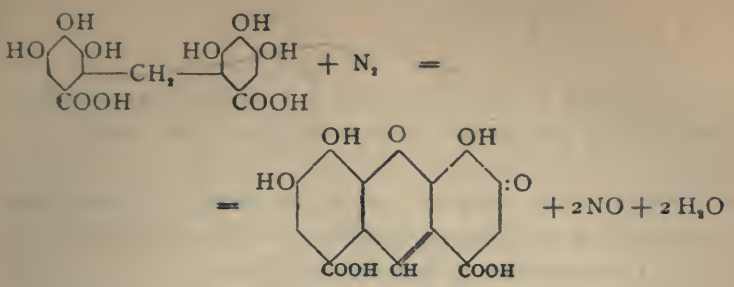
This compound separated from methyl alcohol in dark brown crystalline grains; the dilute alkaline solution exhibited a brown colour and a yellowish green fluorescence. Möhlau and Koch obtained a higher homologue by condensing acetaldehyde and resorcin to "acetaldehydfluoron"; they also prepared the pyronine resulting from acetaldehyde and dimethyl-*m*-amino-phenol. (Compare Kehrmann and S. M. Jones, see below.)

A carboxylic acid of the fluorone series was obtained by J. T. Hewitt and F. G. Pope (*Ber.*, 1896, *29*, 2824) by the oxidation of diacetylcitraconfluorescein; to this the following constitution was assigned.



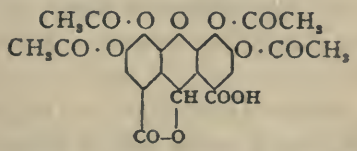
Möhlau and Kahl (*Ber.*, 1898, *31*, 259) further studied the reaction of formaldehyde with gallic acid and obtained four modifications of methylenedigallic acid. Two of these were crystalline and two amorphous; of each pair, one was more easily soluble in water than the other. The amorphous acids were looked on as polymerides of the crystalline forms.

A special study was made of the conversion of the difficultly soluble methylenedigallic acid into trihydroxyfluorone-dicarboxylic acid. This was effected by treating a sulphuric acid solution of the former acid with a nitrosyl sulphate solution at ordinary temperature, condensation and oxidation taking place.



Trihydroxyfluoronedicarboxylic acid, thus obtained, forms a violet crystalline powder giving satisfactory figures on analysis. It is sparingly soluble in water; the sulphuric acid solution is yellowish red; solutions in alkaline carbonates are violet, in ammonia blue, and in caustic alkalies greenish blue. None of the solutions are fluorescent; the compound behaves as a mordant dyestuff.

Acetylation gives a colourless crystalline acetyl derivative, m. p. 140.5—141.5°, to which the constitution



is assigned. On reduction, two atoms of hydrogen are taken up and a colourless leuco-compound (xanthene derivative) is formed.

It might be supposed that resorcin and pyrogallol would condense with monobasic acids giving compounds identical with those formed when these phenols are condensed with aldehydes and the resultant products subsequently oxidised. By heating 1 part of formic acid, 2 parts of resorcin and 2 parts of zinc chloride for one hour to 140—145°, Nencki and Schmid (*J. pr. Chem.*, 1881, II, *23*, 547) obtained a substance which, after purification, formed a brick red amorphous powder, and dissolved in alkalies giving yellowish red, non-fluorescent solutions. At the time, the formula $C_{19}H_{14}O_6$ and structure

$$[C_6H_3(OH)_2]_2C\begin{matrix}O\\|\\C_6H_3OH\end{matrix}$$

were assigned to the compound, but Nencki was unable to make acetyl or benzoyl derivatives (*J. pr. Chem.*, 1882, II, *25*, 279).

Oxalic acid might be expected to react with resorcin to give fluorone compounds, possibly the hydroxyfluoronecarboxylic acid obtained by Hewitt and Pope.

$$2\,C_6H_4(OH)_2 + \begin{matrix}COOH\\|\\COOH\end{matrix} = 2\,H_2O + HO\cdot C_6H_3\begin{matrix}O\\\diagup\\C\\\diagdown\\COOH\end{matrix}\begin{matrix}\diagup\\\\\diagdown\end{matrix}\begin{matrix}C_6H_3:O\\\\\end{matrix}$$

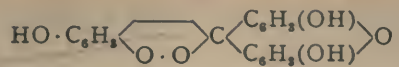
This does not seem to be the case; the reaction between the two compounds has been studied by different experimenters under varied condition; and a number of products of unknown constitution obtained.

Baeyer (*Ber.*, 1871, *4*, 662) heated the two substances with concentrated sulphuric acid obtaining a yellow substance, similar to euxanthone in some of its properties: Baeyer suggested it might be a mixture in which euxanthone was present.

Claus and Andreae (*Ber.*, 1877, *10*, 1305) heated resorcin (1 mol.) with dehydrated oxalic acid (2 mols.) in sealed tubes for 2 or 3 hours at 200°. The product was soluble in alkalies with green fluorescence and was given the formula $C_{13}H_8O_4$. Claus subsequently (*Ber.*, 1881, *14*, 2563) altered this to $C_{20}H_{14}O_7$ or $C_{20}H_{12}O_6$, the composition depending on whether the substance was dried at 100° or 150°.

Meanwhile Gukassianz (*Ber.*, 1878, *11*, 1184) effected condensation by heating with concentrated sulphuric acid to 120°; the compound he obtained was given the formula $C_{14}H_8O_5$.

Von Georgievics (*Mitt. des Technol. Gewerbe-Museums in Wien*, 1898, II, *8*, 364) condensed resorcin with twice its weight of anhydrous oxalic acid heating for 3 hours to 150—160° without pressure or a condensing agent. The product was given the formula $C_{19}H_{12}O_6$ and a provisional constitution



assigned to it.

Hewitt and A. E. Pitt (*Trans. Chem. Soc.*, 1899, *75*, 518) examined the product prepared according to the directions given by Gukassianz and altered the formula to $C_{20}H_{14}O_7$; the percentages of carbon and hydrogen are nearly identical. Salts of the type $C_{20}H_{13}O_7M$ and a triacetylated lactone, $C_{20}H_9O_6(COCH_3)_3$, were prepared. Acetylation in presence of a reducing agent gave a tetracetylated lactone, $C_{20}H_{10}O_6(COCH_3)_4$. Benzoylation probably effects cleavage of the molecule, possibly in accordance with the equation

$$C_{20}H_{14}O_7 + 3\,C_6H_5COCl = C_{14}H_7O_5(C_7H_5O) + C_6H_4(OC_7H_5O)_2 + 3\,HCl$$

Although the compounds prepared by Gukassianz and Claus possess the same formulae, they are isomeric, not identical.

Generally, better defined compounds are obtained by the condensation of resorcin with aromatic aldehydes and acids or the chlorine compounds corresponding to the acids, though Michael and Ryder (*Amer. Chem. J.*, 1884, *5*, 338) obtained a resin of the empirical formula $C_{26}H_{20}O_4$ by adding small quantities of hydrochloric acid to an alcoholic solution of resorcin and benzaldehyde.

O. Döbner (*Annalen*, 1883, *217*, 234) obtained *Resorcinbenzein* by heating resorcin (2 mols.) with benzotrichloride (1 mol.) to 180—190°. After extracting the product with boiling water it was dissolved in caustic soda, reprecipitated with acetic acid and crystallised from a mixture of glacial acetic acid and alcohol. To the compound prepared in this manner, the formula $C_{33}H_{30}O_9$ was assigned, i. e. it was supposed that the first product of the action of benzotrichloride on resorcin was a tetrahydroxytriphenylmethyl chloride which then exchanged chlorine for oxygen.

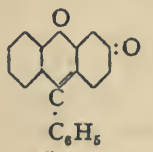
$$C_6H_5\cdot CCl_3 + 2C_6H_4(OH)_2 = 2HCl + C_6H_5\cdot CCl[C_6H_3(OH)_2]_2$$

$$2\,C_{19}H_{15}O_4Cl + H_2O = 2\,HCl + C_{33}H_{30}O_9$$

By loss of water at 130°, a product of the composition $C_{38}H_{26}O_7$ was obtained.

Resorcinbenzein, as prepared by Döbner, forms large violet red prisms, yellow by transmitted light. The compound is insoluble in water, ether and benzene; when freshly precipitated it dissolves readily in hot alcohol though the crystals are very sparingly soluble.

Döbner's material seems to have been impure for F. Kehrmann and O. Dengler (*Ber.*, 1908, *41*, 3445) proved definitely that the compound must be a derivative of 9-phenylfluorone[1] (I or II).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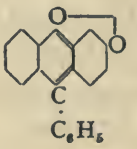
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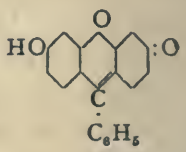
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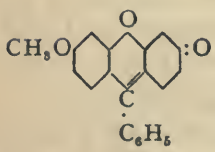
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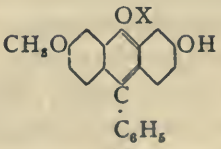
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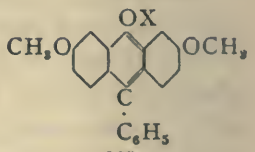
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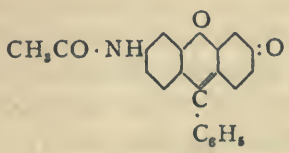
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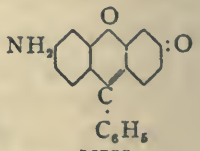
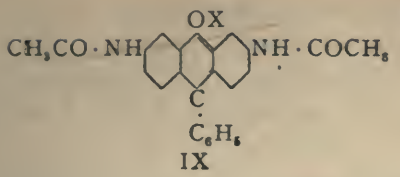
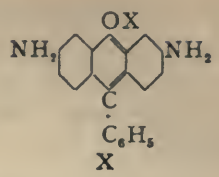

VIII

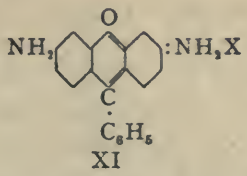
1) Kehrmann represented fluorones, safranones and analogous compounds with *o*-quinonoid oxonium betaine structure (II). Correspondingly, rosamines were represented with an oxonium (X) instead of an ammonium (XI) structure, but since Kehrmann himself now admits *p*-quinonoid constitution in the case of many compounds which he previously looked on as *o*-quinonoid, there seems no reason to do more than refer to views which have been largely abandoned and which the present writer never shared.



IX



X



XI

When *m*-acetylaminophenol was condensed with benzotrichloride, 3:6-diacetamino-9-phenylxanthonium chloride (IX) formed the chief product, but was accompanied by a certain amount of 3-acetamino-9-phenylfluorone (VII) which yielded 3-amino-9-phenylfluorone (VIII) on hydrolysis. By diazotisation and treatment with alcohol, phenylfluorone (I) was obtained, whilst if the diazo solution was boiled with water, 3-hydroxy-9-phenylfluorone (III) resulted. The latter compound was compared with resorcinbenzein obtained by the condensation of benzotrichloride with resorcin and found to be identical. Diacetaminophenylxanthonium salts gave the simplest phenylrosamine (X or XI) on hydrolysis.

Kehrmann and Dengler (*Ber.*, 1909, *42*, 870) further studied the action of methyl sulphate on resorcinbenzein, giving at the same time a method for the purification of the latter substance (*loc. cit.*, 873). The melt obtained from resorcin and benzotrichloride was treated with a current of steam, then dissolved in hot dilute ammonia, and precipitated whilst hot with acetic acid. The dried precipitate was rubbed up with alcohol to a thin paste, allowed to stand half-an-hour, and washed with some alcohol. 20 grams of the filtered product were suspended in 100—150 cc. of alcohol, raised to the boil, and 10—15 cc. of fuming hydrochloric acid added. The material went immediately into solution and then set to a paste of the hydrochloride. After cooling, the salt was collected, again dissolved in alcohol of 80—90 per cent and

reprecipitated by addition of hydrochloric acid. Finally the compound was dissolved in hot ammonia solution, precipitated with dilute acetic acid, collected, dried and crystallised from a boiling mixture of benzene and alcohol, or from hot nitrobenzene.

Resorcinbenzein melts at 333°; if pure, the substance should give a clear yellow solution, and then a separation of pure yellow crystals on adding hydrochloric acid to its alcoholic suspension. The alkaline solution, if concentrated, appeors orange red by transmitted light, the dilute solution appears yellow in thick and rose red in thin layers; it fluoresces like fluorescein, but more feebly.

The following are the chief properties of phenylfluorone and its derivatives.

9-*Phenylfluorone.* Prepared from aminophenylfluorone by diazotisation in fairly concentrated sulphuric acid solution and addition to cold alcohol (*Ber.*, 1908, *41*, 3444, 874). Small orange crystals, m. p. 204°.

3-*Methoxy*-9-*phenylfluorone* (*Ber.*, 1909, *42*, 874). On adding methyl sulphate to a solution of resorcinbenzein (III) in nitrobenzene at 150°, methoxyhydroxyphenylxanthonium methylsulphate (V) is formed; the corresponding chloride may be salted out from its aqueous solution. These salts are orange yellow in colour; their solutions are somewhat readily hydrolysed on warming; addition of sodium carbonate solution precipitates 3-methoxy-9-phenylfluorone (IV). This compound separates from alcohol as chrome red bundles of needles, m. p. 202°. It is more basic than resorcinbenzein; the solution in concentrated sulphuric acid is golden yellow in colour and shows a green fluorescence.

3:6-*Dimethoxy*-9-*phenylxanthonium salts* (VI) are obtained by adding methyl sulphate to a solution of the preceding compound in nitrobenzene at 150°. When sodium carbonate is added to the aqueous solution of the resulting methylsulphate, the corresponding carbinol base is precipitated which, when crystallised from methyl alcohol, yields the cor-

responding colourless methyl ether of m. p. 112°. From the latter, dimethoxyphenylxanthonium chloride is readily obtained by the action of hydrochloric acid and methyl alcohol. The salt is soluble in water with very slight hydrolysis; other salts, e. g. bichromate and iodide, may be obtained by double decomposition.

3-*Acetamino-9-phenylfluorone* (VII, *Ber.*, 1908, *41*, 3443). Shining, chrome red bundles of needles; gives bright yellow salts which exhibit a green fluorescence in solution.

3-*Amino-9-phenylfluorone* (VIII, *loc. cit.* 3444). Obtained by acid hydrolysis of the preceding compound. Dark red needles, m. p. 305°. The salts give yellowish red solutions.

3:6-*Diacetamino-9-phenylxanthonium salts* (IX, *loc. cit.* 3446). The chloride forms yellowish brown needles with blue reflex, soluble in hot water with pure yellow colour and green fluorescence.

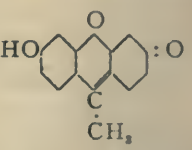
3:6-*Diamino-9-phenylxanthonium salts* or simplest *Rosamine* (X or XI). The preceding compound is hydrolysed by mineral acids, both acetyl groups are removed and salts of type X or XI (more probably the latter) are produced. The orange red chloride is easily soluble and dyes tannined cotton orange.

In a later paper (*Annalen*, 1910, *372*, 287) Kehrmann in conjunction with O. Dengler, K. Scheunert, R. Silzer, S. M. Jones and X. Vogt described a large number of compounds of xanthonium structure. Several 3:6-diacetamino-9-phenylxanthonium salts were described and their analyses given, and the simplest phenorosamine and 3-amino-6-hydroxy-9-phenylxanthonium chloride were more closely examined. Acetylaminophenylfluorone adds on methyl sulphate giving 3-acetylamino-6-methoxy-9-phenylxanthonium methylsulphate from which a number of other salts were prepared. Quinol and toluquinol were found to yield benzeins, and several salts were prepared in each case.

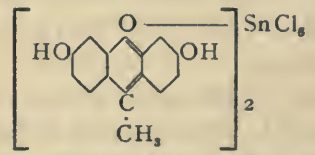
Reference has already been made to the "acetaldehydfluoron" of Möhlau and Koch, Kehrmann and S. M. Jones obtained this compound in a pure condition. By heating

resorcin and 2:4-dihydroxyacetophenone (resacetophenone) with stannic chloride to 160—180°, a stannichloride of the composition $(C_{14}H_{11}O_5)_2SnCl_6$ was obtained; this crystallised in large dark red granules with a blue metallic reflex and furnished 3-hydroxy-9-methylfluorone when treated in aqueous solution with sodium acetate. Condensation had taken place according to the equation

$$C_6H_4(OH)_2 + C_6H_3(OH)_2 \cdot COCH_3 = 2\,H_2O +$$

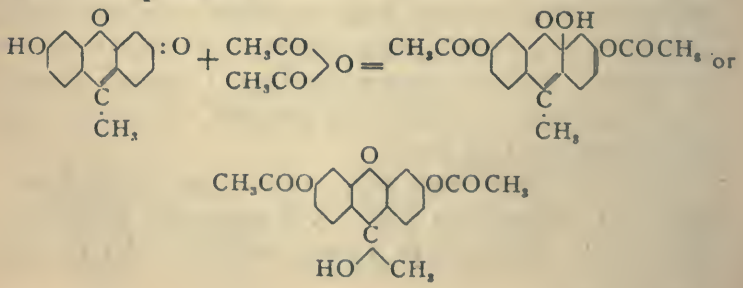


the hydroxymethylfluorone reacting with stannic chloride and hydrochloric acid resulting from the hydrolysis of some of the stannic cloride to form the salt

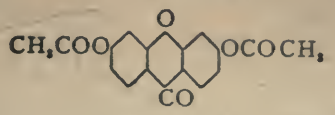


3-*Hydroxy-9-methylfluorone* crystallises in large dark red plates with a blue reflex and melts at 238° with decomposition after previously sintering at 229°. Its yellow solutions show an intense green fluorescence; the compound is identical with the acetfluorescein of Nencki and Sieber. It reacts with acids forming 3:6-dihydroxy-9-methylxanthonium salts; the chloride, bromide, iodide, platinichloride and picrate have been prepared.

On heating with acetic anhydride and sodium acetate, the diacetyl derivative (m. p. 200°) of the corresponding carbinol is produced,

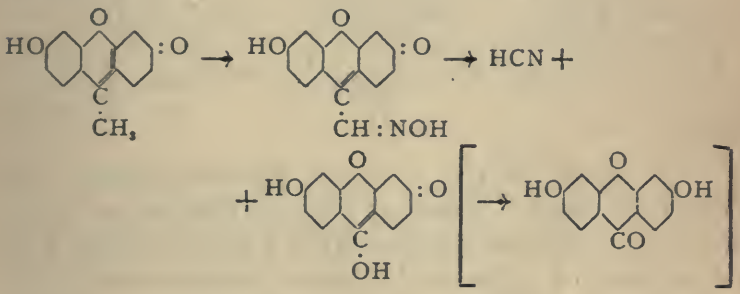


but 3:6-diacetoxyxanthone (m. p. 204°),



is formed at the same time. The parent 3:6-dihydroxyxanthone had been previously obtained by R. Meyer and A. Conzetti by dehydration of 2:4:2':4'-tetrahydroxybenzophenone (*Ber.*, 1897, *30*, 971).

When 3-hydroxymethylfluorone is acted on by glacial acetic acid and sodium nitrite, an oximino-derivative is obtained as dark red prisms with a green reflex and of m. p. 200°. This compound is quantitatively decomposed by caustic soda solution yielding sodium cyanide and 3:6-dihydroxyxanthone.

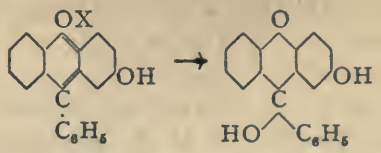


By reducing 3:6-dihydroxyxanthone with sodium amalgam, 3-hydroxyfluorone is obtained. This forms a brick red crystalline powder with a blue reflex; the corresponding dihydroxyxanthonium chloride is yellow.

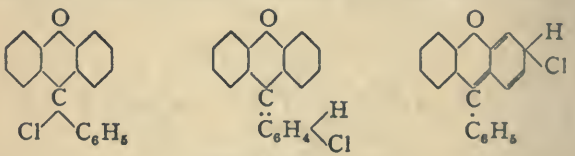
In all Kehrmann's papers of this period, the fluorones were represented with orthoquinonoid formulae whilst paraquinonoid structure has been assigned to these compounds in this book.

Decker held to the view that the free fluorones were paraquinonoid, thus whilst 3-hydroxy-9-phenylfluorone is capable of existence, 2-hydroxy-9-phenylxanthonium salts furnish colourless 2-hydroxy-9-phenylxanthen-9-ol (m. p. 158

to 160°, decomp.) when hydrolysed (W. Kropp and H. Decker, *Ber.*, 1909, *42*, 578).



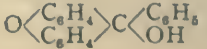
Quite a different view of the constitution of the salts formed by the fluorones with acids was put forward by M. Gomberg and L. Cone (*Annalen*, 1909, *370*, 142). These authors considered the substances in question to be really carbonium salts which like triphenylmethyl chloride can exist in both benzenoid (I) and quinonoid (II and III) forms.

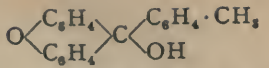


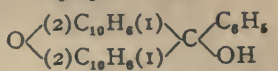
I II III

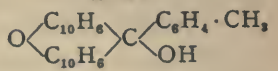
In favour of this view, the following evidence was brought forward. On passing hydrogen chloride into a solution of a xanthenol (xanthydrol) in a neutral solvent a hydrochloride of a xanthenol chloride is obtained as a yellow precipitate; when the molecule of hydrochloric acid is removed a colourless chloride remains which behaves in a similar manner to triphenylmethyl chloride. These colourless, normal xanthenol chlorides give yellow solutions when dissolved in liquid sulphur dioxide, which is considered to show that tautomeric forms exist. Moreover, when phenyl-*p*-bromoxanthenol bromide is treated with silver chloride, phenyl-*p*-chloroxanthenol chloride results.

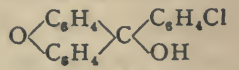
A large number of compounds were prepared and described in the paper referred to, salts derived from the following xanthenols being obtained.

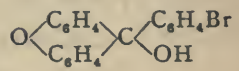
Phenylxanthenol, 

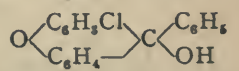
p-Tolylxanthenol, m. p. 150°, 

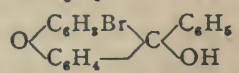
Phenyldinaphthoxanthenol, m. p. 265—268°, 

p-Methoxyphenyldinaphthoxanthenol, 

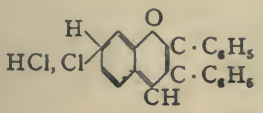
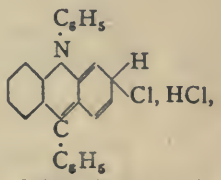
p-Chlorophenylxanthenol, m. p. 173°, 

p-Bromophenylxanthenol, m. p. 183°, 

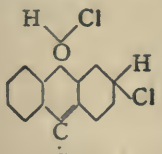
Phenyl-*p*-chloroxanthenol, m. p. 164°, 

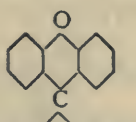
Phenyl-*p*-bromoxanthenol, m. p. 178°, 

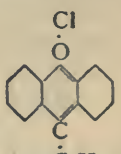
The salts of the pyranols and phenylacridols were considered as having analogous structures, 2:3-diphenylbenzopyranol chloride hydrochloride and 5:10-diphenylacridol chloride hydrochloride being regarded as possessing the constitutions

 and 

Kehrmann (*Annalen*, 1910, *372*, 287) refers to the work of Gomberg and Cone but disagrees with them as to the carbonium structure of the salts derived from the xanthenols. His view is that the highly coloured chloridehydrochloride has a structure represented by (I) and when heated it loses hydrogen chloride passing either into the colourless carbinol chloride (II) or the coloured oxonium chloride (III)


I

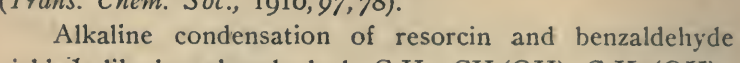

II


III

3-Hydroxy-9-phenylfluorone may also be obtained from resorcin and benzaldehyde, a clean method of condensation having been worked out by F. G. Pope and H. Howard (*Trans. Chem. Soc.*, 1910, *97*, 78).

Alkaline condensation of resorcin and benzaldehyde yielded dihydroxybenzhydrol, $C_6H_5 \cdot CH(OH) \cdot C_6H_3(OH)_2$, which when heated with resorcin and zinc chloride gives 3:6-dihydroxy-9-phenylxanthene, m. p. 136°.

$$C_6H_5 \cdot CHOH \cdot C_6H_3(OH)_2 + C_6H_4(OH)_2 =$$

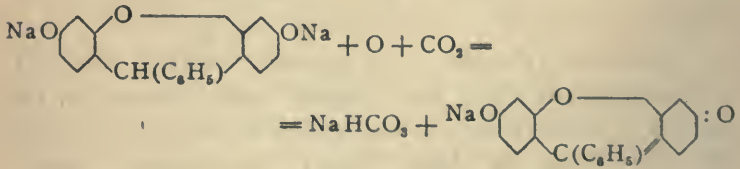


$$= H_2O + HO \cdot C_6H_3 \langle O\text{-}\rangle C_6H_3 \cdot OH$$

$$\text{(CH(C}_6\text{H}_5\text{))}$$

This general method is capable of wide application and Pope and his co-workers have produced many xanthene and dihydroacridine derivatives by the use of various phenols and primary bases.

Pope and Howard (*Trans. Chem. Soc.*, 1910, *97*, 1026) oxidised the 3:6-dihydroxy-9-phenylxanthene to 3-hydroxy-9-phenylfluorone by solution in N/1 caustic soda solution and passage of a current of air for two or three days. On addition of acid, a dark brown precipitate was obtained which was crystallised from alcohol, it separated from this solvent in dark brown scales with a deep blue reflex.



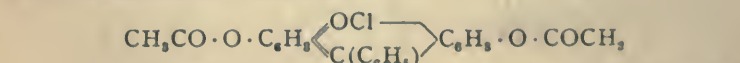
$$NaO \langle O\text{-}\rangle ONa + O + CO_2 =$$

$$\text{(CH(C}_6\text{H}_5\text{))}$$

$$= NaHCO_3 + NaO \langle O\text{-}\rangle :O$$

$$\text{(C(C}_6\text{H}_5\text{))}$$

The substance gave satisfactory results on analysis, formed a hydrochloride, yielded a dark brown monoacetyl derivative with acetic anhydride and fused sodium acetate, whilst acetyl chloride converted it into 3:6-diacetoxy-9-phenylxanthonium chloride

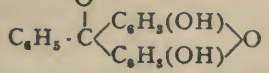


$$CH_3CO \cdot O \cdot C_6H_3 \langle OCl\text{-}\rangle C_6H_3 \cdot O \cdot COCH_3$$

$$\text{(C(C}_6\text{H}_5\text{))}$$

But a brief reference will be made to H. von Liebig's views as to the constitution of resorcinbenzein (*J. pr. Chem.*,

1908, II, *78*, 534). Having obtained resorcinbenzein by the condensation of resorcin with benzoic anhydride or benzil, von Liebig expressed the structure by the formula



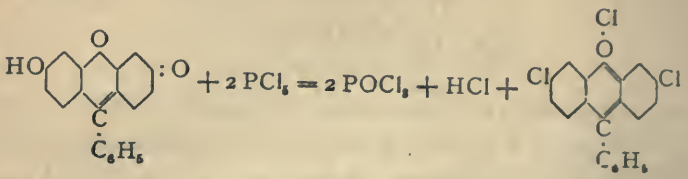
This agrees with the composition assigned by Döbner to his resorcinbenzein after drying at 130°. Cohn also formulated the product of the action of benzoic acid on resorcin in presence of zinc chloride as $C_{38}H_{26}O_7$ (*Ber.*, 1893, *26*, 2064; (*J. pr. Chem.*, 1893, II, *48*, 387). Von Liebig obtained other anhydrides such as $C_{76}H_{52}O_{13}$, C_2H_5OH, whilst in later papers it was assumed that the Döbner method of synthesis gave rise to a mixture of products (*J. pr. Chem.*, 1912, II, *85*, 97, 241; 1913, II, *88*, 26). Of these compounds α-resorcinbenzein has the formula $C_{19}H_{12}O_3$; it is hydroxyphenylfluorone. Other compounds isolated are β-resorcinbenzein $(C_{19}H_{12}O_3)_2$, C_2H_5OH, γ-resorcinbenzein, $(C_{19}H_{12}O_3)_4$, H_2O, C_2H_5OH and the dihydroxybenzophenone compound of the γ-benzein.

The constitution of the oxonium salts of the fluorescein ether-esters formed the subject of a further communication (von Liebig, *Ber.*, 1913, *46*, 2736) which led to a reply on the part of Kehrmann (*ibid.* 3028) and a counter reply from von Liebig (*ibid.* 3593).

In view of the decisive results obtained by F. G. Pope and H. Howard, there is no necessity to discuss von Liebig's views further since several of the compounds he described possessed different formulae to those assigned to them. Following up their earlier work, Pope and Howard (*Trans. Chem. Soc.*, 1911, *99*, 545) condensed dihydroxybenzophenone with phenol to 9-phenylfluorone which on treatment with acetyl chloride yielded 3-acetoxy-9-phenylxanthonium chloride. Condensation with 2-naphthol gave 11-phenylphenonaphthofluorone, m. p. 237°.

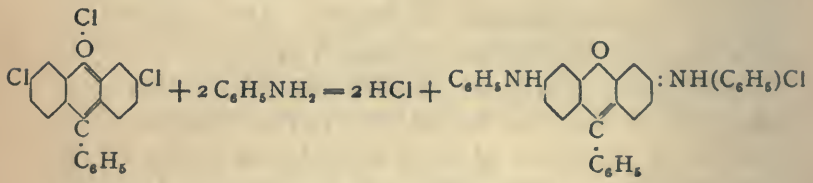
From 3-hydroxy-9-phenylfluorone a number of interest-

ing compounds were obtained through 3:6-dichloro-9-phenylxanthonium chloride. This reddish-yellow compound (decomposes about 200°) was obtained by the action of phosphorus pentachloride on hydroxyphenylfluorone in presence of phosphoryl chloride.



Potassium cyanide in alcoholic solution gives 3:6-dichloro-9-cyano-9-phenylxanthene which can be hydrolysed to the corresponding carboxylic acid, whilst sodium alkyloxides convert dichlorophenylxanthonium chloride into 3:6-dichloro-9-phenylxanthyl ethers.

Towards bases, the dichloroxanthonium chloride is reactive, the chlorine atoms in positions 3 and 6 being replaced by amine residues.



This reaction was studied with aniline, *o*- and *p*-toluidines, 2-naphthylamine, *p*-phenylenediamine and *p*-aminophenol. These rosamines gave blue to violet solutions which were generally fluorescent.

The normal manner in which 3-hydroxy-9-phenylfluorone reacts led Pope and Howard (*Trans. Chem. Soc.*, 1914, *105*, 251) to repeat much of von Liebig's work. Compounds were prepared according to his directions and compared with known products. The different varieties of resorcinbenzein described by von Liebig were all found to be 3-hydroxy-9-phenylfluorone and the same held for the two anhydroresorcinbenzeins. The *α*-, *β*- and *γ*-hydrochlorides all had the

formula $C_{19}H_{12}O_3$, HCl, i. e. they were simply dihydroxy-9-phenylxanthonium chloride. The barium salt, acetyl derivative and acetylated reduction product were all found to be quite straightforward compounds, whilst it was shown that the products of alkaline fusion are resorcin and dihydroxybenzophenone and not a pair of compounds $C_{38}H_{30}O_9$ and $C_{19}H_{10}O_3$ as von Liebig had stated.

Trihydroxyfluorones

C. Liebermann and S. Lindenbaum (*Ber.*, 1904, *37*, 1171) examined the behaviour of benzaldehyde towards the three trihydroxybenzenes; in the case of 1:2:4-trihydroxybenzene a definite fluorone was obtained.

2:3:7-*Trihydroxy-9-phenyl-6-fluorone* was obtained by dissolving 5 grams of benzaldehyde and 20 grams of 1:2:4-trihydroxybenzene in 200 cc. of alcohol, adding 32 grams of concentrated sulphuric acid diluted with 160 cc. of water and heating the mixture in a boiling water-bath for 5 or 6 hours. On cooling, much of the sulphate of the dyestuff separated as small yellow needles; the remainder was recovered from the mother liquor; the best total yield was 55 per cent.

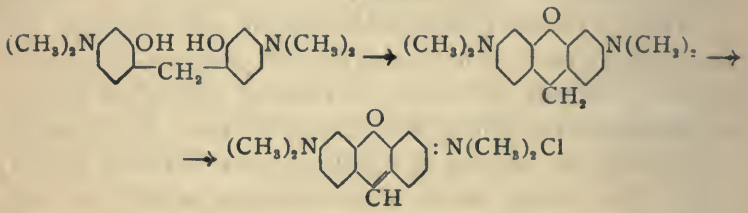
The free fluorone does not melt below 300° and is sparingly soluble in all solvents. The alcoholic solution shows a green fluorescence, the alkaline solution has a beautiful carmine colour. A triacetyl derivative and various salts were prepared.

2:3:7-Trihydroxy-9-methyl-6-fluorone was obtained from 1:2:4-trihydroxybenzene and paraldehyde in 90 per cent alcoholic solution by adding about 2 per cent of concentrated sulphuric acid. It is fixed by mordants; alumina gives a bright orange yellow, iron mordants a brownish violet.

CHAPTER XII

PYRONINES AND ROSAMINES

Though the fluorones possess considerable interest they are technically of little importance except in so far as the chloroxanthonium chlorides are capable of reacting with amines and giving pyronine dyes. The latter may, however, be obtained more readily by condensing formaldehyde with *m*-aminophenols to diaminodihydroxydiarylmethanes, closing the xanthene ring and oxidising the resulting leuco-compound to a dyestuff. This may be illustrated by reference to the production of Pyronine G from dimethyl-*m*-aminophenol and formaldehyde.



Pyronine

The first patents (Brit. P. 8673/1889; F. P. 198785; D. R. P. 54190/1889) relating to the production of pyronines were taken out by F. Bayer and Co., who found that methylene chloride and dimethyl-*m*-aminophenol reacted with one another. 3.4 kilos of the former and 11 kilos of the latter were heated for 3 or 4 hours at 130—140° under pressure, and the mass slowly introduced into 60 kilos of concentrated sulphuric acid (66° Bé.) whereupon hydrogen chloride and sulphur dioxide escaped.

After heating for half-an-hour at 160° the mixture was poured into 200 litres of cold water and the excess of sulphuric acid neutralised with milk of lime. After thorough boiling and settling, the solution was decanted and filtered and the colour base precipitated by an excess of caustic soda. The resinous base was dissolved in 9 kilos of hydrochloric

acid (33 %) and 50 litres of water, and the colour salted out as a double zinc salt by the addition of sodium and zinc chlorides. Although a resinous precipitate was thus obtained, it became crystalline on standing for 24 hours; it was then dried at 30—40°.

A. Leonhardt and Co. (D. R. P. 58955/1889) showed that for the conversion of dialkyl-*m*-aminophenols into diphenylmethane derivatives, formaldehyde could be used instead of methylene halides as in Bayer's patent.

Example 1. An aqueous solution (30 per cent) of three kilos of formaldehyde is added to 28 kilos of dimethyl-*m*-aminophenol in 60 litres of alcohol; the solution becomes warm and after some time the tetramethyldiaminodihydroxydiphenylmethane crystallises out. After a recrystallisation from spirit it is obtained as shining leaflets, m. p. 180°.

Example 2. Add a 30 per cent aqueous solution of 3 kilos of formaldehyde to a solution of 33 kilos of diethyl-*m*-aminophenol in 70 litres of methyl alcohol and 10 litres of concentrated hydrochloric acid. After standing for some time at the ordinary temperature, add a solution of 15 kilos of sodium acetate in 30 kilos of methyl alcohol, filter off the condensation product and recrystallise. M. p. 165°.

The same firm took out additional patents, simplifying the procedure and using other aminophenols.

Thus the use of an alcohol as a solvent is omitted in D. R. P. 63081/1892.

Example 1. 14 kilos of dimethyl-*m*-aminophenol or 16 kilos of diethyl-*m*-aminophenol are dissolved in 100 litres of water and 11.1 litres of concentrated hydrochloric acid. 3.8 kilos of 40 per cent formaldehyde solution are added and when the smell of the latter has disappeared, the tetraalkyldiaminodihydroxydiphenylmethane is precipitated by addition of sodium carbonate solution.

Example 2. In this case the condensation is carried out in alkaline solution, the quantities of dialkyl-*m*-aminophenols mentioned in example 1 being dissolved in 12 kilos of 33 per cent lye diluted with 100 litres of water. 3.8 kilos of 40 per

cent formaldehyde solution are added, and when the smell of the aldehyde has disappeared, the base is precipitated by acetic acid.

A. Leonhardt and Co. deal with the condensation of aminocresol ($CH_3 : NH_2 : OH = 1 : 2 : 4$) in another patent. (D. R. P. 75 373/1893.)

Example 1. 12 kilos of the aminocresol are dissolved in 12 litres of 30 per cent hydrochloric acid, and 200 litres of water and 3.8 kilos of 40 per cent formaldehyde solution added. When the smell of the aldehyde has disappeared, the mixture is warmed to 60° and finally precipitated by sodium carbonate.

Example 2. 12.5 kilos of the aminocresol in 300 litres of water acidified with 2.5 kilos of concentrated sulphuric acid are treated with 3.8 kilos of 40 per cent formaldehyde solution in the cold; in this case the condensation product is isolated as the sparingly soluble sulphate.

Leonhardt's first patents for the manufacture of pyronine were taken out in 1899 (Brit. P. 13 217/1889; U. S. P. of Bender 359 916; F. P. 200 401; D. R. P. 59 003) and marks G and B were placed on the market. The procedure is illustrated as follows.

Example 1. 2.7 kilos of tetramethyldiaminoxanthene are dissolved in hot dilute hydrochloric acid (4 kilos of concentrated acid to 120 litres of water). After cooling, aqueous sodium nitrite is added as long as formation of colouring matter takes place, about 0.8 kilo of nitrite being necessary. The dyestuff is then salted out with sodium and zinc chlorides.

Example 2. The oxidation of 5 kilos of tetramethyldiaminoxanthene dissolved in 4 kilos of concentrated hydrochloric acid, 4 kilos of 50 per cent acetic acid and 200 litres of water is effected by adding an aqueous suspension of about 4 kilos of lead peroxide. The lead in solution is removed by addition of sodium sulphate solution and the dyestuff salted out with sodium and zinc chlorides.

Example 3. 10 kilos of tetraethyldiaminoxanthene are dissolved in about 200 litres of dilute sulphuric acid (about

20 per cent) and treated with 30 kilos of ferric chloride solution of s. g. 1.14. The mixture is then heated for some time on the water-bath until dyestuff formation is complete, the solution allowed to cool, the dyestuff filtered off and purified by recrystallisation.

The dye prepared from diethyl-*m*-aminophenol gives bluer shades than the ordinary pyronine.

Pyronine G (Leonhardt, Sávoz et Boasson, Bayer) is soluble in water and alcohol with red colour and yellow fluorescence. (Absorption, $\lambda = 548.3$ and 509.6.) Hydrochloric acid gives a bright orange solution, concentrated sulphuric acid a reddish yellow solution becoming red on dilution. Caustic soda gives a pale red precipitate, soluble in alcohol or acetone with red colour and yellow fluorescence, the benzene solution does not fluoresce. Cotton (tannin and antimony mordant), silk and wool are dyed carmine red, moderately fast to light and soap.

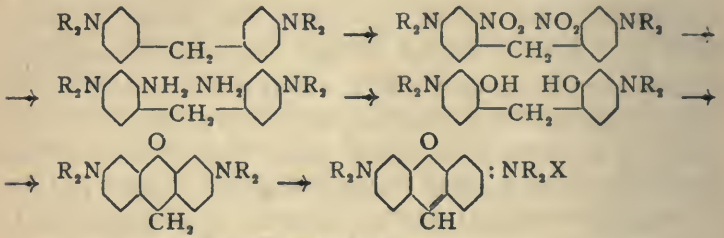
Pyronine has formed the subject of scientific investigations, R. Meyer and P. Koch (*Ber.*, 1894, *27*, 2896) refer to it briefly and J. Biehringer (*Ber.*, 1894, *27*, 3301; *J. pr. Chem.*, 1896, II, *54*, 217) at greater length. The latter author finds that tetramethyldiaminodihydroxydiphenylmethane melts at 178°, tetramethyldiaminoxanthene at 116°. Biehringer also synthesised the compound (*loc. cit.*, 240) starting with tetramethyldiaminodiphenylmethane which was dinitrated in the ortho positions to the methane carbon atom. The nitro-groups were reduced to amino-groups which were in turn replaced by hydroxyl. After closing the ring and oxidising the resulting xanthene derivative, Pyronine G was obtained. Incidentally this shows that the "Rose" of Gerber and Co. (D. R. P. 60 505/1889) is identical with Pyronine.

By the alkaline oxidation of Pyronine G with ferricyanide (*loc. cit.*, 235) Biehringer obtained tetramethyldiaminoxanthone, m. p. 240 243°. This compound dissolves in acids with yellow colour and beautiful green fluorescence.

Biehringer has also described the condensation of diethyl-

m-aminophenol with formaldehyde and the preparation of the corresponding tetraethylpyronine.

As mentioned above, A. Gerber and Co. of Basel (D. R. P. 60 505/1889) obtained dyes known as "Rose" and "Kasan Red" identical with Pyronine G. The process followed was to start with tetramethyldiaminodiphenylmethane which is obtained by the action of formaldehyde on dimethylaniline and then carry out the series of reactions indicated by the scheme



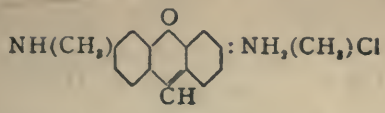
R = alkyl, X = acid radide.

10 kilos of tetramethyldiaminodiphenylmethane dissolved in 200 kilos of concentrated sulphuric acid are nitrated at 0° (5° at the highest) by a mixture of 9.5 kilos of nitric acid (53 per cent) and 10 kilos of concentrated sulphuric acid. After standing some hours the solution is poured into 1000 litres of ice water and the solution directly reduced with 40 kilos of zinc dust. After reduction, the solution is filtered, cooled to 5—10° by addition of ice and diazotised by 57 kilos of sodium nitrite in 100 litres of water; the diazonium compound loses nitrogen in the cold with much foaming.

To produce the dyestuff, 50 kilos of 30 per cent ferric chloride solution are added and the temperature gradually raised to boiling; the deep cherry red solution is then salted out as the zinc chloride double salt by the addition of 200 kilos of sodium chloride. The precipitate may be purified by crystallisation.

Acridine Red. By oxidation of Pyronine G with potassium permanganate, two methyl groups are apparently removed and a dye is produced which was marketed as "Acri-

dine Red" B, BB, 3 B; the constitution appears to be represented by



The commercial dye forms a brown powder soluble in water with a red colour and dyeing cotton (tannin and antimony mordant) rose red, fast to washing and moderately fast to light.

The patents (Brit. P. 1231/1892; U. S. P. 489 623 of Bender and Kämmerer; F. P. 219 023; D. R. P. 65 282/1892) dealing with the preparation of the so called acridine red claim that the bluish red colouring matters obtained from dialkyl-*m*-aminophenols (phthaleins, succineins, benzeins, pyronines) are converted into yellower dyestuffs by oxidation.

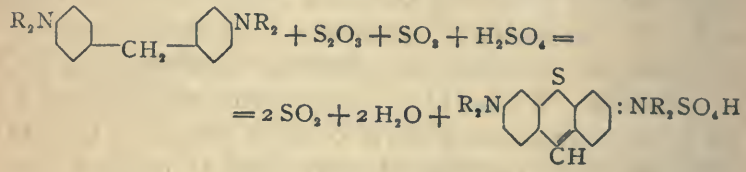
Example. 8 kilos of succinrhodamine are dissolved in 400 litres of water and 50 litres of acetic acid and 4 kilos of permanganate in 100 litres of water added to the cold solution with constant stirring. After standing some time the mixture is boiled, filtered and the filtrate salted out with zinc chloride.

A. Leonhardt and Co. (Brit. P. 12 323/1893; D. R. P. 75 138/1893) oxidise the diaminoditolylmethane oxide obtained from aminocresol ($CH_3 : NH_2 : OH = 1 : 2 : 4$) with peroxides, bichromates or ferric chloride. Thus a solution of 2.5 kilos of the base in 70 litres of 15 per cent sulphuric acid is treated with 12 litres of ferric chloride solution (s. g. 1.14), 12 litres of zinc chloride solution (s. g. 1.45) and 25 litres of saturated brine. The mixture is frequently stirred at ordinary temperature, the colouring matter filtered off and purified by solution in hot water and salting out with sodium and zinc chlorides.

Additional patents (Brit. P. 1414/1894; F. P. 200 401; D. R. P. 84 955) describe the alkylation of the above mentioned dyestuff, 2 kilos of the colour base being heated with 25 litres of alcohol and 2 kilos of ethyl bromide for 3 hours

at 130—140°. After cooling and dilution with 200 litres of water, the alcohol is boiled off and the colouring matter salted out. The British and French patents further deal with the production of a dyestuff from ethylaminocresol ($CH_3 : NHC_2H_5 : OH = 1 : 2 : 4$) and formaldehyde; this forms the subject matter of a separate German patent, 84988/1895 (additional to D. R. P. 58955). The oxidation of the dyestuff so obtained is dealt with in D. R. P. 86967/1895.

Thiopyronines. J. R. Geigy and Co. (D. R. P. 65739/1892) found that the solution of sulphur sesquioxide in concentrated sulphuric acid, which is obtained by dissolving flowers of sulphur in oleum, converts tetraalkyldiaminodiphenylmethanes into sulphur analogues of the pyronines.



A dye produced by such a process was introduced under the name of *methylene red.*

According to the patent, 2 kilos of flowers of sulphur are dissolved in 20 kilos of fuming sulphuric acid (25 per cent anhydride), and 2 kilos of tetramethyldiaminodiphenylmethane are stirred in at 30—35°; the temperature must not be allowed to rise above this point. The stirring is continued for 2 hours; the sulphuric acid solution is then poured into water, boiled, filtered from sulphur and salted out with sodium and zinc chlorides.

The green metallic, crystalline powder dissolves in water with red colour and brick red fluorescence. The solution in concentrated sulphuric acid is orange yellow; this colour turns to bluish red on dilution. Caustic soda decolourises the aqueous solution precipitating a reddish white flocculent precipitate which redissolves on addition of acid with intense bluish red colour.

Dyestuffs prepared from chloral hydrate and dialkyl-

m-aminophenols have been described by the Badische Co.; these are stated to belong to the rhodamine group but may possibly be pyronines. (Brit. P. 15859/1894; F. P. 240216; D. R. P. 81042/1894). According to the patentees, chloral hydrate and metaaminophenols react energetically with one another giving a mixture of blue, violet and red dyestuffs as well as their leuco-compounds, the mixture being very difficult to separate. It is, however, possible to operate in four stages as follows.

(a) Prepare a crystalline condensation product of equimolecular quantities of the components, one molecule of water being split off.

(b) Obtain the leuco-compound of a greenish blue dyestuff by condensing the first product with a second molecule of *m*-aminophenol which may be the same as or different to that used in operation (a).

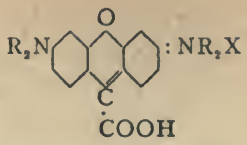
(c) Oxidise the leuco-compound to a greenish blue dyestuff.

(d) Convert the greenish blue into a red dyestuff, this may be effected by allowing its aqueous solution to stand for some time in the cold, or more rapidly by warming.

If a symmetrical dyestuff is desired, the first stages may be combined, 1 molecular proportion of chloral hydrate being condensed with 2 molecular proportions of the dialkyl-*m*-aminophenol, an excess being used for preference.

The German patent is somewhat remarkable in that a rather lengthy description of processes and properties is given but no hint as to the constitution of the compounds obtained.

The condensation of chloral hydrate with resorcin has been studied by H. Causse (*Bull. soc. chim.*, 1890, III, *3*, 861) and J. T. Hewitt and F. G. Pope (*Trans. chem. Soc.*, 1896, *69*, 1265; 1897, *71*, 1084) but the results obtained throw little light on the course of the reactions described by the Badische Co. It is possible that the final product may be of the type



Example 1. 1 part of finely powdered chloral hydrate and 3 parts of powdered diethyl-*m*-aminophenol are rubbed together; after incipient liquefaction the product sets to a dry, nearly colourless mass. After about an hour, the powdered mixture (it still contains excess of the aminophenol) is warmed on plates or dishes for 3 hours at 40—50°; the temperature is then gradually raised to 50° to 60° (3 hours) and then from 60° to 70° in the course of 6 hours. During the process the mixture melts and then solidifies.

The brittle mass is suspended in 5 times its weight of water, brought into solution by cautious addition of dilute acid and dilute ferric chloride solution added to the cold solution with continuous stirring. The oxidation of the leuco-base is complete when a filtered sample shows no further dyestuff formation on addition of ferric chloride. If common salt is also added, the blue dye is salted out as produced and its premature conversion into the red dye avoided; the precipitate is however tarry, but a soluble nitrate brings down the nitrate of the blue dye in a crystalline condition.

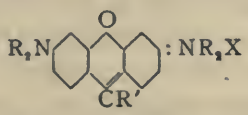
If an aqueous solution of the easily soluble chloride be allowed to stand for 12 hours until it has taken on a pure red shade, and on testing with sodium acetate and shaking out with ether shows that the blue dye is absent, addition of dilute nitric acid (until the red colour passes into bluish violet) brings down the nitrate of the red dye as needles showing a green reflex.

The dyestuff dissolves in water and alcohol with bluish red colour and yellow fluorescence. Addition of mineral acids turns the solution bluish violet, and in considerable excess to orange red. The colour of the red solution (mono-acid salt) is not altered by addition of alkaline carbonates.

Wool is dyed red shades, tannined cotton, violet red.

Example 2. In this case the preparation of an unsymmetrical dye is described, one molecule of chloral hydrate being condensed with one molecule of a dialkyl-*m*-aminophenol and the resulting product melted with a molecule of a different dialkyl-*m*-aminophenol.

The name of Rosamine has been applied to aryl derivatives of the pyronines, e. g. to compounds of the type



where R = alkyl and R' = phenyl or other aryl.

The first rosamines were prepared from resorcinbenzein (Meister, Lucius and Brüning, D. R. P. 51 348/1889; F. P. 200 347) by conversion into "resorcinbenzeinchlorid" and acting on this compound with amines; the resulting dyestuffs were named "Rosindamines" by the patentees. From the method of preparation there can be no doubt that "resorcinbenzeinchlorid" is simply 3:6-dichloro-9-phenylxanthonium chloride, the patent prescribing the following mode of operation.

Equal weights of dry resorcinbenzein, $C_{19}H_{14}O_4$,[1] and phosphorus pentachloride are intimately mixed and heated slowly to 100° and finally to 140°, being kept at the higher temperature until no further reaction is noticeable. The resulting product is ground and washed with water and then sufficient 1 per cent caustic soda solution added to give a permanent alkaline reaction; it is then filtered off, pressed and dried. The compound can be crystallised from ether and is then obtained as pale yellow shining prisms of m. p. 149°.

"Tetramethylrosindamine" is prepared by heating a mixture of 3.4 kilos of "Resorcinbenzeinchlorid", 1.7 kilos of dimethylamine hydrochloride and 1.7 kilos of ammonium acetate gradually to 120°, and then to 150—160°. After 1 to $1^1/_2$ hours the melt solidifies; it is ground, dissolved in dilute

1. This formula is taken from the German Patent.

hydrochloric acid, filtered and salted out with sodium and zinc chlorides.

Thus obtained, the dyestuff forms brown needles with a green metallic reflex; it is easily soluble in water and alcohol with red colour and yellowish red fluorescence. Wool and silk are dyed red from a feebly acid bath; on the latter fibre a yellow red fluorescence is observed.

An additional patent (D. R. P. 52 030/1889) claims the reaction between "resorcinbenzeinchlorid" and primary aromatic amines; those mentioned are aniline, *o*- and *p*-toluidines, xylidine and the naphthylamines. The rosindamines obtained in this way are sparingly soluble and give violet shades on silk. Both patents were allowed to lapse in 1890.

The "Benzorhodamines" described by the Badische Anilin und Soda Fabrik (D. R. P, 56 018/1889) are probably identical with the compounds produced from "resorcinbenzeinchlorid" and amines or from benzaldehyde and dialkyl-*m*-aminophenols. 10 kilos of benzotrichloride and 15 kilos of diethyl-*m*-aminophenol are heated with 20 kilos of toluene at water-bath temperature in an enamelled vessel, air being excluded as far as is practicable.

$$C_6H_5\cdot CCl_3 + 2\,C_6H_4(OH)(NR_2) = 2\,HCl + H_2O + C_6H_5\cdot C\begin{<}\begin{matrix}C_6H_3\cdot NR_2\\ O\\ C_6H_3{:}NR_2Cl\end{matrix}$$

According to Friedländer (III, 168) the dyes are of little interest.

A. Thauss and O. Schebler (D. R. P. 79 168/1893) replaced the benzotrichloride of D. R. P. 56 018 by monocarboxylic acids which were condensed with dialky-*m*-aminophenols according to the equation

$$R'\cdot COOH + 2\,C_6H_4(OH)(NR_2) + HX = 3\,H_2O + R'\cdot C\begin{<}\begin{matrix}C_6H_3\cdot NR_2\\ O\\ C_6H_3{:}NR_2X\end{matrix}$$

The acids which can be employed are limited in number since it is essential that they should, by themselves, be capable of withstanding the action of a condensing agent for several hours at 175—185°; obviously salicylic acid, gallic acid and

phenylglycine must be rejected. The reaction is claimed to differ from other reactions in which carboxylic acids are also employed; thus when oxalic acid is used, it is the products of its decomposition which really matter.

The acids which the patentees found most suitable were acetic acid and its halogen substituted derivatives, substituted benzoic acids, especially those containing nitro and sulphonic groups, and certain individual acids, e. g. phenylacetic. The processes employed are illustrated by certain examples.

Example 1. Dissolve 2 parts of diethyl-*m*-aminophenol in 6 to 7 times its weight of concentrated sulphuric acid, add one part of *m*-nitrobenzoic acid and warm for 4 or 5 hours at 175—185°.

Example 2. Heat 2 parts of ethyl salicylate, 3 parts of diethyl-*m*-aminophenol and 4 parts of zinc chloride with frequent stirring and exclusion of air for 5 hours to 175 to 185°.

Example 3. Dissolve 5 parts of diethyl-*m*-aminophenol in 20 to 30 parts of concentrated sulphuric acid, add 1 part of glacial acetic acid and heat for 5 hours to 175—185°.

The typical condensation of benzaldehyde with dialkyl-*m*-aminophenols, whereby (new)[1] red dyestuffs are produced, is described by Bayer & Co. in D. R. P. 62 574/1889. Besides benzaldehyde itself, various substituted derivatives can also be used, claims being made in the cases of *m*- and *p*-nitro-, *o*-, *m*- and *p*-hydroxy- and dimethyl-*p*-amino-benzaldehydes which can be brought to reaction with dimethyl- (or diethyl-) *m*-aminophenol &c.

Example 1. 10.6 kilos of benzaldehyde are added very gradually within 12 hours to a solution of 27.4 kilos of dimethyl-*m*-aminophenol and 30 kilos of zinc chloride in 22 kilos of 33 per cent hydrochloric acid at 100°. The melt is kept at 100° for a further 12 hours with frequent stirring

1 ' Since the product of the condensation is dehydrated and then oxidised, the final dyestuffs must surely be identical with those obtained according to the patents of Meister, Lucius and Brüning and of the Badische Co.

and finally raised gradually with stirring and access of air to 200°. The red melt obtained in this way is subsequently worked up.

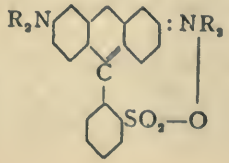
Example 2. 5 kilos of dimethyl-*p*-aminobenzaldehyde, 10 kilos of dimethyl-*m*-aminophenol and 40 kilos of concentrated sulphuric acid are heated for 2 to 3 hours to 100° and then for some time to 140—150° until a sample when poured into water and treated with alcohol shows the desired shade and fluorescence.

Example 3. 9.1 kilos of monoethyl-*m*-aminophenol, 10 kilos of zinc chloride and 30 kilos of alcohol are liquefied and 5 kilos of *p*-nitrobenzaldehyde gradually added. After warming for one hour on the water-bath under reflux and with continuous stirring, the alcohol is distilled off and either the zinc chloride is removed from the residue by digestion with water, or the melt is dissolved in hydrochloric acid and the resulting leuco-base precipitated by excess of alkali or of sodium acetate. The nitro leuco-base can be converted into the nitro-dyestuff by concentrated sulphuric acid, or this may be prefaced by reduction of the nitro-group so that ultimately an amino-substituted dyestuff is obtained.

Sulphonated Rosamines

Introduction of sulphonic acid groups into rosamines leads to the production of acid dyes; one may start by using components which already contain sulphonic groups or else one may prepare rosamines containing radicles such as benzyl which are very readily sulphonated.

By the action of benzaldehyde-*o*-sulphonic acid on dialkyl-*m*-aminophenols, J. R. Geigy & Co. (D. R. P. 90487/1896) obtained condensation products which after closing of the xanthene ring and oxidation gave rosamines of the type



The necessary benzaldehyde-*o*-sulphonic acid is prepared according to D. R. P. 88952/1896 of the same firm by heating 20 kilos of *o*-chlorobenzaldehyde for 8 hours at 190 to 200° (oil-bath temperature, pressure in autoclave 8 atmospheres) with a solution of sodium sulphite made by diluting 50 litres of 40 per cent bisulphite solution with 50 litres of water and exactly neutralising with caustic soda. After removal of any unaltered chlorobenzaldhyde and *o*-chlorobenzoic acid the aldehyde-sulphonic acid is salted out as sodium salt by addition of sodium sulphate.

57 kilos of a 10 per cent solution of benzaldehyde-*o*-sulphonic acid and 7 kilos of diethyl-*m*-aminophenol are boiled for 8 hours under reflux, the solution evaporated and the quite dry residue powdered and heated to 135—140° for one hour with 40 kilos of concentrated sulphuric acid. The mass is then diluted with 400 litres of water, boiled up, cooled, filtered and treated with 18 kilos of 33 per cent ferric chloride solution. The mixture is then heated for 4 or 5 hours at 80 to 90°. Much of the dye separates during the process, the remainder is salted out. Washing with hot, saturated sodium chloride solution removes adhering iron salts, and other impurities are extracted by boiling with aqueous ammonia.

The residue crystallises from alcohol or acetic acid (the solutions are bluish red and fluoresce yellow red) as a crystalline powder with green reflex; it is scarcely soluble in water even when hot. The compound dissolves in hydrochloric acid and dilute sulphuric acid with yellow red colour; this changes to bluish red on dilution. Wool and silk are dyed from an acid solution in very clean bluish red shades which are stable to alkalies.

Dimethyl-*m*-aminophenol gives a similar dyestuff which is less soluble; the acid solution also dissociates more readily.

An alternative method may be used in preparing the dye, the sulphobenzaldehyde and diethyl-*m*-aminophenol (both dry) being condensed by sulphuric acid in which they are first heated for some hours at 100° and finally at 130—140°.

Some years after the granting of Geigy's patent, Meister,

Lucius and Brüning (D. R. P. 205 758/1906) claimed that dyestuffs prepared from *m*-aminophenols and benzaldehyde-2:4-disulphonic acid possess considerable advantages over those made from benzaldehyde-2-sulphonic acid. This is chiefly due to the greater solubility in water and greater affinity for cotton so that they are very suitable for mixed goods whilst the dye baths are also more completely exhausted.

Example 1. A dilute aqueous solution of 31 kilos of sodium benzaldehyde-2:4-disulphonate and a solution of 33 kilos of diethyl-*m*-aminophenol feebly acidified with sulphuric acid are boiled together under reflux until the separation of the tetraethyldiaminodihydroxytriphenylmethanedisulphonic acid is complete. The acid is notable for its very sparing solubility in water; to close the pyrone ring it is heated for 2 to 3 hours with about 5 times its amount of concentrated sulphuric acid above 100°. The resulting leucodisulphonic acid is oxidised subsequently in dilute sulphuric acid solution by means of ferric chloride.

Example 2 resembles example 1 but the dimethyl-*m*-aminophenol is replaced by 30.2 kilos of monoethyl-*o*-amino-*p*-cresol.

In D. R. P. 229 466/1910 (U. S. P. 1 003 738/1911 of W. Emmerich) the process is extended to cover the condensation of one molecule each of a mono- and a di-alkyl-*m*-aminophenol; thus e. g. 31 grams of sodium benzaldehydedisulphonate are boiled in feebly acid solution with 16.5 grams of diethyl-*m*-aminophenol and 15.1 grams of monoethylamino-*p*-cresol.

Acid dyestuffs can be obtained by sulphonation of benzylated rosamines prepared by the condensation of aromatic aldehydes (e. g. benzaldehyde and its 2-monochloro-, 2:5-dichloro- and 3-sulpho-derivatives) with benzylethyl- (or methyl-) *m*-aminophenol (Badische Co., Brit. P. 19 994/1897; U. S. P. 624 877 of J. Schmid and H. Rey; F. P. 269 821 and D. R. P. 97 015/1897).

Example 1. A solution of 5.3 parts of benzaldehyde and

23 parts of ethylbenzyl-*m*-aminophenol in 100 parts of alcohol is boiled for 12 hours under reflux with 100 parts of 10 per cent sulphuric acid. On cooling, the condensation product crystallises; it is purified by recrystallisation from alcohol.

1 part of the pure leuco-compound and 3 parts of concentrated sulphuric acid are heated for $1^1/_2$ hours to 130°, poured on to ice and the precipitate filtered off, pressed and dissolved in 40 parts of water with addition of the necessary amount of sodium carbonate. The solution is oxidised at water-bath temperature by addition of a 10 per cent ferric chloride solution containing $^1/_2$ part of ferric chloride and 1 part of hydrochloric acid. The colouring matter acid separates, it is dissolved in sodium carbonate solution, filtered and salted out.

The dyestuff dissolves in water with carmine red colour and yellow fluorescence; concentrated sulphuric acid gives a brownish yellow solution from which dark red flocks separate on dilution. Wool and silk are dyed bluish red from an acid bath, the shades are fast to acid and alkali.

Example 2. Dissolve 20.8 parts of sodium benzaldehyde-*m*-sulphonate in 200 parts of 10 per cent sulphuric acid and add 46 parts of ethylbenzyl-*m*-aminophenol dissolved in 100 parts of alcohol. Warm for 10 to 12 hours on the water-bath and proceed as in example 1.

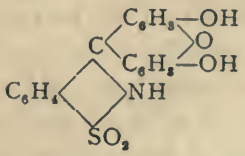
Example 3. 8.75 parts of dichlorobenzaldehyde (1 : 2 : 5) are dissolved in 50 parts of spirit and a solution of 23 parts of ethylbenzyl-*m*-aminophenol in 110 parts of 10 per cent sulphuric acid added. After standing for 10 hours, the leuco-compound is filtered off and converted into the pyrone compound.

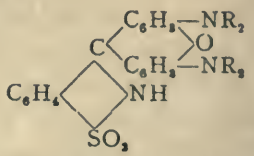
Although the pyrone compound is easily soluble in dilute sodium carbonate solution, the dyestuff obtained from it is sparingly soluble. It is desirable, therefore, to dry the pyrone compound after separation and convert it into higher sulphonic acids by solution in 5 parts of oleum (24 per cent SO_3). This also effects most of the necessary oxidation, but little

ferric chloride being subsequently employed. This dyestuff gives much bluer shaded reds than the preceding dyes.

Saccharеins

The condensation of saccharin with resorcin and *m*-aminophenols leads to dyestuffs





having properties very similar to those possessed by fluorescein and rhodamine (Soc. chim. des Usines du Rhône, Brit. PP. 21 196 and 21 197/1896; F. P. 267 442/1897; D. R. P. 100 779/1896). The preparations are described somewhat fully in the patents.

Example 1. 18 grams of saccharin, 22 grams of resorcin and 2.2 grams of aluminium chloride are heated to 200 to 220°. The mass is at first mobile but thickens as the reaction proceeds becoming a thick paste after 7 hours. On cooling, this sets to a brittle mass which is powdered and extracted with cold, dilute sodium carbonate solution. From this solution, acids precipitate the dyestuff.

To prepare the saccharein in a state of purity, 10 grams of the crude material and 30 grams of acetic anhydride are boiled for one hour under reflux, allowed to cool and poured into 100 parts of alcohol. The acetyl derivative separates as a faintly yellow, crystalline powder which is filtered, washed with alcohol, dissolved in glacial acetic acid and again precipitated by alcohol: m. p. 286°. The acetyl derivative is hydrolysed by boiling with alcoholic potash, diluted with water and precipitated by acetic acid; after crystallisation from alcohol, the resorcin-saccharein is obtained with m. p. 265—267°. It forms feebly reddish coloured leaflets, soluble in alkalies with yellow colour and green fluorescence.

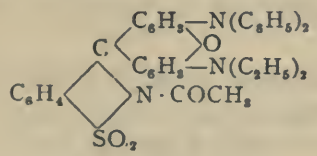
Example 2. 100 grams of diethyl-*m*-aminophenol and 200 grams of saccharin are heated for 36 hours to about

165°; if a condensing agent is used, the time of reaction can be shortened. The cooled product is powdered, suspended in a solution of 100 grams of sodium carbonate, boiled, cooled and filtered off. The residue forms a brown mass with metallic reflex and is now digested for some hours with caustic soda solution and again filtered. Hot, dilute hydrochloric acid takes up the base, the beautiful red solution deposits the hydrochloride on cooling in the form of small crystals showing a green metallic reflex. The salt is relatively sparingly soluble in water and is easily dissociated; bases, e. g. ammonia, precipitate the colourless base (m. p. 240 to 245°) immediately.

The great sensitiveness to alkalies makes the substance worthless as a dyestuff; this disadvantage may be rectified by acetylation. (Brit. P. 18017/1897; D. R. P. 100780/1897.) This is effected by boiling it with 4 times its weight of acetic anhydride for 2 hours and distilling off the excess of anhydride under reduced pressure. The new dye gives a very blue shade of red which fluoresces on the fibre; the melting point of the colour base is 232°.

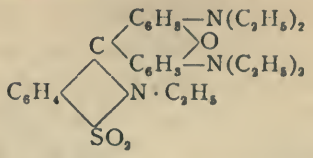
A further description of these compounds has been given by P. Monnet and J. Koetschet (*Bull. soc. chim.*, 1897, III, *17*, 690, 1030). Bromine and iodine in presence of sodium chlorate give halogenated resorcin-saccharеins; the bromo and iodo compounds dissolve in alkalies giving red and reddish violet solutions respectively.

The acetyl derivative of the saccharein from diethyl-*m*-aminophenol



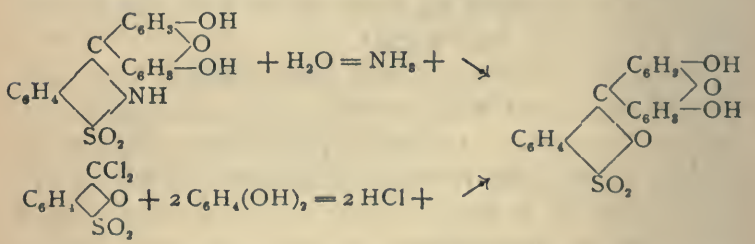
is a colourless compound of m. p. 230—232°; it is very soluble in benzene, fairly so in alcohol, chloroform and ether; in petroleum spirit it is nearly insoluble. The alcoholic and chloroform solutions are red, the solutions in ether and light

petroleum are nearly colourless. On treatment with sodium ethoxide and ethyl iodide, the saccharein gives an ethyl derivative (m. p. 220—222°)



which is colourless; the salts are readily hydrolysed by boiling water.

P. Sisley (*Bull. soc. chim.*, 1897, III, *17*, 821) claims that several of the derivatives described by Monnet and Koetschet had been previously obtained by himself in conjunction with Seyewetz or by I. Remsen and A. Linn (*Amer. Chem. J.*, 1889, *11*, 73). Concentrated sulphuric acid removes the elements of ammonia from the saccharеins leaving substances identical with the "sulphureins" which result from the condensation of phenols with the chlorides of *o*-sulphobenzoic acid.

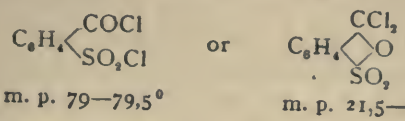


As is evident from D. R. P. 90487, similar derivatives are obtained by condensing *o*-sulphobenzaldehyde with dialkyl-*m*-aminophenols and oxidising the resulting leuco-compounds.

"Sulphone-fluorescein", $C_{19}H_{12}O_6S$, has been examined by C. C. Blackshear (*Amer. Chem. J.*, 1892, *14*, 455). Ammonium-*o*-sulphobenzoate, $COOH \cdot C_6H_4 \cdot SO_2 \cdot ONH_4$, (15 grams), when heated with resorcin (12 grams) to 170–175° until water ceases to be evolved, gives ammonium dihydroxybenzoylbenzenesulphonate, $C_6H_3(OH)_2 \cdot CO \cdot C_6H_4 \cdot SO_2 \cdot ONH_4$. When the acid is heated with concentrated sulphuric acid at

160—180°, it yields "sulphone-fluorescein" which after collection and drying is dissolved in aqueous alkali and reprecipitated by acid.

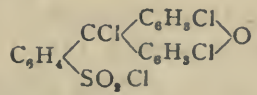
Sulphone-fluorescein is also formed when either of the chlorides derived from *o*-sulphobenzoic acid, viz. —



m. p. 79—79,5° or m. p. 21,5—22,5°

is condensed with resorcin (I. Remsen and S. R. McKee, *Amer. Chem. J.*, 1896, *18*, 794; compare Remsen, *ibid.*, 1895, *17*, 309).

It seems to be impossible to preapare sulphone-fluorescein by directly condensing *o*-sulphobenzoic acid with resorcin. Some of the reactions of the compound exhibit peculiarities; thus with bromine, a dibromo-derivative is chiefly formed, whilst phosphorus pentachloride gives a tetrachloro-derivative which may be



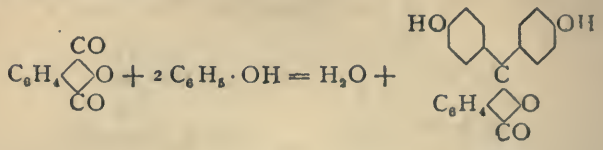
(J. White jun., *Amer. Chem. J.*, 1896, *17*, 545).

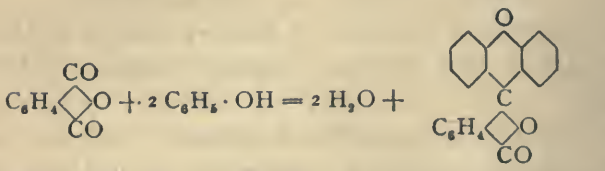
CHAPTER XIII.

THE CONSTITUTION OF FLUORESCEIN AND ANALOGOUS COMPOUNDS

Fluorescein was discovered by A. von Baeyer in the course of his researches on the condensation of phthalic anhydride with various phenols (*Ber.*, 1871, *4*, 457, 555, 658). In the case of phenol itself, two compounds were formed, phenolphthalein in larger quantity, the so-called phenolphthaleinanhydride (fluoran) in smaller amount. The first of these resulted from a para condensation and the two

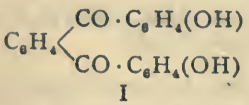
hydroxyl groups of the original phenol molecules were preserved intact; fluoran resulted from an ortho condensation and subsequent closing of a pyrone ring; this is represented by the two equations





The behaviour of phthalic anhydride towards resorcin was also examined in 1871, one molecule of the former condensing with two of the latter whilst two molecules of water were eliminated. In the light of the above equations, one draws the conclusion that the resorcin molecules are substituted most probably in position 4 (OH : OH = 1 : 3); substitution in position 2 is, however, a possibility.

The relationship of phenolphthalein to phthalide was not recognised at the time, and in Baeyer's first collective publication on the compounds formed from phthalic acid and phenols (*Annalen*, 1876, *183*, 1), the following constitutions are assigned to phenolphthalein (I), phenolphthalein anhydride (II), hydrated fluorescein (III) and fluorescein (IV).



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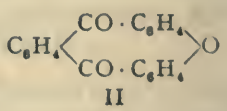

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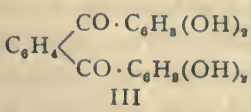
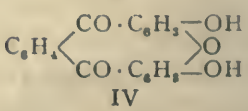
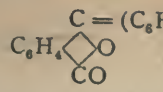


III



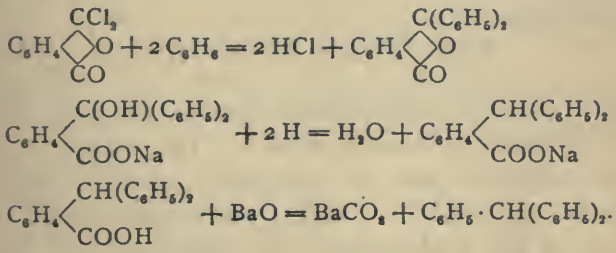
IV

That phenolphthalein really possesses an isomeric structure, viz, that of a dihydroxydiphenylphthalide,

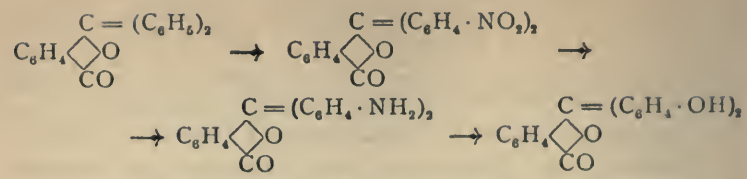


was proved by Baeyer himself a few years later.

Diphenylphthalide was discovered by Friedel and Crafts who obtained it by condensing phthalyl chloride with benzene in presence of aluminium chloride (*Ann. chim. phys.*, 1884, VI, *1*, 523; this paper collects much earlier work, Friedel and Crafts having published their first notice of diphenylphthalide in 1877). Its constitution is proved by its degradation to triphenylmethane; this was effected by Baeyer (*Annalen*, 1880, *202*, 50) who reduced the compound with alkali and zinc dust to a triphenylmethanecarboxylic acid which broke up into triphenylmethane and carbon dioxide on fusion with caustic baryta.



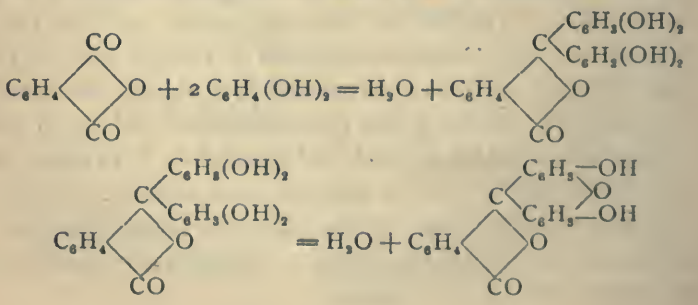
Diphenylphthalide gives a mixture of two dinitro-derivatives when added to 10 times its weight of nitric acid of s. g. 1.5 (Baeyer, *loc. cit.*, 66). When the mixture is reduced with tin and hydrochloric acid and the reduction product crystallised from hot alcohol, the so-called α-diaminodiphenylphthalide separates first; it forms the greater portion of the mixed bases, crystallises in thick plates and melts at 179 to 180°. When this diamino-compound is treated with nitrous acid, the amino groups are replaced by hydroxyl and phenolphthalein is produced. Since phenolphthalein is formed when phthalic anhydride is heated with phenol, it is evident that, when diphenylphthalide is nitrated, one nitro group enters each phenyl group and that the phthalic residue remains unattacked; the relationships of the compounds mentioned must be represented by the scheme,



So far, no direct proof is given that the two hydroxyl groups of phenolphthalein stand in the para position to the grouping methane carbon atom; indirect evidence is furnished by the fact that *p*-chlorophenol and *p*-cresol simply give substances analogous to "phenolphthalein anhydride" when condensed with phthalic anhydride. A direct proof of the structure is afforded by the fact that phenolphthalein yields *p*, *p*'-dihydroxybenzophenone when fused with caustic potash

The dihydroxybenzophenone thus obtained by Burckhardt and Baeyer (*Annalen*, 1880, *202*, 127) melted at 206° and was identified with the compound previously prepared by Staedel and Gail (*Ber.*, 1878, *11*, 746), Caro and Graebe (*ibid.*, 1348) and Liebermann (*ibid.*, 1434). It was subsequently prepared by the condensation of *p*-hydroxybenzoic acid and phenol in presence of stannic chloride at 120° (*Amer. Chem. J.*, 1883, *5*, 86).

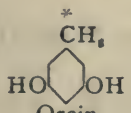
The way in which phthalic anhydride condenses with phenols having thus been elucidated, it is likely that in the case of resorcin, the reaction takes place as follows.



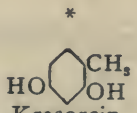
Substitution of a phenol usually takes place in the ortho- or para-position relatively to a hydroxyl group; that this rule holds during the formation of fluorescein was not recognised immediately, the definite proof being much delayed.

Emil Fischer (*Annalen*, 1876, *183*, 63) found that one molecule of phthalic anhydride condensed with two molecules of orcin yielding an orcin-phthalein, $C_{22}H_{18}O_5$, apparently homologous with fluorescein. The compound dissolves in dilute alkalies and ammonia with an intense dark red colour but shows no fluorescence.

Some years afterwards, E. Knecht (*Annalen*, 1883, *215*, 83) prepared an isomeride of orcin, viz. 2:4-dihydroxytoluene ("kresorcin") which he condensed with phthalic anhydride to a compound also of the formula $C_{22}H_{16}O_5$, resembling fluorescein completely. Now orcin is 3:5-dihydroxytoluene, i. e. the two hydroxyl groups are not merely meta to one another, but are also both in the meta position with regard to the methyl group, whilst in "kresorcin" the meta position is unoccupied.

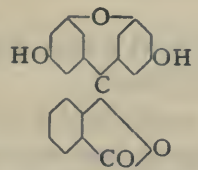


Orcin



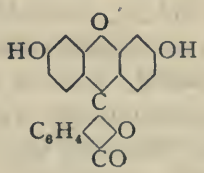
Kresorcin

The conclusion was drawn that in order to produce a true fluorescein the position marked with an asterisk must be unsubstituted, i. e. that the phthalic anhydride attacks resorcin meta to its hydroxyl groups and fluorescein possesses the constitution.



This view seems to have been generally adopted except by Richard Meyer (*Ber.*, 1888, *21*, 3376) who thought that an ortho-para-condensation was far more probable. Taking the accumulated evidence regarding the directive influence of

hydroxyl and amino groups on further substitution, he was of opinion that phthalic anhydride attacks phenol chiefly in the para-position, the resulting phenolphthalein being *p*, *p*'-dihydroxydiphenylphthalide as Baeyer had already shown (*Annalen*, 1880, *202*, 43, 126). In a lesser degree, phenol is attacked in the ortho-position, the *o*, *o*'- dihydroxydiphenylphthalide losing water as represented above; in other words, phenolphthalein does not form an anhydride, and Meyer used the name *fluoran* for the compound described by Baeyer as "phenolphthaleinanhydrid". The view was definitely expressed that fluorescein results from the phthalic anhydride attacking both molecules of resorcin in position 4, so that fluorescein is a dihydroxyfluoran of the constitution (I)



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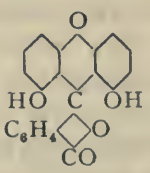
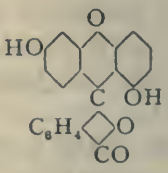


II



III

though the possibilities of structures II and III must also be reckoned with.

For a complete elucidation of the relationships, it is necessary to prove the following points.

I. "Phenolphthalein anhydride" possesses the constitution of fluoran.

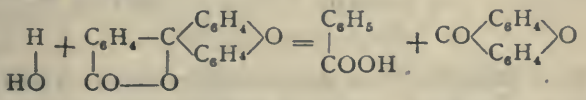
II. Fluoran can be obtained from fluorescein or, alternatively, an identical compound can be obtained from fluoran and fluorescein.

III. The two hydroxyl groups occupy the positions assigned to them in structure I.

Meyer obtained a considerable stock of phenolphthalein anhydride by working up residues derived from the manufacture of phenolphthalein, and expressed the intention of trying to convert the substance into phenylacridine (*Ber.*, 1891, *24*, 1418). This was not followed up since it was found (Meyer and Hoffmeyer, *Ber.*, 1892, *25*, 2118) that "phenol-

phthalein anhydride"(as such or as the reduction product) yielded xanthone and benzene on distillation with lime.

The reaction is easily explained; decomposition at a high temperature gives rise to a certain amount of water which in presence of the lime effects fission of the fluoran in the following sense.



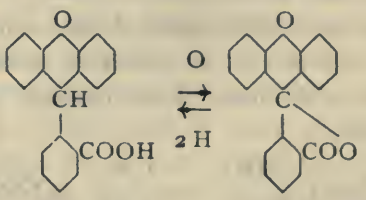
The benzoic acid then undergoes the usual decomposition into benzene and carbon dioxide in presence of an excess of lime.

That "phenolphthalein anhydride", or fluoran as it should now be called, is the parent substance from which fluorescein is derived had been proved shortly before by Meyer and Hoffmeyer (*Ber.*, 1892, *25*, 1385). Fluorescein may be readily converted into "fluorescein chloride" (Baeyer, *Annalen*, 1880, *202*, 350) by the action of phosphorus pentachloride according to the equation

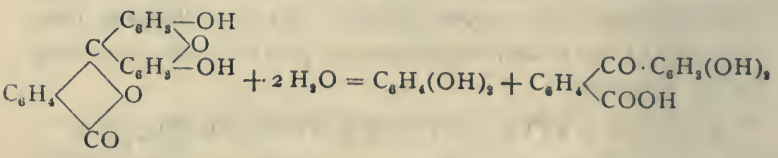
$$C_{20}H_{12}O_5 + 2\,PCl_5 = 2\,POCl_3 + 2\,HCl + C_{20}H_{10}O_3Cl_2$$

but neither Baeyer nor Meyer and Hoffmeyer were able to eliminate the chlorine by reduction. The latter authors found, however, that if fluorescein were treated with phosphorus pentabromide, the two hydroxyl groups as well as a hydrogen atom were replaced by bromine and a compound of the formula $C_{20}H_9O_3Br_3$ produced, replacement of hydrogen being probably due to the dissociation of the phosphorus pentabromide into tribromide and bromine. By prolonged reduction of this compound with alkali and zinc dust in alcoholic solution, the three bromine atoms were replaced by hydrogen, two further hydrogen atoms added and, on acidification, an acid was isolated identical with the substance obtained by Baeyer by the reduction of phenolphthalein anhydride and which he called phenolphthalin anhydride. Meyer refers to the substance as "Hydrofluoransäure"; its constitution is evidently that of *o*-carboxyphenylxanthene which

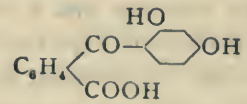
may be easily oxidised back to fluoran, the lactone of *o*-carboxyphenylxanthenol.



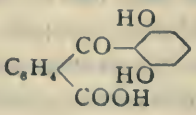
Thus fluorescein is a dihydroxy derivative of fluoran and it remains to decide which of the three constitutions given on page 274 represents correctly the orientation of the hydroxyl groups. Meyer was strongly in favour of formula I; a publication by Gräbe (*Ber.*, 1895, *28*, 28) apparently made this view improbable. Baeyer had found that fluorescein splits off one molecule of resorcin when fused with potash yielding a dihydroxybenzoylbenzoic acid



If fluorescein has the constitution represented by Formula I, the dihydroxybenzoylbenzoic acid must possess the structure

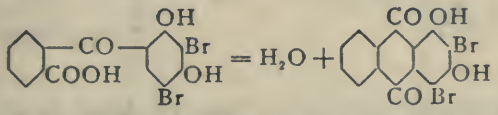


Such a compound might be expected to lose water when acted on by sulphuric acid; this reaction was not realised and Gräbe drew the conclusion that the constitution of the acid had to be represented by the alternative structure

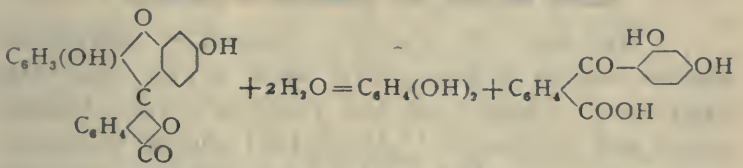


This would necessitate the constitution II or III for fluorescein itself; of these, Gräbe preferred the more symmetrical formula.

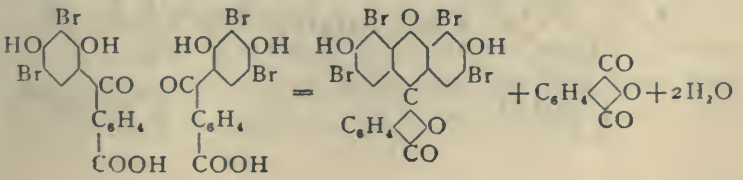
The fallacy of the conclusion was proved shortly afterwards by Heller (*Ber.*, 1895, *28*, 312). If the dihydroxybenzoylbenzoic acid is brominated, a dibromo-derivative is obtained which may be readily condensed by two hours heating on the water-bath with 8 times its weight of 20 per cent fuming sulphuric acid to dibromoxanthopurpurin.



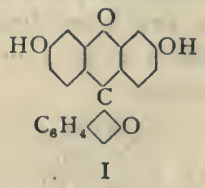
Hence it follows that in the fluorescein from which the dihydroxybenzoylbenzoic acid is obtained, of the two hydroxyl groups, one at least must be in the para position with regard to the grouping methane carbon atom.



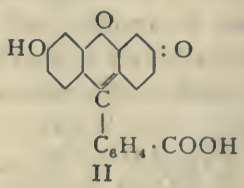
Gräbe's unsuccessful attempt to obtain xanthopurpurin directly from the dihydroxybenzoylbenzoic acid must be attributed to sulphonation of the dihydroxyphenyl group. Heller's result does not definitely prove that the other hydroxyl group is in the para position; the desired result was obtained shortly afterwards by R. Meyer and H. Meyer (*Ber.*, 1896, *29*, 2623). By heating the dibromodihydroxybenzoylbenzoic acid referred to above with one-fifth of its weight of zinc chloride for 20 minutes to 235–240° in a current of hydrogen, tetrabromofluorescein was produced, identical in all respects with eosine obtained by the direct bromination of fluorescein.



All doubt as to fluorescein being produced by an ortho-para-condensation with regard to both of the molecules of resorcin is set aside. As to the constitution of fluorescein, the only question left to consider is whether the compound is actually dihydroxyfluoran (I) or possesses a tautomeric quinonoid structure (II)



I



II

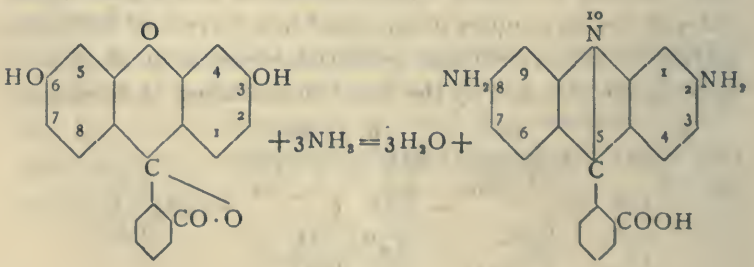
This question is referred to later (p. 280); fluorescein furnishes derivatives of both types and at present we shall simply look upon it as 3:6-dihydroxyfluoran.[1])

General Reactions and Tautomerism of Fluorescein

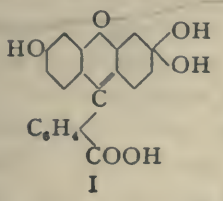
1. *Hydration.* The precipitate obtained on acidifying an alkaline solution of fluorescein is yellow and flocculent; this passes into a yellowish red, fine crystalline powder. Analysis agrees with the formula $C_{20}H_{12}O_5, H_2O$ whereas fluorescein recrystallised from alcohol and dried at 130° has a composition corresponding with $C_{20}H_{12}O_5$.

Solutions of the two forms in alkali show no difference; possibly the hydrated form is to be represented by struc-

[1]) It is regrettable that numbering in the acridine and xanthene series should not correspond. Thus the compound obtained by the action of ammonia on 3:6-dihydroxyfluoran is 2:8-diamino-5-*o*-carboxyphenylacridine.



ture I; there is no reason to suppose the pyrone ring has been opened as in structure II.



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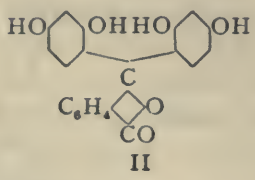
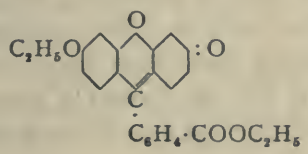


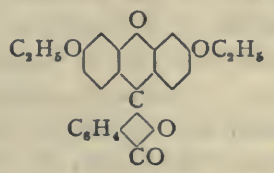
II

We shall see later that fluoresceins produced from halogenated phthalic acids form very stable hydrates which only lose the molecule of water on heating to 100° or an even higher temperature, whilst cases occur where two forms of hydrates of substituted fluoresceins have been obtained.

2. *Acylation.* The hydroxyl groups of fluorescein may be esterified, the methods usual in the case of phenolic compounds being employed. Thus acetic anhydride, benzoyl chloride and phosphorus pentachloride produce diacetylfluorescein, dibenzoylfluorescein and 3:6-dichlorofluoran respectively; these substances are colourless and derived from the phenolic (non-quinonoid) form of fluorescein.

3. *Alkylation.* One or two alkyl groups may be substituted for hydrogen; in the latter case two isomerides are known, a coloured ether-ester and a colourless dialkyl ether.

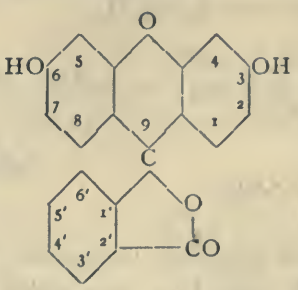




4. *Ammonia, Amines &c.* The exhaustive action of ammonia on fluorescein ends in the production of 2:8-diamino-5-*o*-carboxyphenylacridine. Aniline gives rise to an anilide, hydroxylamine to a so-called oxime; reference is made to these compounds below.

5. *Acids.* In addition to its weakly acidic properties, fluorescein is also capable of forming salts with acids; these are generally considered to be of oxonium type.

6. *Substitution.* Positions 2, 4, 5 and 7 are those which



are most readily attacked by substituting agents such as bromine or nitric acid. Thus bromine reacts with fluorescein to give di- or tetra-bromo-derivatives (Baeyer, *Annalen*, 1876, *183*, 36; the existence of a monobromofluorescein is also mentioned) whilst nitric acid gives either di- or tetranitrofluorescein (Baeyer, *loc. cit.*, 29), or perhaps pentanitrofluorescein (Bogert and Wright, *J. Amer. Chem. Soc.*, 1905, *27*, 1310).

In the case of nitration, L. Matras showed that positions 4 and 5 were first substituted, for the alkaline fission of dinitrofluorescein results in the formation of 2-nitroresorcein (*Chem. Zeit.*, 1895, *19*, 408; *Arch. Sci. phys. nat.*, 1895, III, *33*, 285). Hewitt and Woodforde (*Trans. Chem. Soc.*, 1902, *81*, 893) proved that bromine first attacks positions 4 and 5, for nitration of dibromofluorescein yields a different compound to that produced by brominating dinitrofluorescein. 4 : 5-Dibromo-2 : 7-dinitrofluorescein is not only formed by the action of nitric acid on dibromofluorescein but also by the action of bromine on tetranitrofluorescein.

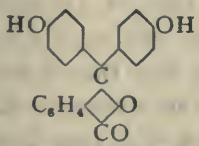
Fluorescein derivatives substituted in the phthalic residue are made by condensing the corresponding substituted phthalic anhydrides with resorcin.

Tautomerism of Fluorescein.

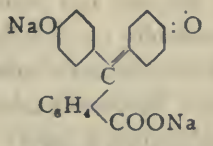
A. Bernthsen (*Chem. Zeit.*, 1892, *16*, 1956; see also Dehnst, *ibid.*, 1893, *17*, 654) seems to have been the first to draw attention to the possibility of tautomeric change in the

fluorescein series; he assigned a quinonoid structure to the alkaline salts whilst fluorescein itself was apparently regarded as having the constitution of a true dihydroxyfluoran.

Not long afterwards, P. Friedländer (*Ber.*, 1893, *26*, 172) came to the conclusion that the colourless phenolphthalein possesses the constitution of *p*,*p*′-dihydroxydiphenylphthalide assigned to it by Baeyer, whilst the coloured alkali salts are derived from a tautomeric quinonoid form.

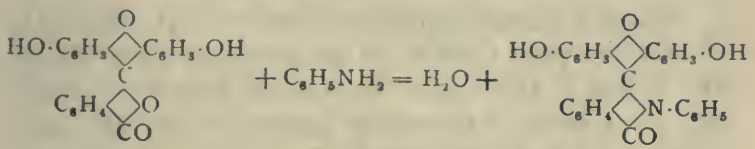


Phenolphthalein



Alkaline solution

O. Fischer and E. Hepp (*Ber.*, 1893, *26*, 2236) took the question a step further, showing that fluorescein and aniline give a colourless anilide, soluble in alkalies with green fluorescence. The reaction probably follows the course



for the substance readily gives a very stable, colourless dimethyl ether which only exhibits fluorescence when dissolved in concentrated sulphuric acid.

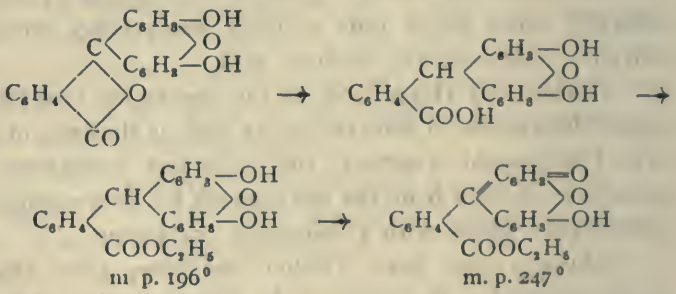
Fischer and Hepp came to the conclusion that the coloured derivatives of fluorescein, as well as fluorescein itself, are of quinonoid structure; the colourless derivatives have structures derived from the old formula for fluorescein which should correspond with a colourless compound.

About a year later, Fischer and Hepp (*Ber.*, 1894, *27*, 2790) returned to the study of the dimethyl ether of fluorescein anilide and found that by heating with glacial acetic and sulphuric acids under pressure, the aniline was split off; from the residue they recovered a colourless dimethyl ether of fluorescein of m. p. 198°.

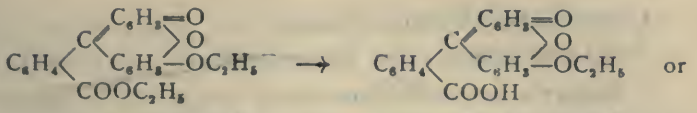
At the same time the ethylation of fluorescein anilide was described; the resulting ether melted at 162—164° and on removal of aniline gave a colourless diethyl ether of fluorescein of m. p. 181—182°. Baeyer (*Annalen*, 1876, *183*, 17) had previously described a diethyl ether of fluorescein as forming bright yellow tables; no melting point was given the quantity obtained being extremely small.

In order to obtain undoubted carboxylic esters of fluorescein, Nietzki and Schröter (*Ber.*, 1895, *28*, 44) endeavoured unsuccessfully to esterify fluorescein with alcohol and sulphuric or hydrochloric acid. Failing in this, they reduced fluorescein to fluorescin and alkylated this directly with alcohol and hydrochloric acid; this reaction had been carried out previously by Herzig (*Monatsh.*, 1892, *13*, 422). The ethyl ester of fluorescin (m. p. 196°) when oxidised by ferricyanide in alkaline solution gave fluorescein ethyl ester of m. p. 247°; treated with bromine it furnished the ethyl ester of eosine which is also known as the dyestuff *Erythrine*.

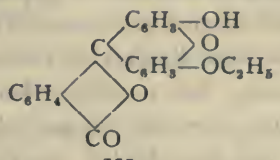
Baeyer's monoethylfluorescein (*loc. cit.*, 15), obtained by the action of ethyl bromide on the potassium salt of fluorescein, melted at 155—156°. The steps in Nietzki and Schröter's preparation of fluorescein carboxylic ester are represented by the following scheme



By acting on the ester with sodium ethoxide and ethyl bromide, the diethyl ether-ester, m. p. 159°, was obtained as dark yellow needles; its constitution is expressed by the formula I.



I m. p. 159° II m. p. 251°



III

It will be at once apparent that it differs radically in properties from the diethyl ether of Fischer and Hepp; this difference is emphasised by the fact that it readily undergoes alkaline hydrolysis losing the ethyl group attached to carboxyl and giving a monoethyl ether which crystallises in yellow rhombic leaflets and melts at 251°; the constitution of this compound must be represented by one of the formulae II or III.

There is some discrepancy between the results given by Baeyer and those obtained by Nietzki and Schröter; the latter (*loc. cit.*, 49) therefore re-examined the reaction between ethyl bromide and the potassium salt of fluorescein. After removing the excess of ethyl bromide, the reaction product was shaken with sodium carbonate solution and ether; the latter solvent dissolved the two diethyl derivatives, from the sodium carbonate solution the two monoethyl compounds were precipitated by carbon dioxide, whilst unattacked fluorescein remained in solution. By partial crystallisation from alcohol, colourless diethyl fluorescein ether was separated from the isomeride, the latter being identified by bromination to erythrine. The melting point of the colourless ether was found to be 183°, whilst Fischer and Hepp gave 181—182° for the substance obtained by the fission of the diethyl ether of fluorescein anilide. It is thus seen that fluorescein gives the following ethyl derivatives.

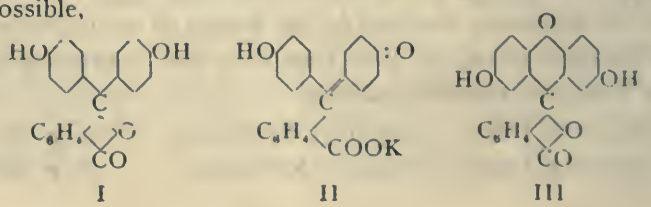
Monoethyl ether (Hydroxyl derivative)	m. p. 251°
Monoethyl ester (Carboxyl derivative)	m. p. 247°

Diethyl ether (Diethoxyfluoran)	m. p. 183°
Ethyl ether-ethyl ester (Quinonoid)	m. p. 159°

Baeyer's monoethylfluorescein (m. p. 156°) has to be reconciled with this scheme; it proved to be really the coloured quinonoid diethyl derivative. The analytical difference between mono- and di-ethyl derivatives is small, and it is scarcely surprising that in 1876, when the possibility of isomeric derivatives was not suspected, Baeyer should have taken one of the two diethyl derivatives for a monoethyl ether of fluorescein.

The researches of A. G. Green and P. King (*Ber.*, 1906, *39*, 2365; 1907, *40*, 3724; 1908, *41*, 3434) on the behaviour of quinolphthalein towards esterifying agents have thrown much light on the function of the lactone ring in fluoran derivatives.

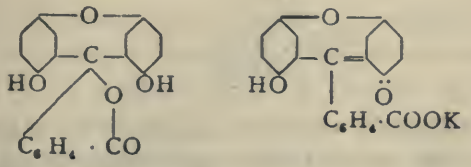
Quinolphthalein was first obtained by Grimm (*Ber.*, 1873, *6*, 507) who condensed two molecules of quinol with one of phthalic anhydride in presence of sulphuric acid at 130 to 140°. Ekstrand (*Ber.*, 1878, *11*, 714) effected the condensation by means of stannic chloride and the study of the substance was resumed at a later date by R. and H. Meyer (*Ber.*, 1895, *28*, 2959) in connection with the question of the quinonoid structure of phthaleins generally which, as we have seen above, received considerable attention about that date. The assumption of quinonoid structure for the alkaline salts had become fairly general in the case of phenolphthalein and fluorescein; the position of the hydroxyl groups para to the grouping carbon atom renders this form of tautomerism quite possible. But in quinolphthalein (III), the hydroxyl groups must be meta to this carbon atom and rearrangement of linkages such as is supposed to take place when phenolphthalein (I) is converted into a monopotassium salt (II) is impossible,



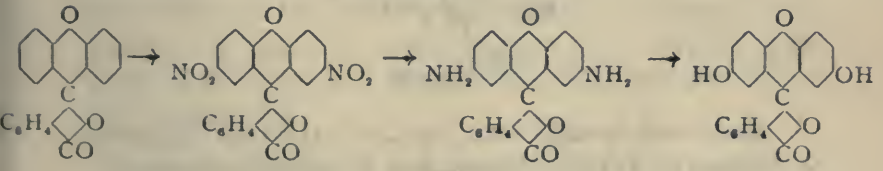
I II III

though, as we have seen already, fluorescein, which is isomeric with quinolphthalein, gives rise to two sets of derivatives.

Now quinolphthalein resembles phenolphthalein in giving a violet solution in alkalies although the compound itself is colourless. The possibility of quinolphthalein having a structure



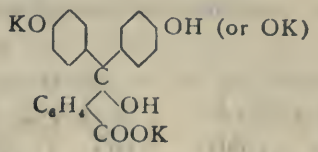
with hydroxyl groups ortho to the grouping carbon atom and so being capable of furnishing quinonoid salts, may be put entirely on one side since Meyer and Friedland (*Ber.*, 1898, *31*, 1739) obtained it from fluoran by successive nitration, reduction and diazotisation.



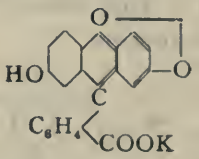
Another explanation must consequently be found for the violet colour of the alkaline solutions of quinolphthalein. R. Meyer and Spengler (*Ber.*, 1903, *36*, 2950) turned to Ostwald's theory of indicators and attributed the colour change to ionisation alone. "Die freien, farblosen Phthaleine enthielten hiernach die unveränderten Molekeln, während die Farbe ihrer Alkalilösungen den bei der Salzbildung auftretenden Ionen zuzuschreiben wäre."

Meyer and Spengler practically reject the idea of tautomeric change for the phthaleins generally. Shortly after the appearance of their paper, A. G. Green and A. G. Perkin (*Trans. Chem. Soc.*, 1904, *85*, 398) brought forward evidence to show that in the case of phenolphthalein the colour change produced on addition of alkali was due to transition from

the lactonoid to the quinonoid configuration, whilst the decolourisation produced by excess of alkali was due to addition of the elements of alkaline hydroxide with production of a non-quinonoid salt containing more than one atom of alkali metal.

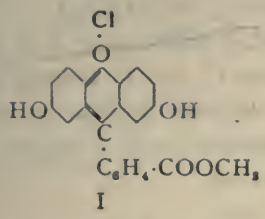


Quinolphthalein was also examined in respect to its behaviour with one and more equivalents of alkali; it resembled phenolphthalein so closely that Green and Perkin assigned to its monopotassium salt an orthoquinonoid structure involving a quadrivalent oxygen atom in the pyrone ring

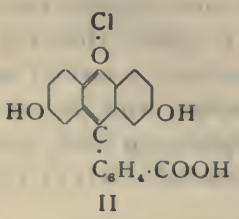


Meyer and Spengler (*Ber.*, 1905, *38*, 1318) took exception to Green and Perkin's formulation of quinolphthalein salts and showed moreover that an excess of either quinol- or phenol-phthalein when treated with a solution of caustic soda yields a solution in which only one molecule of the phthalein has been dissolved for every two molecules of alkali.

This led to the work on the esterification of phthaleins to which reference has already been made. In the first paper of the series, Green and King (*Ber.*, 1906, *39*, 2370) showed that quinolphthalein was converted into a dark red crystalline mass when its solution in five parts of methyl alcohol was saturated with hydrogen chloride and allowed to stand. Methoxyl and chlorine were estimated in the product; the results were in excellent agreement for the chloride of an oxonium ester to which the constitution I was assigned.



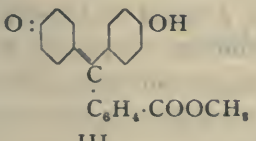
I



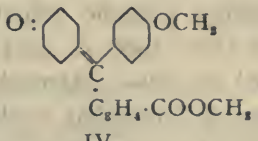
II

A corresponding hydrochloride of quinolphthalein was prepared by leading a stream of hydrogen chloride into its solution in warm glacial acetic acid. The salt (II) separated in glittering red crystals on cooling; in contact with water it is instantly decomposed with regeneration of quinolphthalein, whilst the ester of formula I is somewhat soluble in water with a reddish orange shade and is only slowly hydrolysed on boiling.

Phenolphthalein was also found to be capable of furnishing a coloured methyl ester (*loc. cit.*, 2369) which had a great tendency to hydrolyse; its method of preparation was subsequently improved (*Ber.*, 1907, *40*, 3726) and the compound isolated in a pure condition as orange coloured, prismatic needles (III).



III

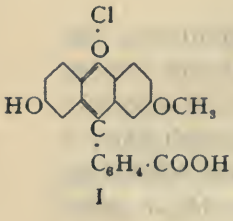


IV

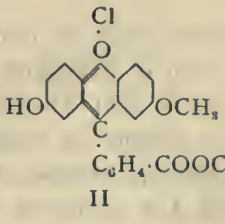
By esterification of the lactonoid monomethyl ether of phenolphthalein with methyl alcohol and hydrochloric acid gas, a monomethylphenolphthalein methyl ester (IV above) was obtained; this is orange red in colour and isomeric with the colourless dimethyl ether (dimethoxydiphenylphthalide) usually obtained by direct methylation of phenolphthalein with alkali and methyl iodide.

Green and King (*loc. cit.*, 3730) also prepared some remarkable derivatives of quinolphthalein, starting out with the lactonoid mono- and dimethyl ethers of quinolphthalein

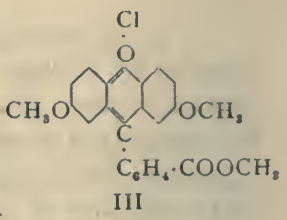
which were already known (R. Meyer and Spengler, *Ber.*, 1905, *38*, 1328). Thus the monomethyl ether gave a hydrochloride and a methyl ester chloride (I and II below) corresponding with the compounds obtained previously from quinolphthalein itself, whilst the dimethyl ether furnished an ester chloride (III) in a similar manner.



I



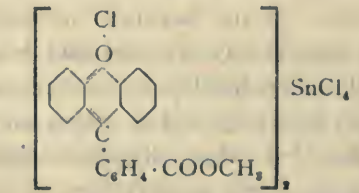
II



III

The last of these compounds was isolated as an orange red, double zinc salt, $2\,C_{19}H_{10}OCl(OCH_3)_2(COOCH_3), ZnCl_2$, which dissolved readily in water giving a fairly stable orange solution from which alkalies precipitated the colourless dimethylquinolphthalein ether.

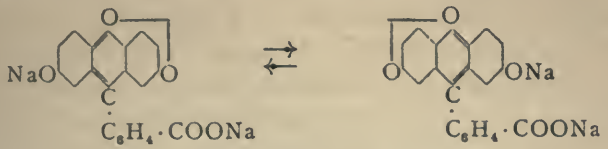
Green and King eventually extended their esterification methods to fluoran itself as well as to 2:7-dimethylfluoran and 2:7-dichlorofluoran, the respective products obtained by condensing phthalic anhydride with *p*-cresol and *p*-chlorophenol (*Ber.*, 1908, *41*, 3434). The oxonium compounds were isolated as yellow stannichlorides whose aqueous solutions decompose somewhat readily with separation of the parent fluorans. As an example, the formula



may be given as representing the salt isolated from fluoran itself.

Respecting the coloured salts produced by the action of alkalies on quinolphthalein, Green (*J. Soc. Chem. Ind.*, 1909,

28, 640) inclines to the view that their structures are ortho-quinonoid, the linkages oscillating between the two quinol residues.



At the same time he does not entirely reject the possibility that they may have a metaquinonoid constitution, which, however, he thinks is less probable.

Somewhat similar views have been suggested by W. Kropp and H. Decker (*Ber.*, 1909, *42*, 578), fluorescein and quinolphthalein being both regarded as possessing ortho-quinonoid betaine constitutions. Salts of toluquinolphthalein and its ethers have been described by F. Kehrmann and R. Silzer; they exhibit very similar properties (*Annalen*, 1910, *373*, 355).

CHAPTER XIV

FLUORESCEIN AND RELATED DYESTUFFS

The condensation of phthalic anhydride with resorcin gives fluorescein as chief product; this holds whether the two substances are simply heated together until the reaction is completed as far as possible or whether a condensing agent is also employed.[1]

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1 It should be kept in mind that phenols are capable of condensing in various ways with phthalic anhydride; thus in the case of phenol itself it has been pointed out that both para and ortho condensations occour simultaneously, and phenolphthalein, the chief product of the reaction, is always accompanied by smaller amounts of fluoran or phenolphthalein anhydride.

The following chart is taken from a paper by Copisarow (*Trans.*

Fluorescein was discovered by A. von Baeyer (*Ber.*, 1871, *4*, 558, 662) and soon attracted considerable attention on account of the beautiful fluorescence of its alkaline solutions as well as by its employment as a yellow dyestuff. In the autumn of 1871, Baeyer handed a specimen of fluorescein to Caro of the Badische Anilin und Soda Fabrik and received news from him a few days afterwards that he had discovered a beautiful dyestuff by brominating the compound. Baeyer suggested to Emil Fischer the desirability of examining fluorescein more fully and as a result the diacetyl and dibenzoyl derivatives, the chloride and the sulphate were prepared and described (*Ber.*, 1874, *7*, 1211; *Dissertation*, Strassburg, 1874).

Meanwhile, Caro undertook the task of preparing the necessary intermediates on a technical scale and discovered the method of purifying tetrabromofluorescein by means of its potassium salt, so that by the summer of 1874, the Badische

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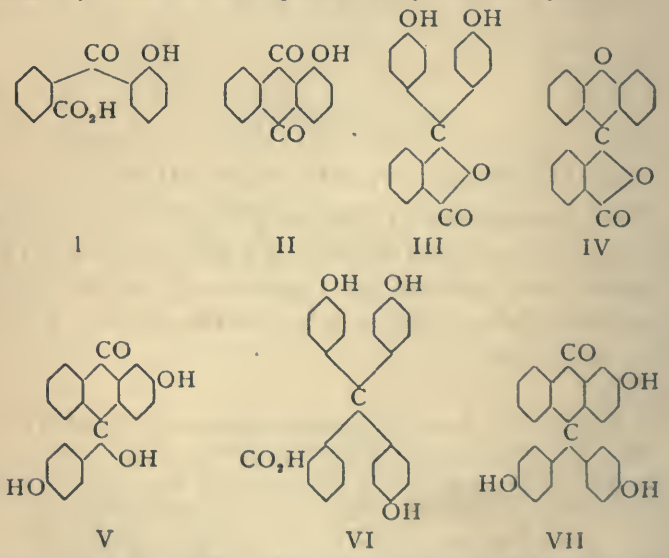
Chem. Soc., 1920, *117*, 209); it shows the substances which may be obtained by condensation of phthalic anhydride with phenol



Copisarow points out the influence of certain condensing agents in favouring particular reactions; he also gives an useful list of references.

Co were in the position to place the salt on the market under the name of *Eosine*.

At that date, the German Patent Law afforded very little protection and the decision was made to keep the process secret. By December 1874, Gnehm suspected that eosine was allied to Baeyer's phthalein dyestuffs, and shortly afterwards Hofmann (*Ber.*, 1875, *8*, 66) revealed the secret which had been kept for almost a year. (See von Baeyer, *Annalen*, 1876, *183*, 146.)

Preparation of fluorescein. Baeyer gives the following directions: 5 parts of phthalic anhydride and 7 parts of resorcin are heated in an oil-bath to 195—200°; after some time the mass froths owing to escape of water vapour and finally becomes solid; with small quantities this happens after 2 or 3 hours, with larger after 6 or 7. The mass is then crushed and boiled out with water.

Impurities originating from the resorcin are removed by washing with alcohol which also dissolves some of the fluorescein; the greater amount remains as a red powder. For crystallisation, the fluorescein is dissolved in dilute caustic soda solution, precipitated with dilute sulphuric acid and extracted with ether, this solvent taking up the hydrated form of fluorescein with great ease. Some absolute alcohol is added to the ethereal solution and the ether distilled off; the fluorescein then separates as crystalline crusts.

Von Baeyer gives the following alternative mode of purification. The fluorescein is boiled with an amount of dilute caustic soda solution insufficient to dissolve the whole; in this way the impurities are precipitated by the fluorescein. When a very impure product has to be dealt with, the solution in caustic soda may be treated with calcium chloride solution, the dark brown precipitate filtered off, excess of calcium precipitated by sodium phosphate, the brown coloured calcium phosphate removed and the fluorescein thrown out of solution by means of an acid.

It should be remarked that the resorcin used by Baeyer was not of the degree of purity expected at the present time,

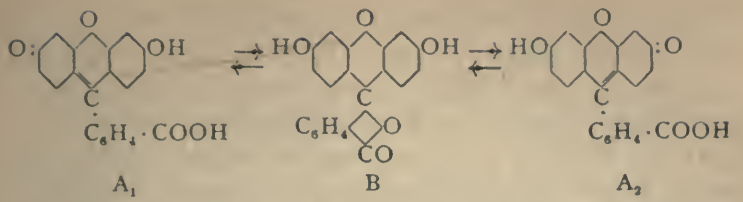
so that if fluorescein is required simply for conversion into other derivatives, a sufficiently pure material may generally be obtained by fractional precipitation of the alkaline solution.

By the direct precipitation of fluorescein on acidifying its alkaline solution, the substance is obtained in an amorphous yellow flocculent condition, which on warming, drying or even being allowed to remain under the surface of the liquid is transformed into a yellowish red, fine crystalline powder. Analyses of precipitated fluorescein agree with the formula $C_{20}H_{12}O_5, H_2O$ (*Ber.*, 1871, *4*, 662), whereas the material after crystallisation from alcohol and drying at 130° has the composition $C_{20}H_{12}O_5$ and forms a dark red powder.

H. von Liebig states that in addition to the ordinary form of fluorescein, various other modifications exist, though polymeric formulae are assigned in some cases; all are stated to be unimolecular in solution. Reference has already been made to this author's work on resorcinbenzein. (See further, *J. pr. Chem.*, 1912, II, *85*, 97, 241.)

Fluorescein does not melt; on heating it remains unaltered up to 280°, above 290° it becomes very brown and finally decomposes completely. Freshly precipitated fluorescein dissolves easily in alcohol and ether; after crystallisation, continued boiling is necessary to get it into solution; it is fairly soluble in hot acetic acid but hardly at all in chloroform and benzene. The alcoholic solution is yellowish red and shows a green fluorescence; the solutions in alkalies (caustic or mild) are deep red becoming yellow on dilution, and exhibit a very lively green fluorescence visible at extreme dilutions, so that they are very suitable for tracing the course of underground streams. Measurements of the absorption were published by Le Royer (*Annalen*, 1887, *238*, 360).

Respecting the cause of the fluorescence, R. Meyer supposed that it depended on the fluorophoric pyrone ring (*Zeitschr. physikal. Chem.*, 1897, *24*, 468). J. T. Hewitt, on the other hand, attributed it to tautomeric change between the lactonoid and quinonoid configurations (*Proc. Chem. Soc.*, 1900, *16*, 3; *Zeitschr. physikal. Chem.*, 1900, *34*, 5).



A_1 B A_2

The quinonoid form A may be derived from the lactonoid B by displacements with respect to either of the phenolic residues, so that a molecule of structure A_1 might swing through position B to A_2, the oscillations resembling in some degree those of a pendulum. Fluorescent organic compounds usually show this sort of double symmetrical tautomerism.

Salts with bases. Fluorescein forms salts in which two hydrogen atoms are replaced by metal; a few have been analysed, e. g. $CaC_{20}H_{10}O_5, 4\,H_2O$ and $BaC_{20}H_{10}O_5, 9\,H_2O$ (Schreder, *Ber.*, 1878, *11*, 1342). The ammonium salt is precipitated in a flocculent state when ammonia is passed into an ethereal solution of fluorescein; it loses ammonia on exposure to the air.

The violet solution produced by boiling fluorescein with a large excess of caustic soda very probably contains salts in which the pyrone ring has been ruptured and consequently more nearly the analogues of phenolphthalein salts. Such a solution alters its shade on dilution with water, and finally shows the colour of an alkaline solution of fluorescein, the latter compound being precipitated on acidification. The violet colour is conserved if the dilution be effected with alcohol; acids then produce a yellow precipitate which dissolves in ether with a yellow shade. A caustic alkali solution is coloured violet if brought in contact with this ethereal extract. When fluorescein is fused with alkali, the two resorcin molecules are split off in succession, dihydroxybenzoylbenzoic and phthalic acids being produced (Baeyer).

Salts with acids. Fluorescein dissolves in concentrated sulphuric acid with dark red colour and green fluorescence. Baeyer (*Annalen*, 1876, *183*, 27) isolated a compound to which he assigned the formula $C_{20}H_{12}O_5, SO_3$, this product being

obtained by condensing resorcin and phthalic anhydride with concentrated sulphuric acid at 100°, extracting unaltered resorcin and sulphuric acid with cold water, and crystallising from methyl alcohol. Well formed prismatic yellowish crystals were obtained in this way; Baeyer's formula agrees with the structure of a fluoresceinsulphonic acid, but he himself negatived this possibility by showing that the compound was readily decomposed into fluorescein and sulphuric acid on warming with water.

At a later date, Gattermann and Öhmichen (*Ber.*, 1899, *32*, 1135) obtained an addition compound of fluorescein with hydrochloric acid, $C_{20}H_{12}O_5$, HCl, which was recorded without attracting any interest. Shortly afterwards, Hewitt (*Zeitschr. physikal. Chem.*, 1900, *34*, 7) assumed the existence of an oxonium salt in the fluorescent solution obtained by dissolving fluorescein in concentrated sulphuric acid. The existence of such salts was regarded with suspicion by R. Meyer (*Jahrbuch der Chemie*, 1901, *10*, 3819), but Hewitt and Tervet (*Trans. Chem. Soc.*, 1902, *81*, 665) prepared and analysed a monohydrochloride, a monosulphate and a disulphate of fluorescein. Baeyer's compound was evidently the monosulphate, the percentage of sulphur (7.88) recorded in his analysis being quite indecisive for $C_{20}H_{12}O_5$, SO_3 which requires 7.77 per cent and for $C_{20}H_{12}O_5$, H_2SO_4 which requires almost as much, viz, 7.44 per cent.

Ethers and esters of fluorescein. The alkyl derivatives of fluorescein have been treated at some length in discussing the tautomerism of the compound. Acylation leads to colourless derivatives of the lactonoid form, i. e. to substituted fluorans in all cases.

Chloride, (3:6-*Dichlorofluoran.*) Baeyer (*Annalen*, 1876, *183*, 18) obtained this compound by warming fluorescein with two molecular proportions of phosphorus pentachloride; an energetic reaction set in at 70° and was completed by heating for two hours to 100°. The resulting dark red mass was boiled out several times with water and unchanged fluorescein then removed by digestion with caustic soda solution.

After several extractions with boiling alcohol, the compound was crystallised by solution in hot toluene, addition of one or two volumes of alcohol, and cooling.

Dichlorofluoran forms small, colourless prisms, melts at 252°, is insoluble in water, difficultly soluble in alcohol, ether, acetone and acetic acid, easily soluble in chloroform, benzene and toluene. The compound may be reconverted into fluorescein by heating with a small amount of water and an excess of lime in a sealed tube to 230°; the chlorine is also replaceable by amine residues. The halogen atoms are evidently less firmly bound to the aromatic nucleus than they are in the case of chlorobenzene. On the other hand, heating with an excess of fuming hydriodic acid to 150° fails to remove the chlorine atoms though the compound adds on two atoms of hydrogen at the lactone ring giving a carboxylic acid (M. p. 229—230°).

Dichlorofluoran has also been obtained by the condensation of 3-chlorophenol with phthalic anhydride in presence of zinc chloride. 3:4-Dichlorophenol, 2-chloro-4-cresol and 2-bromo-4-cresol undergo similar condensations giving 2:3:6:7-tetrachlorofluoran (m. p. 255°), 2:7-dimethyl-3:6-dichlorofluoran (m. p. 285°) and 2:7-dimethyl-3:6-dibromofluoran (m. p. 284—285°) respectively. (Badische Co., Brit. P. 9675/1904; U.S.P. 785003/1904 of P. Julius; F. P. 342518/1904; D.R.P. 156333/1903.)

Diacetylfluoran. This is obtained by gently boiling fluorescein with 3 to 4 times its weight of acetic anhydride until a sample furnishes yellow crystals on dilution with alcohol. Excess of acetic anhydride is destroyed by pouring into alcohol, allowing to stand for one day, collecting the separation and purifying this by solution in glacial acetic acid and pouring into several volumes of alcohol. Colourless needles, m. p. 200°. Baeyer obtained pure fluorescein by hydrolysing the diacetylderivative with alcoholic potash, diluting with water and acidifying.

Dibenzoylfluorescein. Baeyer prepared this compound by heating fluorescein with four times its weight of benzoyl

chloride to 140° for one hour, boiling out the product with water and crystallising from acetone. Colourless crystals, m. p. 215°.

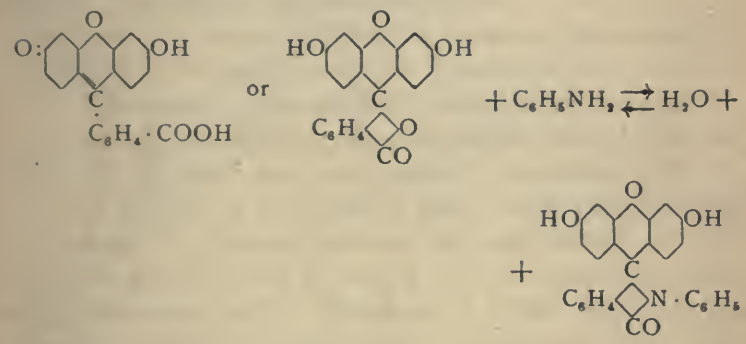
Fluorescein bisphenylcarbamate. $C_{20}H_{10}O_3(O \cdot CO \cdot NH \cdot C_6H_5)_2$, is obtained by heating fluorescein with phenylcarbimide. It forms pale yellow, microcrystalline grains, melts at 195°, and, whilst somewhat soluble in acetone, is very slightly soluble in most organic solvents. Phenolphthalein behaves in a similar manner. (Haller and Guyot, *Compt. rend.*, 1893, *116*, 121.)

Thiofluorescein. (3:6-*Dithiolfluoran.*) This compound is formed by boiling 5 grams of dichlorofluoran with 50 cc. of concentrated alcoholic potassium hydrosulphide for half-an-hour, filtering off the potassium chloride, diluting the intensely blue solution with water and carefully precipitating with dilute hydrochloric acid. For purification, the compound can be dissolved in very dilute ammonia and the solution filtered into excess of dilute hydrochloric acid. Free thiofluorescein is thus obtained as a greyish white, amorphous powder which cannot be obtained in a crystalline condition; it is almost insoluble in alcohol, ether and benzene; it dissolves more easily in carbon disulphide, but is recovered as a resin on evaporation (Gattermann, *Ber.*, 1899, *32*, 1127). Colourless aromatic ethers of thiofluorescein are obtained by acting on dichlorofluoran with alcoholic potash and thiophenol or its analogues. These substances differ from the free thiofluorescein in being readily crystallisable.

Fluorescein-anilide. $C_{20}H_{12}O_4(:N \cdot C_6H_5)$. Colourless compounds are obtained by replacing oxygen in the lactone ring of fluorescein by groups of the type RN.

O. Fischer and E. Hepp (*Ber.*, 1893, *26*, 2236) obtained fluorescein-anilide by boiling 1 part of fluorescein with 4 parts of aniline and 2 parts of aniline hydrochloride for 6 hours under reflux, driving off the excess of aniline in a current of steam and crystallising the residue from hot dilute alcohol and then from ethyl acetate. The colourless leaflets turn red

on heating to 200° and give a reddish sublimate. Fluorescein-anilide is insoluble in water and gives colourless solutions in alcohol, glacial acetic acid and alkalies; the alkaline solutions have a strong green fluorescence. The solution in concentrated sulphuric acid is yellow and shows a feeble green fluorescence. Dilute alkalies and acids do not hydrolyse the compound, but fluorescein and aniline are regenerated when a concentrated alcoholic solution is subjected to prolonged boiling with 40 per cent sulphuric acid.



Fluorescein is red and tautomeric, its anilide is colourless and only yields colourless dimethyl (m. p. 207—208°) and diethyl (m. p. 162—164°) ethers.

The monomethyl ether of fluorescein may be similarly converted into an anilide, $C_{20}H_{10}O_2(OH)(OCH_3)(:N \cdot C_6H_5)$, m. p. about 280°, which is colourless and dissolves in alkali giving a colourless solution without any trace of fluorescence Fischer and Hepp, *Ber.*, 1895, *28*, 397).

Fluorescein-phenylhydrazide, $C_{20}H_{12}O_4(:N \cdot NH \cdot C_6H_5)$, is obtained by gently boiling 3 grams of fluorescein with 10 grams of phenylhydrazine, diluting with ether and crystallising from dilute acetic acid. The substance is colourless, and gives colourless, fluorescent solutions in alkalies (Gattermann and Ganzert, *Ber.*, 1899, *32*, 1133). The same authors obtained a colourless phenylhydrazide of 3:6-dichlorofluoran, $C_{20}H_{10}O_2Cl_2(N_2HC_6H_5)$, which melts at 265°.

Substitution Derivatives of Fluorescein

Replacement of hydrogen atoms in fluorescein may take ploce either in the resorcin or phthalic residues. It has already been mentioned (p. 280) that substituting agents first attack positions 4 and 5 and then 2 and 7, whilst compounds substituted in the phthalic residue are usually prepared by condensing resorcin with correspondingly substituted phthalic anhydrides. The colour of the compounds depends more on substitution in the resorcin residues than in the phtalic group.

2:7- (? 4:5-) *Dichlorofluorescein*, $C_{20}H_{10}O_5Cl_2$. A dichlorofluorescein can be obtained by the direct chlorination of fluorescein; apparently the same compound is formed by condensation of phthalic anhydride with chlororesorcin, but attempts further to chlorinate the compound lead to destruction of the molecule. (Meister, Lucius and Brüning, D. R. P. 230737/1909; U. S. P. 990224/1911 of A. Brunner.) The German Patent does not mention how the fluorescein is chlorinated, neither does it specify the orientation of the chlororesorcin which is condensed with phthalic anhydride, but claims that further introduction of bromine or iodine leads to the production of valuable dyestuffs.

Example 1. 20 kilos of dichlorofluorescein (from chlororesorcin and phthalic anhydride) are suspended in alcohol and treated with 16 kilos of bromine. The mass becomes warm and the product separates in a short time. The compound forms red, shining leaflets; it dissolves in alkalies with a red colour and green fluorescence, and dyes wool in shades resembling those given by eosine.

Example 2. 13 kilos of iodine are introduced into 15.8 kilos of the product obtained by the action of chlorine on fluorescein. The new dye gives shades resembling those given by erythrosine (Tetraiodofluorescein).

It seems very improbable that the dichlorofluorescein of example 1 can be the same as that used in example 2. Direct chlorination of fluorescein must almost certainly give rise to 4:5-dichlorofluorescein which would also be produced by condensation of phthalic anhydride with 2-chlororesorcin.

The patentees do not mention the source of the chlororesorcein they employed; the compound obtained by Reinhard (*J. pr. Chem.*, 1878, II, *17*, 328) was probably 4-chlororesorcin since, as Mettler points out (*Ber.*, 1912, *45*, 803), sulphuryl chloride has a pronounced tendency to chlorinate phenols exclusively in the para position.

2:4:5:7-*Tetrachlorofluorescein*, $C_{20}H_8O_5Cl_4$, was discovered in the laboratory of the Geigy works. (C. Mettler, *Ber.*, 1912, *45*, 800), the method employed being to heat dichlorodihydroxybenzoylbenzoic acid. (Compare the production of eosine from dibromodihydroxybenzoylbenzoic acid by R. Meyer.)

To obtain dichlorodihydroxybenzoylbenzoic acid, 125 grams of sulphuryl chloride were allowed to drop into a well cooled (ice) mixture of 100 grams each of dihydroxybenzoylbenzoic acid and dry ether under continual mechanical stirring. After some hours the ether was distilled off and the product dissolved in sodium carbonate solution and reprecipitated by acid, 122 grams of crude product being obtained. For complete purification, the compound was crystallised from glacial acetic acid. M. p. 222°.

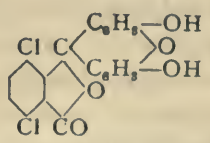
44 grams of dichlorodihydroxybenzoylbenzoic acid were melted, 10 grams of zinc chloride added and the mixture heated to 240° for 20 minutes. After cooling, the tetrachlorofluorescein was dissolved in sodium carbonate solution, filtered and precipitated by acid, purification being effected through the red, crystalline ammonium salt. After crystallisation from glacial acetic acid and drying at 100°, the compound was still hydrated, its percentage of chlorine agreeing with the formula $C_{20}H_8O_5Cl_4, H_2O$.

The substance softened at 295° and was completely fused at 305°, the flesh colour giving place to a deep red. The shades produced by this dyestuff on the fibre are possibly somewhat yellower than those given by eosine.

A dyestuff of unknown constitution was obtained by Wilm, Bouchardat and Girard by the action of bleaching powder or chloride of soda and a slight excess of hydro-

chloric acid on fluorescein. This was called "Aureosin"; its alkaline solution was rose red and showed a green fluorescence, so that possibly it was dichlorofluorescein. A. beautiful red dye, "Rubeosin", was obtained by its nitration. (D. R. P. 2618/1877, lapsed in 1880.)

3':6'-*Dichlorofluorescein.*



In order to modify the shade of eosine, Noelting introduced the use of chloro-derivatives of phthalic acid which were condensed with resorcin to substituted fluoresceins and then brominated. The "phloxine" of P. Monnet et Cie. was produced by this method from a dichlorophthalic acid; the latter compound was examined at some length by Le Royer (*Annalen*, 1887, *238*, 350) and taken for a derivative of *o*-dichlorobenzene. It was not until 1900 that Graebe (*Ber.*, *33*, 2019; and with Gourevitz, *ibid.*, 2023) examined the technical "*β*-dichlorophthalic acid" really systematically when it was found to furnish *p*-dichlorobenzene on degradation.

Le Royer condensed dichlorophthalyl chloride (1 mol.) with resorcin (2 mols.) at 200°, dissolved the melt in ammonia, precipitated the filtered solution with hydrochloric acid and crystallised the dichlorofluorescein from methyl alcohol. The substance was thus obtained as $C_{20}H_8O_5Cl_4, H_2O$; when boiled under water it melted and was transformed into the granular anhydrous compound. The alkaline solution resembled that of fluorescein but was redder in shade, the absorption band being shifted in the direction of greater wavelength.

3':4':5':6'-*Tetrachlorofluorescein*, $C_{20}H_8O_5Cl_4$, is obtained by heating 13 parts of tetrachlorophthalic anhydride with 10 parts of resorcin for 2 or 3 hours at 200° (Gräbe, *Annalen*, 1887, *238*, 333). When an alkaline solution is precipitated by acid and the producet crystallised from ether, the

substance is obtained as reddish yellow needles of the hydrate, $C_{20}H_{10}O_6Cl_4$, which remains practically unchanged at 150—160° but loses water at 180—200° giving yellow red anhydrous substance. The *diacetyl derivative* was obtained as somewhat yellowish crystals.

Monobromofluorescein. Baeyer (*Annalen*, 1876, *183*, 36) suspended fluorescein in four times its weight of glacial acetic acid and added the calculated quantity of bromine as a 20 per cent solution in glacial acetic acid in one lot. The amorphous substance was not analysed; it could not be purified by crystallisation or by means of an acetyl derivative. The evidence for the existence of monobromofluorescein as a chemical individual is scanty.

4:5-*Dibromofluorescein*, $C_{20}H_{10}O_5Br_2$. This was obtained in a somewhat similar manner using two molecular proportions of bromine, the compound being purified by solution in alcohol, addition of acetic acid and evaporation. It was thus isolated as reddish brown thick needles melting at 260—270°. The solution in alkalies is reddish yellow and feebly fluorescent (green); on boiling, the colour of the solution turns first violet then blue. *Diacetyl derivative.* M. p. 208—210° (Baeyer). *Dibenzoyl derivative.* M. p. 240—244° (Hewitt and Woodforde).

2:4-*Dibromoflurocein* was obtained by Heller and H. L. Meyer (*Ber.*, 1909, *42*, 2188) by condensing dibromodihydroxybenzoylbenzoic acid with resorcin in presence of 20 per cent of zinc chloride at 170°. A small amount of fluorescein produced during the condensation is removed as hydrochloride by adding alcoholic hydrochloric acid to the solution in acetone. The compound melts at about 300°. Silk is dyed yellow from an acetic acid bath but without fluorescence; alkaline solutions show fluorescence intermediate between fluorescein and eosine. On alkaline fusion, dihydroxybenzoylbenzoic acid is formed. *Diacetyl derivative*, m. p. 173° with evolution of gas.

2:4:5:7-*Tetrabromofluorescein.* (*Eosine.*) Baeyer (*Annalen*, 1876, *183*, 39) states that this dyestuff is obtained

by adding a 20 per cent solution of bromine in glacial acetic acid to fluorescein mixed with four times its weight of glacial acetic acid, the tetrabromofluorescein separating in a crystalline condition on standing. Alternatively, bromine may be added to a mixture of fluorescein and alcohol avoiding too great a rise in temperature; on the other hand it is necessary not to operate too slowly or dibromofluorescein crystallises out and escapes the further action of the halogen. For final purification, Baeyer recommends conversion into the crystalline potassium salt and crystallisation of the regenerated eosine from six times the quantity of absolute alcohol.

On a manufacturing scale, bromination in alcoholic suspension was resorted to, an oxidising agent (alkaline chlorate, cupric salt etc.) being added so that only four atomic proportions of bromine were necessary instead of eight, though this does not appear in the accounts given by Bindschedler and Busch (*Monit. sci.*, 1878, *20*, 1170) and Mühlhäuser (*Dingler's Polyt. J.*, 1887, *263*, 100).

Bindschedler and Busch describe two processes for the technical preparation of eosine. According to the first method, 1 kilo of finely powdered fluorescein is suspended in 10 litres of alcohol and 1.1 kilo of bromine added very slowly through a fine jet with continuous stirring. At this stage the partially brominated dyestuff is all in solution, bromination is continued with a further 1.1 kilo of bromine, added as before described. Each drop gives a crystalline precipitate of tetrabromofluorescein. The liquid is then decanted, the residue washed with a small amount of alcohol, suspended in boiling water, caustic soda added to neutralisation and the resulting solution evaporated, the eosine being obtained as a crystalline powder. The alcoholic mother liquors from the deposit of tetrabromofluorescein are worked up to yield an inferior eosine and the bromine in solution as hydrobromic acid is also recovered.

In the second process, 5 kilos of fluorescein and the necessary amount of caustic soda are dissolved in 200 litres of boiling water. On the other hand, 11 kilos of bromine are

dissolved in sufficient caustic soda to give a colourless solution. The two solutions are mixed and hydrochloric acid run in very slowly in sufficient quantity to render the mixture acid. The product is filtered off, washed, dissolved in caustic soda solution and evaporated as described for the first method.

Mühlhäuser adds some further details. 20 kilos of fluorescein and 80 kilos of alcohol (96°) are raised to boiling in an enamelled, steam jacketted vessel provided with an enamelled stirrer. The contents of 4 bottles, each containing 13 kilos of bromine, are added in the course of 50 minutes, the heating is then continued for 3 hours at $1^1/_2$ atmospheres (Überdruck). Afterwards the material is washed and dried, yield 27 to 31 kilos.

The Société chimique des Usines du Rhône obtain eosine by anodic oxidation of a solution of fluorescein and bromine in dilute sodium carbonate (D. R. P. 108838/1899).

F. Alefeld and W. Vaubel (*Chem. Zeit.*, 1898, *22*, 297) had made somewhat similar experiments but introduced the halogen in the form of hydracid into the kathodic compartment; the dyestuffs they obtained in this way were apparently not pure since they gave duller shades than the dyestuffs made by the usual substitution processes.

According to the patent referred to above, eosine may be obtained in great purity by the following procedure. 1 kilo of fluorescein is dissolved in a solution of 1 kilo of sodium carbonate in 30 kilos of water and 1 kilo of bromine is added whilst the mixture is stirred. Electrolysis is then effected, a diaphragm being used whilst a dilute solution of sodium hydroxide or carbonate is used as the kathode liquid. The kathode is of iron sheet or gauze, the anode of platinium gauze and the liquid is kept stirred during the operation. The current density is 2 to 3 ampères per square metre and the time taken is determined by finding when the desired shade is arrived at. According to the duration of the electrolysis, dyes giving orange yellow to bluish red may be obtained.

Eosine crystallises from alcohol with one molecule of solvent; it loses this at 100°. When the potassium salt of eosine is heated with concentrated caustic potash, it passes into solution and the colour changes to an intense blue which is not immediately discharged on dilution. On allowing the diluted solution to stand for some time, it becomes red, but the concentrated solution will remain blue. The diluted blue solution gives a reddish yellow precipitate on acidification which redissolves in alkalies with a blue colour; this precipitate was not analysed but is probably the substance produced by hydration of the pyrone ring.

If the potassium salt is heated to 140° with 20 times its weight of 50 per cent caustic soda, it undergoes fission, dibromoresorcin (m. p. 92°) and dibromodihydroxybenzoylbenzoic acid (m. p. 218—220°) being produced. Baeyer was unable to confirm Hofmann's statement (*Ber.*, 1875, *8*, 64) that dibromoresorcin can be obtained from eosine by heating with hydrochloric acid to 150°.

By boiling eosine with 20 times its weight of concentrated sulphuric acid for 5 minutes, a substance was obtained which when purified gave figures agreeing with the formula $C_{40}H_{13}O_{10}Br_7$. It formed dark, steel blue needles, difficultly soluble in organic solvents with violet colour, soluble in dilute alkalies with greenish blue shade.

Salts of eosine with many metals have been described.

$Na_2C_{20}H_6O_5Br_4$. In a crystallised state, this was used for silk dyeing under the name of Eosine A extra (Heumann, *Anilinfarben*, 1888, 1, 471).

$K_2C_{20}H_6O_5Br_4$. Described as crystallising with 5 or 6 H_2O, or with 1 C_2H_5OH. It is very soluble in water. Baeyer prepared the pentahydrate by adding 100 parts of alcohol to a warm solution of the commercial salt ("water soluble eosine") in 50 parts of water and allowing to stand. Large, measurable leaflets were obtained, red by transmitted light and showing blue and yellow green reflexes. The crystals were described by Groth.

$(NH_4)_2C_{20}H_6O_5Br_4$. Analysis of the salt obtained by

concentrating an alcoholic ammoniacal solution of eosine points to some loss of ammonia. The dye sold as "Eosine B extra" was made by exposing eosine to ammonia gas until completely water soluble. Heumann states that 31.8 kilos were obtained from 30 kilos of tetrabromofluorescein in practice.

$Ag_2C_{20}H_6O_5Br_4$. Dark red precipitate, slightly soluble in water and alcohol.

$CaC_{20}H_6O_5Br_4, {}^1/_2H_2O$. Yellow needles, fairly soluble in water.

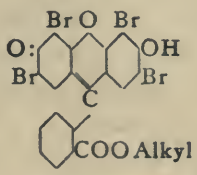
$BaC_{20}H_6O_5Br_4, 2H_2O$. Yellowish red rhombic tablets, sparingly soluble in cold water.

$CdC_{20}H_6O_5Br_4, ?H_2O$. Well crystallised, not analysed.

$PbC_{20}H_6O_5Br_4$ and $(PbOH)_2C_{20}H_6O_5Br_4$. Red amorphous precipitates.

Amorphous precipitates were also obtained with the salts of various other metals.

Monomethyl ester (*Methylerythrine*). Baeyer (*loc. cit.* 53) describes the compound as fine needles or small red crystals, difficultly soluble in alcohol, fairly easily in chloroform. The erythrines were taken for ethers of eosine; their true ester constitution



was proved by Nietzki and Schröter. (See p. 282.)

The preparation of methylerythrine is described by Bindschedler and Busch (*Monit. sci.*, 1878, *20*, 1172). 5 Kilos of tetrabromofluorescein, 10 kilos of methyl alcohol and 9 kilos of sulphuric acid (66° Bé.) are heated for 4 hours on the water bath and poured into a large excess of cold water. The precipitate is collected and converted into the potassium salt by boiling with a solution of potassium carbonate. On filtering, the desired compound is left as a solid whilst any

tetrabromofluorescein which has escaped esterification is contained in the mother liquor.

Monoethyl ester (*Erythrine*). Baeyer (*loc. cit.* p. 46) obtained a monoethyl derivative of eosine by heating the potassium salt with alcohol and potassium ethyl sulphate for 5 hours at 140—150°; the reaction with ethyl bromide proceeded less smoothly. The compound gives salts containing one atom of an alkali metal and was introduced as a dyestuff under various names, e. g. Erythrine, Spriteosin, Primerose à l'alcool, Rose J. B. à l'alcool.

It was discovered subsequently that it might be more easily obtained by acting on eosine with alcohol and sulphuric or hydrochloric acid from which it appeared probable that the compound was really an ester. This was confirmed by Nietzki and Schröter (*Ber.*, 1895, *28*, 46) who showed that it could be obtained by the bromination of fluorescein ethyl ester of m. p. 247°. Since the latter compound is obtained by the oxidation of fluorescin ethyl ester, no doubt remains as to the ester character of the compound.

In manufacturing ethyl eosine, Mühlhäuser (*Dingler's Polyt. J.*, 1887, *263*, 101) gives the following directions for converting the ethyl tetrabromofluorescein into its potassium salt. $2^1/_2$ parts of water and $1^1/_2$ parts of alcohol are mixed, then 1 part of dye is added, the mixture raised to boiling and the calculated amount of caustic potash heated to 80° added in a thin stream in the course of 15 minutes. The apparatus is opened after 3 days, the crystals pressed, washed with hot water, again pressed and dried.

Baeyer (*loc. cit.*, 50) describes the preparation of mono- and di-ethyl derivatives by acting on the silver salt of eosine with ethyl iodide at 100°. Extraction of the reaction product with alcohol removed the colourless monoethyl compound together with small quantities of the red diethyl derivative; these were separated by a solution of alkali in 50 per cent alcohol. The alkaline solution was treated with acetic acid and sufficient dilute alcohol to keep the substance in solution whilst warm; on cooling, the monoethyl-compound separated

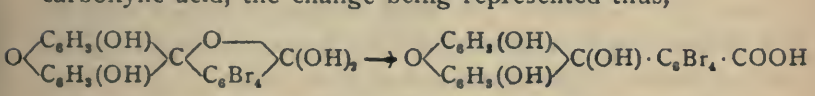
in fine yellow needles which were obtained colourless by repeating the process.

The residue left after removing the ethyl ether from the reaction product of ethyl iodide on silver eosinate was extracted with a hot solution of caustic potash in 50 per cent alcohol and crystallised from chloroform. The small red crystals dissolved with difficulty in alcohol and ether but easily in chloroform and glacial acetic acid. Since the same compound was subsequently obtained by alkylating the coloured ethyl ester of eosine, there is no doubt as to it being a quinonoid diethyl ether-ester of eosine.

Baeyer also described *Diacethyleosine* and *Eosine chloride* (3 : 6-*dichloro*-2 : 4 : 5 : 7-*tetrabromofluoran*).

3' : 4' : 5' : 6'-*Tetrabromofluorescein*, $C_{20}H_8O_5Br_4$. This compound is prepared by the condensation of resorcin with tetrabromophthalic anhydride[1] (D. S. Pratt, G. F. Hutchinson and A. W. Harvey, *J. Amer. Chem. Soc.*, 1919, *41*, 1293).

The colour of the alkaline solution is similar to that of fluorescein; on acidification, a precipitate of the yellow hydrate is formed, but at 100° this is converted into the brick-red quinonoid tetrabromofluorescein; the latter gives a yellow benzenoid form when wetted with acetone or ethyl acetate. The yellow hydrate gives a very pale yellow isomeride when treated with alcohol; this is supposed to be the carbinol-carboxylic acid, the change being represented thus,



The bright red *diammonium* salt and the colourless *diacetyl* derivative have been prepared.

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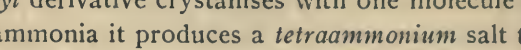
1 Tetrabromophthalic anhydride (m. p. 279.5—280.5°, corr.) was obtained by D. S. Pratt and C. O. Young (*J. Amer. Chem. Soc.*, 1918, 40, 1415) by allowing phthalic anhydride and bromine to react with one another in presence of iodine, hot fuming sulphuric acid being used as solvent. Numerous derivatives were prepared; by condensation with phenol in presence of fuming sulphuric acid (15% SO_3) a mixture of the tetrabromoderivatives of phenolphthalein and fluoran was produced.

2:4:5:7:3′:4′:5′:6′-*Octabromofluorescein*, $C_{20}H_4O_5Br_8$ is obtained by the action of bromine on the preceding tetrabromofluorescein. It is nearly colourless but extremely sensitive to alkalies giving coloured salts; it dyes silk pink. The *diacetyl* derivative crystallises with one molecule of benzene; with ammonia it produces a *tetraammonium* salt to which the following structure is assigned.



A *Diiodofluorescein*, $C_{20}H_{10}O_5I_2$, was sold by Monnet under the name of *Pyrosine J*, probably the positions 4 and 5 were occupied by halogen. The ammonium salt was also known as *Erythrosine G* as well as *Dianthine G.*

2:4:5:7-*Tetraiodofluorescein*, $C_{20}H_8O_5I_4$, was marketed in the form of the sodium salt under the names of *Erythrosine B*, *Rose B à l'eau*, *Pyrosine B*, *Primerose soluble*, *Jodeosin B*, *Eosine bleuâtre* and *Diathine B.*

Eosine bleuâtre (soluble à l'eau) was introduced by the firm of Bindschedler and Busch in 1876, the process being based on the experiments of Kussmaul. The following description of the manufacture is of interest (*Monit. sci.*, 1878, *20*, 1171). Fluorescein and iodine are dissolved independently in dilute caustic soda lye and the solutions mixed; on acidification the tetraiodofluorescein is precipitated in a finely crystalline condition. The precipitate is converted into the sodium salt whilst iodine is recovered from the mother liquors by potassium bichromate and sulphuric acid.

Mühlhäuser (*Dingler's Polyt. J.*, 1887, *263*, 106) states that better results are obtained when an organic acid is used to liberate the iodine.

The electrolytic preparation of erythrosine has been described by the Société chimique des Usines du Rhône (D. R. P. 108838/1899). 1 kilo of fluorescein and 1.5 kilos of finely ground iodine are dissolved in a solution of 1 kilo of sodium carbonate in 30 kilos of water. The solution is then oxidised anodically under the conditions described for

the corresponding preparation of eosine. The patent also refers to the substitution of hydrogen by halogen in the case of the chlorofluoresceins.

3':4':5':6'-*Tetraiodofluorescein*, $C_{20}H_8O_5I_4$, was obtained by D. S. Pratt and A. B. Colemann (*J. Amer. Chem. Soc.*, 1918, *40*, 236) by condensing resorcin with tetraiodophthalic anhydride[1] in presence of zinc chloride.

The alkaline solution is yellowish red in colour and exhibits a vivid green fluorescence thus differing markedly from erythrosine. On acidifying the alkaline solution, a golden yellow hydrate is precipitated which after air-drying for some days retains approximately one molecule of (carbinol) water; this can be expelled at 120°, the colour changing to reddish-brown. This colour change is attributed to the production of a certain amount of the quinonoid form. The colour of the anhydrous compound is altered to a clear canary yellow if a drop of acetone, alcohol or ethyl acetate is applied; in this case it is assumed that the structure undergoes rearrangement and that the more stable benzenoid modification is produced.

The freshly precipitated, golden-yellow hydrate is immediately converted into a very pale yellow isomeride by a little methyl or ethyl alcohol, the change being explained as due to the production of a carbinol-carboxylic acid; a similar case has been mentioned with regard to the corresponding tetrabromofluorescein.

Besides *potassium* and *diammonium* salts, the authors describe *monomethyl-* (bright red, decomposes near 251°), *diacetyl-* (yellow), and *dibenzoyl-* (pale yellow, m. p. 288°) derivatives.

2:4:5:7:3':4':5':6'-*Octaiodofluorescein*, $C_{20}H_4O_5I_8$, was prepared by Pratt and Colemann by heating an alcoholic solution of the preceding compound with iodine and iodic

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1 Tetraiodophthalic anhydride, yellow needles, m. p. 320—325° corr. is obtained by heating phthalic anhydride with iodine and fuming sulphuric acid; several derivatives have been prepared. (D. S. Pratt and A. F. Shupp, *J. Amer. Chem. Soc.*, 1918, *40*, 254.)

acid for twelve hours. It forms clear yellow crystals which become dark red at 140°; this is attributed to quinonoid transformation. The yellow additive compound with acetone is resolved into its constituents at 120°. A red *tetraammonium* salt, a violet *silver* salt, and *monomethyl-*, *diacetyl-* and *dibenzoyl* derivatives are described.

3':6'-*Dichloro*-2:4:5:7-*tetrabromofluorescein*, $C_{20}H_6O_5Cl_2Br_4$. The sodium salt was introduced by P. Monnet et Cie. under the name of *Phloxine*. Le Royer gives a brief account of the substance (*Annalen*, 1887, *238*, 358) which he obtained by dissolving dichlorofluorescein in methyl alcohol and gradually adding eight equivalents of bromine diluted with glacial acetic acid. The yellow, granular precipitate was dissolved in caustic potash, evaporated and the residue extracted with alcohol and ether. The salt was then dissolved in water, precipitated by hydrochloric acid, redissolved in ammonia and again precipitated. The alkaline solution is of a bluer shade than that of eosine.

3':4':5':6'-*Tetrachloro*-2:4:5:7-*tetrabromofluorescein*, $C_{20}H_4O_5Cl_4Br_4$. Even bluer shades are produced by this dye, it was used at one time under the names of *Phloxine TA*, *Eosine 10 B* and *Erythrosine B*.

Cyanosine, $C_{22}H_8O_5Cl_4Br_4$, is the *ethyl* derivative of the preceding compound. The corresponding *methyl ester* has also been manufactured.

The chlorofluoresceins substituted by halogen in the phthalic residue may also be substituted by iodine in that part of the molecule derived from resorcin. In this way, dyestuffs of pronounced blue shade are formed.

3':6'-*Dichloro*-2:4:5:7-*tetraiodofluorescein*, $C_{20}H_6O_5Cl_2I_4$. This dyestuff was introduced as a sodium or potassium salt under the name of *Rose Bengale*. Le Royer (*Annalen*, 1887, *238*, 359) prepared the substance by heating an alkaline solution of dichlorofluorescein on the water-bath and adding a solution of iodine in dilute caustic potash until the fluorescence produced by the dichlorofluorescein disappeared. Dilute hydrochloric acid was

added, the precipitate collected and treated with potassium iodide solution to remove free iodine. The resulting reddish yellow powder was a hydrate, $C_{20}H_8O_6Cl_2I_4$.

The commercial dye is a brown powder giving a red, non-fluorescent solution.

3':4':5':6'-*Tetrachloro*-2:4:5:7-*tetraiodofluorescein*, $C_{20}H_4O_5Cl_4I_4$. An alkaline salt of this compound was marketed as *Rose Bengale B* and *3 B*.

2:4:5:7-*Tetrabromo*-3':4':5':6'-*tetraiodofluorescein*, $C_{20}H_4O_5Br_4I_4$. Pratt and Colemann (*J. Amer. Chem. Soc.*, 1918, *40*, 245) prepared this compound by brominating tetraiodofluorescein in acetic acid solution. A benzenoid constitution was assigned to the substance as it shows no tendency to pass into a highly coloured form. The red alkaline solution exhibits a faint green fluorescence; acids precipitate an amorphous hydrate, $3\,C_{20}H_4O_5Br_4I_4, H_2O$. Besides *diammonium* and *monosilver* salts, a red amorphous *monomethyl ether* and pale yellow *diacethyl*- (m. p. 270—280°) and *dibenzoyl*- (m. p. near 261°) derivatives were described.

Nitrofluoresceins

4:5-*Dinitrofluorescein*, $C_{20}H_{10}(NO_2)_2O_5$, was obtained by Baeyer (*Annalen*, 1876, *183*, 32) by adding 2 parts of fuming nitric acid to a solution of 1 part of fluorescein in 20 parts of concentrated sulphuric acid cooled to 0°. Water precipitates it from the resulting mixture as a reddish yellow precipitate. Baeyer did not analyse the product in this form; in order to obtain a pure substance the precipitate was acetylated, crystallised from alcohol or ethyl acetate and the diacetyl derivative hydrolysed by boiling with alkali. A blue solution was obtained in this way; acids threw down a yellow precipitate which even after recrystallisation dissolved in alkalies with a blue colour, and, as Baeyer showed, possessed the formula $C_{20}H_{12}(NO_2)_2O_6$.

J. T. Hewitt and B. W. Perkins (*Trans. Chem. Soc.*, 1900, *77*, 1324) confirmed these results but showed that if

the acetyl compound were hydrolysed by heating with 80 per cent sulphuric acid for one hour on the water-bath, a canary coloured precipitate was obtained which proved on analysis to be the anhydrous dinitrofluorescein $C_{20}H_{10}(NO_2)_2O_5$. Anhydrous dinitrofluorescein dissolves in cold dilute sodium hydroxide or in sodium carbonate solution with an orange brown colour, and exhibits no fluorescence. If the solution in caustic soda be warmed, the colour changes to a dark blue (no fluorescence); at this stage acids precipitate the hydrate.

Since the salts of dinitrofluorescein and its hydrate are evidently of different series, the simplest explanation is to suppose that the effect of warming with alkali is to open the pyrone ring. Hewitt and Perkins (*loc. cit.*) obtained confirmatory evidence by adding an excess of sodium ethoxide in absolute alcohol to a saturated alcoholic solution of dinitrofluorescein. The orange colour changed to blue on addition of a few drops of water and a purple crystalline paste separated on stirring. After collection and washing with alcohol, the amount of sodium was estimated in the salt and found to agree with the formula $C_{20}H_8O_{10}N_2Na_4$.

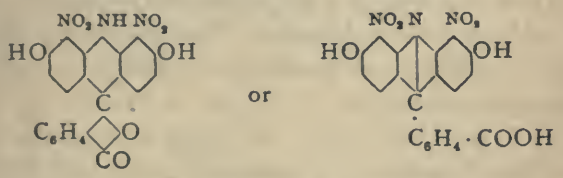
Hewitt and Perkins were under the impression that they were dealing with 2:7-dinitrofluorescein; in this they were mistaken. L. Matras (*Chem. Zeit.*, 1895, *19*, 408; *Arch. Sci. phys. nat.*, 1895, II, *33*, 285) had previously shown that 2-nitroresorcin results from the alkaline fission of dinitrofluorescein and a letter from M. Reverdin caused Hewitt and Woodforde (*Trans. Chem. Soc.*, 1902, *81*, 893) to reexamine dinitrofluorescein and the results of Matras were fully confirmed. The facts established by Hewitt and Perkins therefore relate to the 4:5- and not to the 2:7-dinitro-compound, which so far has not (as far as the present author knows) been prepared, though halogen derivatives such as safrosine are known.

4:5-Dinitrofluorescein possesses tinctorial properties but is of no particular value; its halogenated derivatives do not give shades which render their manufacture profitable.

M. T. Bogert and R. G. Wright (*J. Amer. Chem. Soc.*,

1905, *27*, 1310) reduced dinitrofluorescein with stannous chloride and hydrochloric acid obtaining a substance which was slightly soluble in ether or glacial acetic acid with green fluorescence; the alkaline solutions were red and fluoresced violet. By reducing with stannous chloride and dry hydrogen chloride in alcoholic solution, a substance was obtained which formed bright yellow crystals and melted at 249°.

By acting on dinitrofluorescein with ammonia, Reverdin (*Ber.*, 1897, *30*, 332) found that the pyrone oxygen atom was replaced by the NH group, an acridine derivative



being obtained. The reaction was carried out by adding 75 cc. of 21 per cent ammonia to a paste of 100 grams of dinitrofluorescein and 100 grams of water cooled by ice. The temperature rose to 35—40°; after standing some hours 125 cc. of salt solution were added and the ammonium salt collected. The free acid was liberated, extracted with cold acetone to dissolve impurities and converted into the more stable sodium salt, $C_{20}H_9O_8N_3Na_2$. The colouring matter dyes wool a pure yellow shade from an acid bath; the shades are evener and faster to light than those given by fluorescein derivatives. The ethyl ester behaves in a similar manner.

Aniline reacts in a similar manner with dinitrofluorescein, but in this case it is necessary to heat to 120°; the end of the reaction is detected by a sample no longer giving the characteristic reaction of dinitrofluorescein when warmed with caustic soda.

Meister, Lucius and Brüning protected the reaction (Brit. P. 3944/1896; D. R. P. 89400/1896) describing products resulting from the action of ethylamine and *p*-toluidine on dinitrofluorescein as well as those formed when ammonia acts on the products obtained by dinitrating the fluoresceins

derived from di- and tetra-chlorophthalic acids and nitrophthalic acid. Most of the new dyestuffs are said to give yellow or brownish yellow shades on wool, but the one from dichlorodinitrofluorescein and ammonia is exceptional in dyeing wool brick-red.

2:4:5:7-*Tetranitrofluorescein*, $C_{20}H_8(NO_2)_4$. Baeyer (*Annalen*, 1876, *183*, 33) treated fluorescein with an excess of fuming nitric acid and without cooling; a lively reaction occurred and when it was over, the solution was poured into water. The precipitate was collected, washed with a little alcohol and dissolved in a large quantity (50 parts) of glacial acetic acid by continual boiling. The material separated in crystalline nodules and according to Baeyer's analysis was tetranitrofluorescein.

Hewitt and Perkins (*loc. cit.*, 1329) introduced four nitro groups into fluorescein by nitrating as when preparing dinitrofluorescein, but either allowing the mixture to get warm or else leaving it overnight. The pinkish paste which separated on pouring into an excess of water was collected, washed and dissolved in a hot solution of sodium acetate; on cooling, small, brilliant red tetrahedra separated. From a solution of this salt, acids liberated a substance having the composition of a tetranitrofluorescein hydrate, from which Hewitt and Perkins were unable to remove the elements of water even by boiling with 50 parts of glacial acetic acid for 10 hours; nevertheless, this hydrate showed all the properties assigned by Baeyer to the anhydrous compound. Amongst them may be mentioned the yellowish red colour and yellowish green fluorescence of the alcoholic solution; this colour changes to reddish violet on addition of a drop of hydrochloric acid. The alkaline solutions exhibit no fluorescence.

Von Baeyer prepared an acetyl derivative but gives no analysis; Hewitt and Perkins also obtained such a compound but were unable to analyse it on account of its explosive properties; the latter authors also prepared and analysed salts of the compositions $C_{20}H_8O_{14}N_4Na_2, 8H_2O$ and $C_{20}H_8O_{14}N_4Ba, 4H_2O$.

Derivatives of fluorescein containing nitro groups in the phthalic residue have been prepared by M. T. Bogert and R. G. Wright (*J. Amer. Chem. Soc.*, 1905, *27*, 1310). The compounds obtained by condensing 3- and 4-nitrophthalic acids with resorcin give yellowish red alkaline solutions which have a weak but distinct green fluorescence.

The same authors also studied the reaction between fuming nitric acid and a solution of fluorescein in concentrated sulphuric acid; the product formed a white powder after crystallisation from acetone and appeared to be a penta- and not a tetra-nitro derivative. By acetylation, it seems that four acetyl groups can be introduced into the molecule.

No pure products were obtained on reducing pentanitrofluorescein; the solutions were deep red in colour and showed a blue fluorescence on dilution.

? 4:5-*Dichloro*-2:7-*dinitrofluorescein.* It is possible that the dye named "Rubeosin" by Wilm, Bouchardat and Girard (D. R. P. 2618/1877, lapsed in 1880) possessed the composition $C_{20}H_8Cl_2(NO_2)_2O_5$. A feebly alkaline 10 per cent solution of fluorescein to which bleaching powder or chloride of soda had been added was rendered acid by means of a slight excess of hydrochloric acid. The resulting "Aureosin" was then nitrated either by warming with dilute nitric acid (1 part of ordinary nitric acid to 2 parts of water) or by heating the solution in glacial acetic acid with saltpetre.

4:5-Dibromo-2:7-dinitrofluorescein, $C_{20}H_8Br_2(NO_2)_2O_5$. This compound was described by von Baeyer (*Annalen*, 1876, *183*, 61) who prepared it by the nitration of 4:5-dibromofluorescein; it was introduced as a dyestuff by the Badische Anilin und Soda Fabrik under the name of *Safrosine.*

Hewitt and Woodforde (*Trans. Chem. Soc.*, 1902, *81*, 898) examined the compound further; for its preparation 10 grams of dibromofluorescein were dissolved in 300 grams of concentrated sulphuric acid, the mixture cooled to 0° and a mixture of 5 grams of nitric acid (s. g. 1.36) and 20 grams of concentrated sulphuric acid added drop by drop with continual stirring. After pouring on to ice, the precipitate was

collected and crystallised from acetone. Yield, 90 per cent of the theoretical.

The compound darkens on heating but does not melt even at 310°; it is very sparingly soluble in the usual solvents with the exception of hot acetone. The alkaline solution has a magnificent crimson shade but is non-fluorescent, silk is dyed a crimson purple from a neutral bath containing sodium sulphate but the colour is easily discharged by mineral acids. When the alkaline solution is boiled for some time, no evidence is obtained of opening of the pyrone ring; in this way the compound differs markedly from derivatives of fluorescein containing nitro groups in positions 4 and 5.

The same 4:5-dibromo-2:7-dinitrofluorescein is also produced when tetranitrofluorescein is covered with 8 times its weight of glacial acetic acid and its own weight of bromine added. This affords additional evidence of the greater ease of attacking positions 4 and 5 rather than any other by substituting agents.

The *diacetyl* and *dibenzoyl* derivatives melt at 215° and 301° respectively; the *disodium* salt seems to be anhydrous.

The manufacture of *safrosine* is mentioned by Witt (*Chem. Ind.*, 1886, 9, 4); Mühlhäuser (*Dingler's Polyt. J.*, 1887, *263*, 49, 103); and Bindschedler and Busch (*Monit. sci.*, 1878, 20, 1171).

According to Bindschedler and Busch, 9 kilos of tetrabromofluorescein are dissolved in dilute alkali, 8 kilos of sodium nitrate added and the mixture boiled; 15 kilos of sulphuric acid (66° Bé.) are then added. The intensely red precipitate slowly loses its deep shade ultimately forming flocks of the colour of manganese sulphide. The authors state that the same dye has been known commercially under various other names, e. g. *écarlate lutécienne*, *nopaline* and *coccinine*.[1]

Mühlhäuser stirs 7 kilos of fluorescein in a finely divided

1 The process given has not been tried by the present author; one might suppose that it would yield the valueless 4:5-dinitro-2:7-dibromofluorescein.

condition with 60 kilos of alcohol (96°) and adds 7 kilos of nitric acid (40° Bé.) followed directly by 7.25 kilos of bromine. The yield is 12 to $12^1/_2$ kilos for each 7 kilos of fluorescein.

Another process described by Mühlhäuser consists in making a paste of 30 kilos of "Bromeosin" (? dibromofluorescein) and 25 kilos of glacial acetic acid, stirring in 4 kilos of finely powdered sodium nitrate, covering the vessel and heating it by a water-bath. Reaction begins about 70 to 80°; after 6 or 8 hours heating, the red mass has become flesh coloured and the reaction is finished. The yield is stated to be about 29.5 kilos.

It is also possible to work in aqueous solutions or suspensions, bromination being first effected and then nitration. Even where Mühlhäuser adds nitric acid to the suspension of fluorescein in alcohol and adds the bromine subsequently, it should be noted that the addition of bromine is immediate, so that bromination almost certainly takes place before nitration.

Conversion into the ammonium salt is effected by exposing the dinitrodibromofluorescein to a current of dry ammonia gas.

2:7-*Dibromo*-4:5-*dinitrofluorescein*, $C_{20}H_8Br_2(NO_2)_2O_5$. Hewitt and Woodforde (*loc. cit.*, 895) obtained this isomeride by mixing glacial acetic acid solutions of dinitrofluorescein hydrate (4 parts) and bromine (5 parts), heating the mixture to boiling and allowing to cool. Anhydrous dibromodinitrofluorescein was thus obtained as yellowish brown needles which turn dark red at 270° but do not melt by 310°.

The compound dissolves in the usual organic solvents and in cold dilute caustic soda with a brown colour and no fluorescence; the last named solution readily turns blue when warmed (the shade is greener than that given by dinitrofluorescein) and now contains the hydrate, $C_{20}H_{10}Br_2(NO_2)_2O_6$, which is precipitated on acidification.

The *diacetyl* and *dibenzoyl* derivatives melt at 276° and

315° respectively with decomposition; the *disodium salt* has the formula $C_{20}H_8O_9N_2Br_2Na_2, 2H_2O$.

When silk is dyed ($2^1/_2$ per cent solution of the hydrate), it takes an orange colour, much yellower than that given by eosine and more resembling that given by tetranitrofluorescein.

Chrysolin is the sodium salt of a compound made by condensing phthalic anhydride with a benzyl derivative of resorcin in presence of sulphuric acid. Since the "benzylresorcin" is made by heating benzyl chloride with resorcin, it is possible that the benzyl group has replaced a hydrogen atom of the nucleus of resorcin in which case chrysolin is not a benzyl ether of fluorescein (Reverdin, *Monit. sci.*, II, 7, 860, 1104).

CHAPTER XV.

HYDROXYL DERIVATIVES OF FLUORAN OTHER THAN FLUORESCEIN

Quinolphthalein, $C_{20}H_{12}O_5$. The condensation of two molecules of quinol with one molecule of phthalic anhydride was first effected by Grimm (*Ber.*, 1873, *6*, 507) who caused the reaction to take place in presence of concentrated sulphuric acid at 130—140°. Grimm also prepared the hydrate, $C_{20}H_{14}O_6$, by adding water to the alcoholic solution of the anhydride, whilst by acting with alcohol on the anhydride, he obtained a monoethyl derivative. The hydrate loses water at 160 to 180°, the ethyl derivative at 110°, both compounds regenerating the anhydride.

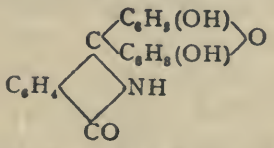
Ekstrand (*Ber.*, 1878, *11*, 714) condensed the phthalic anhydride and quinol by heating with 2 to 3 times the amount of stannic chloride at 120—130°; the product was boiled out with water and crystallised from dilute alcohol.

Quinolphthalein separates from ether in long colourless needles, m. p. 226–227° and dissolves easily in alcohol, glacial

acetic acid and acetone but only slightly in chloroform and benzene. Very little dissolves in hot water the solution depositing the hydrate on cooling. The alkaline solutions are deep violet; they are decolourised by zinc dust with formation of a leuco-compound, $C_{20}H_{14}O_5$.

Ekstrand prepared a *diacetyl* derivative (m. p. 210°) and a *pentabromo* substitution product, $C_{20}H_7O_5Br_5$; the latter is remarkable as giving colourless alkaline solutions.

R. and H. Meyer (*Ber.*, 1895, *28*, 2959) added two further derivatives, a *dibenzoate*, m. p. 252—253°, and an imide



The latter compound was obtained by dissolving 10 grams of quinolphthalein in 150 cc. of concentrated aqueous ammonia and then boiling the solution. The colourless compound gives colourless solutions in alkalies.

The constitution of quinolphthalein has already been dealt with at length (p. 286); it may be remarked that though alkaline solutions of phenolphthalein, quinolphthalein and fluorescein exhibit very different colours, the general character of their absorption spectra is somewhat similar (R. Meyer and K. Marx, *Ber.*, 1907, *40*, 3604).

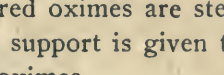
The *dimethyl* and *diethyl* ethers of quinolphthalein prepared with the aid of sodium ethoxide and the respective alkyl halides are colourless, crystalline substances melting at 200° and 164° respectively. (R. Meyer and O. Spengler, *Ber.*, 1903, *36*, 2959). The *monomethyl ether* (m. p. 130—134°) is also colourless but gives coloured alkaline solutions. (Meyer and Spengler, *Ber.*, 1905, *38*, 1330).

Meyer and Spengler prepared an *anilide* by gently boiling 1 part of quinolphthalein for six hours with 4 parts of aniline and 2 parts of aniline hydrochloride; it is colourless, melts at 305°, gives colourless alkaline solutions and yields a colourless *dimethyl ether*, m. p. 183°.

Quinolphthalein-oximes. Three different forms dis-

tinguished as α, β and γ are known. All these result at the same time when an alkaline solution of quinolphthalein is treated with hydroxylamine hydrochloride; the violet colour of the solution gives place to a dirty brown and eventually a cherry red when heated for a short time on the water-bath (Meyer and Spengler, *Ber.*, 1903, *36*, 2961; 1905, *38*, 1330). The separation of the oximes is effected by making use of their different solubilities in methyl and ethyl alcohols. The α-form is colourless and gives a colourless solution in alkali; it melts at 268—269°. The other forms do not melt without decomposition, the β-form gives a yellow solution in methyl alcohol with intense bluish-green fluorescence, whilst the oxime is hardly soluble in organic solvents but dissolves in alkalies with a brownish-yellow colour.

Possibly the coloured oximes are stereoisomerides (*cis*- and *trans*-forms); some support is given to this view by the isolation of two phthaloximes



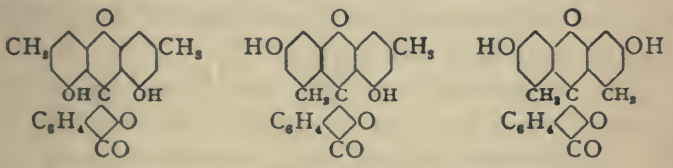
one colourless, the other of a lemon yellow shade. Both of these melt at 220—226° and give red alkaline solutions (W. R. Orndorff and D. S. Pratt, *Amer. Chem. J.*, 1912, *47*, 89).

Orcinphthaleins, $C_{22}H_{16}O_5$. Emil Fischer (*Annalen*, 1876, *183*, 63) obtained an orcinphthalein by heating 3 parts of phthalic anhydride with 5 parts of orcin and 5 parts of concentrated sulphuric acid for 2 hours at 135°. The product was washed with cold water, dissolved in dilute caustic potash, boiled for some time and precipitated by acetic acid. The precipitate was then boiled with water and finally crystallised from dry acetone. In this way, small colourless prisms were obtained which turned brown at 230°.

Whilst the compound was colourless, the alkaline solutions were intensely red but not fluorescent. Fischer also prepared a *hydrochloride*, *mono*- and *di-acetyl* derivatives (m. p. of latter 219—220°) and *tetra*- and *pentabromo* substitution products. The monoacetyl derivative was not observed by R. and H. Meyer.

The lack of colour in the case of the free compound and the non-fluorescence of its alkaline solutions led to considerable confusion at a later date, for if fluorescein is obtained by an ortho-para condensation with formation of a pyrone ring, there seems to be no reason why orcin (3 : 5-dihydroxytoluene) should not behave similarly and give a homologue of fluorescein

The discrepancy was explained by R. and H. Meyer (*Ber.*, 1896, *29*, 2627) who found that orcin and phthalic anhydride condense in three possible ways giving phthaleins of the structures



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Fischer's orcinphthalein, which gives a carmine shade in alkaline solution, was distinguished as α-, the phthalein giving a cherry red as β- and the third isomeride as γ-orcinphthalein respectively. It was found that a relatively greater amount of the γ-phthalein could be obtained if phosphorus pentoxide were used in place of sulphuric acid as condensing agent.

R. and H. Meyer utilised the difference in acidic properties of the three compounds to effect their separation. The α-compound dissolves in caustic potash but not in ammonia or alkaline carbonates, the β-compound dissolves in the latter but not in a solution of ammonium sesquicarbonate, whilst the γ-compound is sufficiently acid to unite directly with ammonia vapour giving a salt which dissolves easily in water.

In addition to the compounds prepared by Fischer, R. and H. Meyer obtained the *benzoyl* derivative of α-orcinphthalein, m. p. 284—285°.

β-Orcinphthalein forms brownish needles or orange leaflets; it retains $^1/_3$ mol. of water even after drying in an

aniline-bath. The *diacetyl* and *dibenzoyl* derivatives melt at 227—228° and 244—245° respectively; the *tetrabromo* substitution derivative is colourless but dissolves in alkalies with a greenish black colour, which after considerable dilution appears dirty red by transmitted light; the substance has no dyestuff character.

γ-Orcinphthalein forms yellowish prisms or orange coloured crystals according to the method of crystallisation. The alkaline solutions are yellow and show a green fluorescence, somewhat feebler than that given by fluorescein. The *diacetyl* derivative melts at 207—208°; the *tetrabromo* substitution product is the analogue of eosine dyeing silk in similar but somewhat weaker shades.

Cresorcinphthalein, $C_{22}H_{16}O_5$. This compound was obtained by heating a mixture of phthalic anhydride and cresorcin (2:4-dihydroxytoluene) for 2 hours to 195—200°. It forms a brick red powder, behaves similarly to fluorescein and yields a *diacetyl* derivative which melts about 260°.

The fluorescein reaction has also been observed with the following homologues of resorcin.

2:6-Dihydroxytoluene, Ullmann, *Ber.*, 1884, *17*, 1964.

2:6-Dihydroxy-1:3-xylene, Wischin, *Ber.*, 1890, 23, 3114.

3:5-Dihydroxy-1:2-xylene, Pfannenstill, *J. pr. Chem.*, 1892, II, *46*, 156.

The fluorescein reaction can also be obtained with phthalic anhydride and 2:6-dihydroxypyridine (Ruhemann, *Trans. Chem. Soc.*, 1893, *63*, 876).

Tetrahydroxyfluorans.

2:3:6:7-*Tetrahydroxyfluoran (Dihydroxyfluorescein)*, $C_{20}H_{12}O_7$, is prepared by heating 1:2:4-trihydroxybenzene (Thiele, *Ber.*, 1898, *31*, 1247) with phthalic anhydride under the conditions described by von Baeyer for the preparation of fluorescein. After repeated extraction with boiling water and crystallisation from alcohol, water being added to the solu-

tion, the substance is obtained as microscopic leaflets showing a golden green reflex (Liebermann, *Ber.*, 1901, *34*, 2300).

The alcoholic solution shows a strong yellowish green fluorescence, the cherry red alkaline solution is non-fluorescent whilst the solution in concentrated sulphuric acid is canary yellow in colour.

An alternative method of preparation is to heat 10 parts of 1:2:4-triacetoxybenzene with 7 parts of phthalic anhydride and 4 parts of concentrated sulphuric acid for a few minutes to 145°.

The compound produces orange shades on wool and silk and acts as an excellent adjective dyestuff on cotton. Alumina mordants give a bright orange, iron a lively violet and chromium a rose colour. The fastness of these shades to soap is said to be very good.

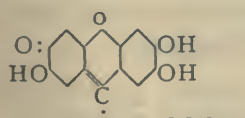
The *ammonium salt*, $C_{20}H_{12}O_7$, NH_3, forms a dark green mass which dissolves easily in water with a reddish brown colour and very strong, dark green fluorescence (J. Thiele and J. Jäger, *Ber.*, 1901, *34*, 2618).

The *tetraacetyl* derivative forms nearly colourless, microscopic prisms, m. p. 264° (Liebermann).

Tetrabenzoyl derivative, large compact crystals (W. Feuerstein and M. Dutoit, *Ber.*, 1901, *34*, 2640).

Ethyl ester, $C_{20}H_{11}O_7 \cdot C_2H_5$, This compound is prepared by esterification with alcohol and sulphuric acid; it forms green leaflets, m. p. 326°. (F. & D.) The *triacetyl* derivative of the ethyl ester forms hard orange yellow crystals with bluish reflex, m. p. 238—239°.

Feuerstein and Dutoit assign a quinonoid structure to dihydroxyfluorescein (I) corresponding to that of the ester (II).



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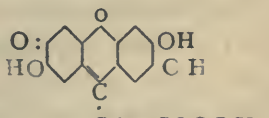


II

Their reasons are summed up as follows;—

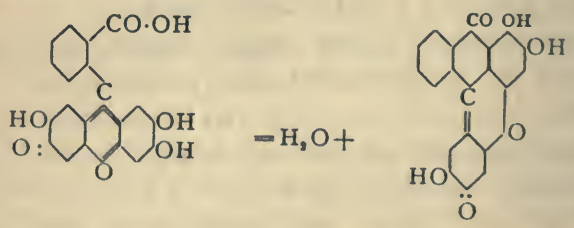
1. Dihydroxyfluorescein contains a carboxyl group since it can be converted into a carboxyic ester by a direct esterification.

2. The ethyl ester must possess constitution II since it only furnishes a triacetyl derivative.

3. The ester and the mother substance show the greatest similarity in tinctorial properties.

4. The acidyl compounds are derived from the lactonoid form.

A further argument in favour of the quinonoid structure is afforded by the fact that dihydroxyfluorescein loses water when heated for 2 hours with 7 to 8 times its weight of concentrated sulphuric acid to 120°, yielding a compound which Thiele and Jaeger (*loc. cit.*, 2619) have called *violein*. This is a dark powder which gives violet solutions in nitrobenzene, glacial acetic acid and aniline; the alkali solutions are indigo blue and the *triacetyl* derivative forms a brownish violet powder. The formation of violein must evidently be represented by the equation



4:5-*Dibromo*-2:3:6:7-*tetrahydroxyfluoran*, formed by the bromination of dihydroxyfluorescein, is a brick red powder difficultly soluble in water, easily in alcohol. It dissolves in sodium acetate solution with eosine red colour and feeble yellow fluorescence; addition of alkalies alters the shade to fuchsine red whilst the fluorescence disappears.

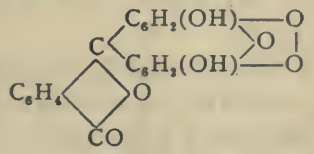
Liebermann and Wölbling (*Ber.*, 1902, *35*, 1762) have condensed other *o*-dicarboxylic acids with 1:2:4-trihydroxybenzene and observed the absorption spectra of the resulting

compounds. The acids employed were 1:2-naphthalene-dicarboxylic, quinolinic, diphenyltetrenic, hemipinic, dibromophthalic and tetrachlorophthalic acids. Some of these dihydroxyfluoresceins were examined more fully by N. Osorowitz (*Ber.*, 1903, *36*, 1076), notably those prepared with the aid of tetrachlorophthalic, 3:6-dichlorophthalic, 4:5-dibromophthalic and 4-hydroxyphthalic acids.

3:4:5:6-*Tetrahydroxyfluoran (Gallein)*, $C_{20}H_{12}O_7$. The condensation of pyrogallol and phthalic anhydride was first effected by von Baeyer (*Ber.*, 1871, *4*, 457, 663) who supposed that the condensation proceeded in the normal manner according to the equation

$$C_8H_4O_3 + 2\,C_6H_6O_3 = 2\,H_2O + C_{20}H_{12}O_7.$$

Some years afterwards the reaction was further studied by Buchka (*Ber.*, 1881, *14*, 1326; *Annalen*, 1881, *209*, 261) and the conclusion arrived at that two hydrogen atoms were removed by oxidation in the course of the condensation, the resulting gallein having the formula $C_{20}H_{10}O_7$ and possessing only two hydroxyl groups, so that it would have to be represented by some such formula as



Since Buchka's results were accepted as correct for several years, his method of preparation and observations with regard to the compound will be given briefly.

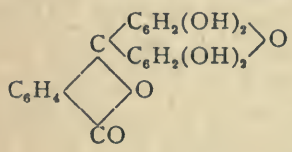
To prepare gallein, 1 part of phthalic anhydride and 2 parts of pyrogallol were heated for some hours to 190 to 200°, the melt dissolved in alcohol and the solution precipitated by water. Solution and precipitation were repeated several times, the gallein then acetylated, the acetyl derivative repeatedly crystallised and finally hydrolysed by alcoholic potash.

Prepared in this way, gallein occurs as a brownish red powder or as small crystals with a green metallic lustre,

difficultly soluble in ether and in hot water. It dissolves easily in alcohol with a dark red colour, but is not taken up by chloroform or benzene. The solution in cold concentrated sulphuric acid is dark red; when this solution is heated to 190°, the gallein loses the elements of water and is converted into coerulein.

A small amount of alkali dissolves gallein with a red colour, but a blue solution is obtained if the alkali is added in excess. From these solutions, acids precipitate gallein; when sulphur dioxide is used as precipitant, some of it remains combined with the gallein. The solutions in ammonia, lime- and baryta-waters are violet in colour.

According to Buchka, reduction with zinc dust and potash first gives *hydrogallein* (I)



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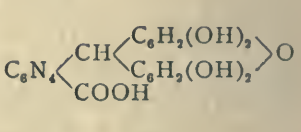


II

and then *gallin* (II). Reduction with zinc and sulphuric acid yields *gallol*, $C_{20}H_{12}O_7$.

Hydrogallein was described by Buchka (*loc. cit.*, 266) as crystalline; it was stated to give a *tetraacetyl* derivative, m. p. 247—248°, on boiling with acetic anhydride. According to Herzig, the correct melting point is 236—237°, whilst Orndorff and Brewer give 241°. The same tetraacetate was formed when 1 part of gallein was boiled with 1 part of fused sodium acetate and 3 to 4 parts of acetic anhydride.

A *tetrabenzoyl* derivative of hydrogallein, m. p. 231° (*B.*) or 226° (O. and B.) was obtained by boiling gallein with benzoyl chloride. This compound crystallised in fine needles from acetone, dissolved in alcohol, chloroform and benzene and was easily hydrolysed by caustic potash solution but not by water.

By adding bromine dissolved in glacial acetic acid to a mixture of 1 part of gallein and 20 parts of glacial acetic

acid, Buchka prepared a dibromogallein to which he assigned the formula $C_{20}H_8Br_2O_7$. This compound formed golden green, glittering crystals; it dissolved readily in alcohol and acetone, difficultly in benzene and chloroform. The alkaline solution was of cornflower-blue colour, that in ammonia a dark violet. On acetylation, a *tetraacetyl* derivative of the formula $C_{20}H_6O_3Br_2(C_2H_3O_2)_4$ was produced; this crystallised from glacial acetic acid in leaflets, m. p. 234°.

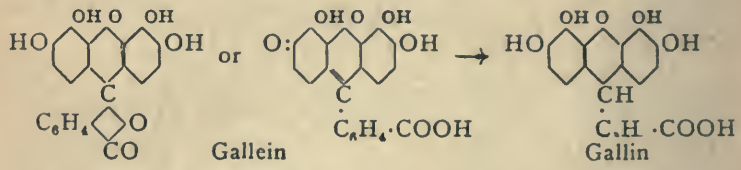
It will have been noticed that according to Buchka, gallein is not a direct condensation product of phthalic anhydride and pyrogallol, but is formed with elimination of two atoms of hydrogen. At the same time, both gallein and dibromogallein yield derivatives of a compound $C_{20}H_{12}O_7$ when acylated, Buchka referring to this parent substance as "hydrogallein", although it should be the direct condensation product from phthalic anhydride and pyrogallol. Further reduction of "hydrogallein" leads to "gallin", just as fluorescein yields fluorescin on reduction.

J. Herzig (*Monatsh.*, 1892, *13*, 422) was struck by the fact that quercetin and other coloured substances of high molecular weight give rise to colourless acetyl derivatives, and the question arose as to whether the latter might not possibly correspond to the leuco-compounds, reduction taking place during the process of acetylation. This view turned out to be incorrect, but it was found that in many cases the acetyl derivatives of corresponding coloured and leuco compounds showed a striking similarity. Acetylfluorescin closely resembles acetylfluorescein in appearance and melts at 200 to 202°, but the substances are not identical.

Herzig extended his work to the acetyl derivatives of gallein and gallin. Hydrogallein, as an intermediate product of reduction, could not be isolated, whilst the melting points given by Buchka for the acetyl derivatives of gallein and gallin respectively were corrected to 234—237° and 211—213°.

The doubt cast on Buchka's results by Herzig led to researches on the part of W. R. Orndorff and C. E. Brewer

(*Amer. Chem. J.*, 1900, *23*, 425; 1901, *26*, 97). Gallein, the direct product of the condensation of phthalic anhydride and pyrogallol, has the formula $C_{20}H_{12}O_7$; on reduction it gives gallin, $C_{20}H_{14}O_7$. These results accord with those obtained by von Bayer (*Ber.*, 1871, *4*, 663), and the relationships of the two compounds may be expressed by the formulae

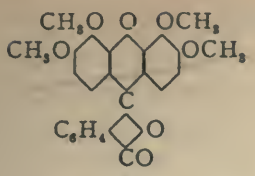


For free gallein, Orndorff and Brewer prefer the quinonoid structure, the substance giving rise to methyl and ethyl esters both of which are crystalline and red by transmitted light. Phenylcarbimide gives a light yellow solid which does not melt sharply; since its formula is $C_{20}H_9O_7(CO \cdot NH \cdot C_6H_5)_3$, it appears that free gallein contains only three phenolic hydroxyls; this agrees with the presence of an easily esterifiable carboxyl group.

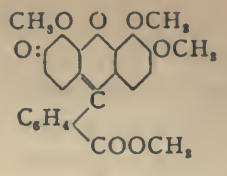
Acylation tends as usual to favour the lactonoid configuration and the *tetraacetate, tetrabenzoate* and *tetrabenzenesulphonate* were all obtained as colourless compounds.

Judging from the analogy of fluorescein, we might expect alkyl derivatives of both the lactonoid and quinonoid forms. The *monomethyl* and *monoethyl esters* mentioned above are coloured and easily hydrolysed, there is no doubt as to their quinonoid structure.

There are two *tetramethyl ethers;* one of them forms colourless needles melting at 195° (I); since it is insoluble in aqueous potassium hydroxide, even on boiling, it must be a tetrahydroxyfluoran. The other tetramethyl ether (II) occurs as dark red monoclinic pyramids, m. p. 199°, and is readily hydrolysed by sodium carbonate solution to a colourless *trimethyl ether,* m. p. 229° (III). The latter compound resembles phenolphthalein and gives an *acetyl* derivative, m. p. 97° (IV)



I



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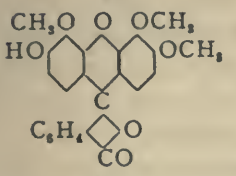
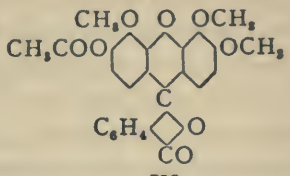


III



IV

Similar tetraethyl compounds have been prepared; the colourless and coloured forms melt at 144 and 155° respectively.

On account of the neighbouring hydroxyl groups, gallein is capable of forming lakes and found a somewhat limited application in cotton printing for the production of greyish violet shades. Fixation can be effected by printing in admixture with aluminium or chromium acetate and subsequent steaming.

In manufacturing gallein, it was found to be unnecessary to use pyrogallol obtained by heating gallic acid, since the latter compound may be condensed directly with phthalic anhydride, carbon dioxide being evolved during the process (Gürke, D. R. P. 30648/1884).

According to the specification, 37.6 kilos of crystallised gallic acid, which may or may not be dehydrated by heating to 100°, are mixed with 17 kilos of phthalic anhydride and heated in an oil-bath to 220—235° until the melt solidifies. The mass is powdered, extracted with water, dried and then treated with 5 parts of alcohol. Gallein passes into solution and after distilling off the alcohol is left in a condition for converting into coerulein.

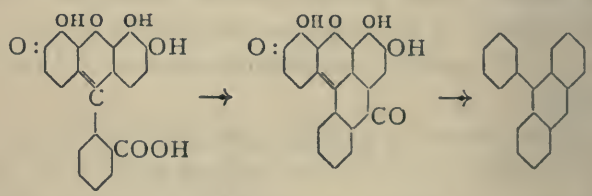
In an additional patent (D. R. P. 32830/1885), Gürke claims the production of chlorinated galleins by condensing chloro-derivatives of phthalic acid with gallic and conversion of the resulting galleins into coeruleins.

Coeruleins.

Coerulein (from Gallein), $C_{20}H_{10}O_6$. According to Baeyer, this compound is formed by heating 1 part of gallein with 20 parts of concentrated sulphuric acid to 200° and pouring into a large excess of water (*Ber.*, 1871, *4*, 556, 663). The bluish black mass assumes a metallic glance when rubbed; it is very sparingly soluble in water, alcohol and ether. Glacial acetic acid dissolves it more readily forming a dirty green solution, the alkaline solutions are green, that in concentrated sulphuric acid is olive brown.

On reduction with ammonia and zinc dust it is converted into the corresponding coerulin which may be oxidised back to coerulein (Buchka, *Annalen*, 1881, *209*, 272).

When coerulein is distilled with zinc dust, phenylanthracene is formed as a product; from this it may be concluded that coerulein is produced from gallein in the following manner



Confirmation of this structure is given by Orndorff and Brewer; coerulein gives a *triacetyl* and coerulin a *pentaacetyl* derivative.

Coerulein found employment in cotton printing, giving dull olive to dark green shades when used in conjunction with aluminium or chromium mordants. A considerable advance in technique was rendered possible by the employment of *Coerulein S*, a compound of coerulein with sodium bisulphite, soluble in water (Brit. P. 3850/1881).

Coerulein from Eosine. Baeyer (*Annalen*, 1876, *183*, 59) found that small quantities of a "Bromcoerulein" were formed by strongly heating tetrabromofluorescein with concentrated sulphuric acid; the process had no technical value.

If, however, the ordinary concentrated sulphuric acid be

replaced by "monohydrate" or fuming sulphuric acid, much better yields of dyestuffs of coerulein type are obtained; this discovery formed the subject of patents taken out by Meister, Lucius and Brüning (Brit. P. 7170/1895; F. P. 246472; D. R. P. 86225/1895).

Example 1. Stir up eosine with 5 times its weight of fuming sulphuric acid (20% SO_3) heat to 125—130° until a sample which has been precipitated by excess of aqueous alkali and some sodium chloride solution gives only a feebly pink filtrate. To reach this point, it is necessary to heat for about $^3/_4$ hour. After cooling, pour into an excess of water, filter off and wash the flocculent precipitate which may be used directly in paste form or converted into the sodium salt by solution in sodium carbonate and salting out with sodium chloride.

The dyestuff thus obtained dissolves in alkalies with a bluish green and in concentrated sulphuric acid with dark cherry red colour; it is insoluble in water, sparingly soluble in alcohol and dyes chromed wool a bright bluish green.

If the dye, obtained as described, be heated with a small quantity of water to 130—150°, it is converted into another product which dyes yet greener shades which are faster to milling. This substance dissolves in alkaline alcohol with bluish green colour which is stable on exposure to light, whilst the colour of corresponding solutions of the first compound soon vanish under the same conditions.

Example 2. 1 part of the dye prepared according to example 1 is heated for 2 or 3 hours with 10 parts of ordinary concentrated sulphuric acid to 150°. The solution is poured into water and the new dye either used as paste or converted into the sodium salt.

Example 3. The operations of the foregoing examples may be combined in the following manner, 1 part of eosine being heated with 5 parts of oleum (20% SO_3) for about $^3/_4$ hour to 125—130°, excess of sulphur trioxide removed by adding ice and the heating continued for 2 or 3 hours at 150°.

The patent states that the shades produced on chromed wool by the dyestuffs prepared from various halogenated fluoresceins are as follows.

Tetrabromofluorescein	Green.
Dibromofluorescein	Blue green; dark shades, black green.
Tetraiodofluorescein	Grey blue.
Dichlorotetrabromofluorescein	Green.
Dichlorotetraiodofluorescein	Green.
Tetrachlorotetrabromofluorescein	Greenish grey.
Tetrachlorotetraiodofluorescein	Grey green.

An additional patent (D. R. P. 97640/1897) states that the product (paste form) formed by heating 20 kilos of eosine with oleum as described in example 1 (D. R. P. 86225) may be converted into a useful dyestuff by dissolving it in 800 litres of water and 9.5 kilos of caustic soda lye (30° Bé.) and warming for one hour to 50—70°, this operation being alternative to the method of heating with ordinary sulphuric acid as previously described.

Coerulein from Fluorescein. Von Baeyer's preparation of a coerulein by heating fluorescein with concentrated sulphuric acid was confirmed by Meister, Lucius and Brüning (D. R. P. 98075/1897) who, however, found it advantageous to add other mineral acids (phosphoric, boric &c.), or their anhydrides, the product being finally halogenated.

Example 1. 15.5 parts of the resorcin-coerulein (in paste form) are suspended in 400—500 parts of alcohol (95%) and 16 parts of bromine slowly added with continual stirring. Much of the dye separates directly, the remainder is obtained by addition of water.

Example 2. 19 parts of resorcin-coerulein in 400 to 500 parts of alcohol are treated with 13 parts of iodine, 3.9 parts of iodic acid and 10 parts of concentrated sulphuric acid. The mixture is well stirred and warmed for one or two hours at 60—70° and the dyestuff precipitated with water.

Example 3. 9 parts of the coerulein prepared from dichlorofluorescein are dissolved in about 750 cc. of water

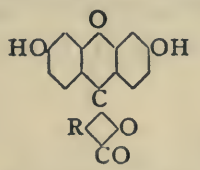
by the aid of 15 parts of caustic soda lye (30% Bé.). 40 to 50 parts of concentrated hydrochloric acid are then added and immediately afterwards 16 parts of bromine dissolved in 32 parts of caustic soda solution of 30° Bé. After stirring one hour, the product is washed and dried.

The products are apparently very similar to those described in D. R. P. 86225.

Sundry compounds of Fluorescein Type.

In addition to phthalic acid and its substitution derivatives, many other dicarboxylic acids may be condensed with resorcin yielding compounds with most of the properties of fluorescein itself. Generally, the dicarboxylic acids employed contain the carboxyl groups attached to neighbouring carbon atoms; thus succinic, maleic, citraconic acids &c. may all be condensed to fluoresceins. On the other hand, resorcin may be replaced by various metadihydroxy-compounds, e. g., 2:6-dihydropyridine, 1:3- (and also 1:6-) dihydroxynaphthalene &c. Since most of these compounds are of no technical importance, they will only be briefly considered except in those cases where attempts, successful or otherwise, have been made to introduce them commercially.

The condensation products of the general type



formed from resorcin and the following acids have been described.

Succinic acid, Nencki and Sieber, *J. pr. Chem.*, 1881, II, *23*, 153.

Maleic acid, Lunge and Burckhardt, *Ber.*, 1884, *17*, 1598; Burckhardt, *Ber.*, 1885, *18*, 2864.

Citraconic acid, Hewitt, *Trans. Chem. Soc.*, 1894, *63*, 677.

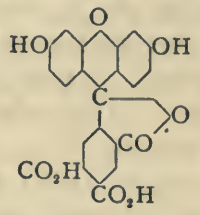
Diphenyltetrenedicarboxylic acid, T. Lanser and B. F. Halvorsen, *Ber.*, 1902, *35*, 1410.

Naphthalic acid and its substitution derivatives, L. Francesconi and G. Bargellini, *Gazzetta*, 1902, *32*, II, 73.

Mellitic and pyromellitic acids, O. Silberrad, C. S. Roy and W. H. Glover, *Trans. Chem. Soc.*, 1906, *89*, 1787.

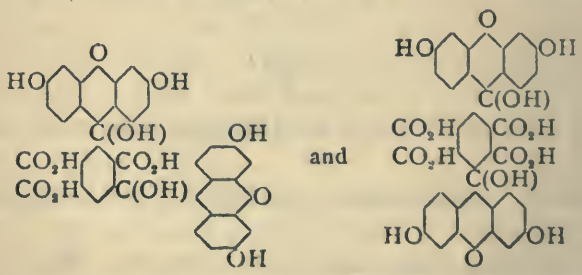
It is only in the case of mellitic acid that an attempt seems to have been made to introduce the condensation products commercially (O. Silberrad, Brit. P. 28638/1902; compare Read Holliday and Sons Ltd. and O. Silberrad, D. R. P. 214252 for a process for manufacturing mellitic acid from charcoal).

Silberrad and Roy found that pyromellitic acid and resorcin gave a diresorcinolpyromellitein



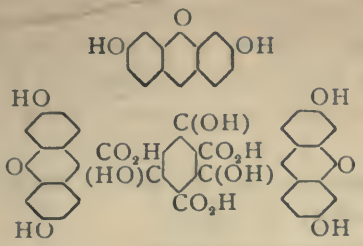
whose tetrabromo-derivative dyed silk and wool a brilliant crimson, whilst the alkaline solutions of the tetraiodo-compound possessed a fine deep red colour.

Dixanthyl derivatives (tetraresorcinolmelliteins) may result from the condensation of mellitic acid with resorcin in either of two ways giving rise to a pair of isomerides



The first of these melliteins dyes silk and wool in brownish yellow, the octabromo-derivative in pink shades. The second (symmetrical) mellitein dyes silk and wool yellow, the octabromo-derivative gives a brownish pink.

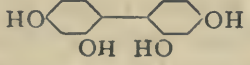
The hexaresorcinolmellitein



dyes silk and wool yellow, the corresponding dodecabromo-compound red with a tinge of violet and the dodecaiodo-compound pink.

The patent referred to also describes nitro-compounds as well as the condensation of pyromellitic and mellitic acids with dialkyl-*m*-aminophenols.

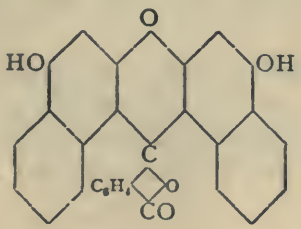
A colouring matter is obtained when 44 parts of di-resorcin, m. p. 222°,



are heated for 3 or 4 hours with 15 parts of phthalic anhydride and 18.5 parts of zinc chloride to 160° (Bayer and Co., D. R. P. 90341/1896). The melt is extracted with hot water and dissolved in hot dilute sodium carbonate solution; saturation with sodium chloride separates impurities which are filtered off and the dyestuff is precipitated from the filtrate on acidification.

Wool is dyed from an acetic acid bath in fiery bluish red shades. The lakes obtained with chromium salts are said to be fast to milling.

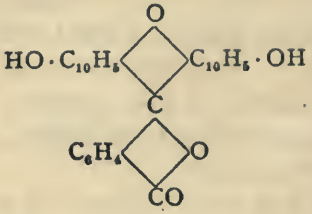
Naphthofluorescein,



was prepared by Bayer and Co. (D. R. P. 84990/1895) by condensing 45 parts of naphthoresorcin (1:3-dihydroxynaphthalene, and 25 parts of phthalic anhydride either by heating with 20 parts of zinc chloride for 10 hours at 200° or for the same time with 40 parts of phosphorus pentoxide at 130°.

The compound much resembles ordinary fluorescein but dyes silk red instead of yellow,

6:6'-*Dihydroxynaphthofluoran*

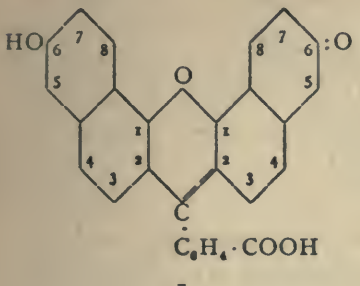


This compound was discovered by E. König and its preparation patented by Meister, Lucius and Brüning (D. R. P. 275897/1913). According to the specification, 10 grams of 1:6-dihydroxynaphthalene and 10 grams of phthalic anhydride are heated in an oil-bath to 180—200°; steam is abundantly disengaged for the first half hour, the melt then goes solid. It is dissolved in dilute caustic soda and precipitated by acetic acid. The proportions of the components may be varied and zinc chloride may be added to assist the condensation.

The alkaline solution is deep greenish blue, the solution in concentrated sulphuric acid is orange red and shows a very strong yellow fluorescence. Dyed on fibres and developed by alkali ("alkalisch entwickelt", no details being given as to the alkaline treatment), deep bluish green shades are produced.

The condensation product from 1:6-dihydroxynaphthalene and 1:4-dichlorophthalic acid exhibits a greener shade in alkaline solution, whilst the solution in concentrated sulphuric acid inclines towards a bluish tint and shows an orange fluorescence.

Further details as to the properties of dihydroxynaphthofluoran appear in a joint paper by O. Fischer and E. König (*Ber.*, 1914, *47*, 1076).



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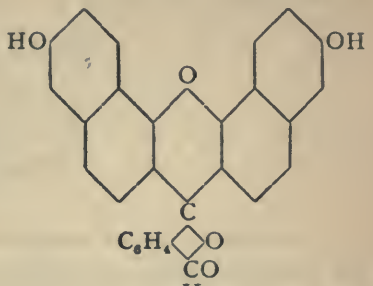

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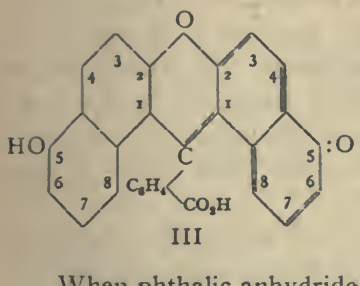
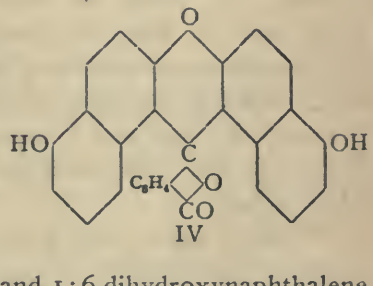


III



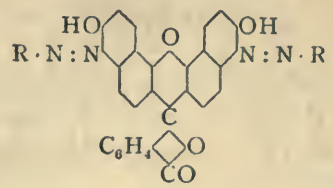
IV

When phthalic anhydride and 1:6-dihydroxynaphthalene are condensed together there are two possibilities; either the naphthalene nucleus is attacked in position 2 or in position 5. In the first case 6:6'-dihydroxyfluoran will be formed and to this one may assign either a quinonoid formula (I) or a lactonoid formula (II). In the second eventuality, 5:5'-dihydroxyfluoran (III or IV) will be the product of the reaction.[1] Formula I corresponds to the structure of 2:6- or *amphi*-naphthaquinone, a compound which had already been isolated by R. Willstätter and J. Parnas (*Ber.*, 1907, *40*, 1406, 3971). Formula III corresponds to a hypothetical 1:5-(*ana*-)naphthaquinone, the possibility of whose existence had been foreseen by Willstätter and Parnas.

The evidence given by Fischer and König points to the formulation of the compound as the 6:6'-dihydroxy-compound

1 The numbering adopted is that used by Fischer and König.

since diazonium salts give rise to bisazo-compounds which are insoluble in both caustic and carbonated alkali; i. e. the bisazo-compound behaves as if it were derived from 2-naphthol and possessed the constitution



According to the conditions, the substance may be represented by either the quinonoid formula (I) or the lactonoid formula (II). When the alkaline solution is acidified with acetic acid the dihydroxyfluoran separates as a voluminous red precipitate and dries to a red powder. The freshly precipitated substance dissolves readily in ether; the dried powder is nearly insoluble but if covered with ether, the red colour disappears, the compound being converted into a greyish white powder.

Fischer and König studied the action of a number of solvents; the coloured quinonoid form seems to be favoured by water and traces of acids as well as by petroleum ether. The separation of colourless crystals, supposed to contain the lactonoid form, is favoured by those solvents such as acetone, methylal, pyridine and benzene which themselves partly separate with the dihydroxynaphthofluoran as solvent of crystallisation. Thus colourless crystals, $C_{28}H_{16}O_5$, $2(C_2H_5)_2O$, are obtained by dissolving dihydroxynaphthofluoran in methylal, filtering from any dark resinous flocks, adding 3 to 4 volumes of ether and a small amount of petroleum spirit, again rapidly filtering, if necessary, from any coloured substance and allowing to crystallise. Colourless crystals of the composition $C_{28}H_{16}O_5$, $2\,C_3H_6O$ are also known; they lose their acetone of crystallisation on heating to 140° and leave the red quinonoid form.

Colourless *diacetyl-* (m. p. 180°) and *dibenzoyl*-derivatives were prepared; methylation gave a mixture of com-

pounds (some of them coloured) from which a colourless *dimethyl ether* was isolated. The last named compound darkens on heating above 200° and decomposes completely about 293°.

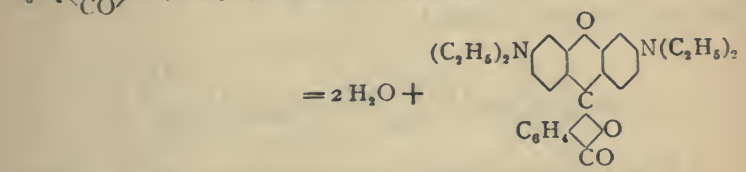
The *hydrochloride*, $C_{28}H_{16}O_5$, HCl, separates as a scarlet, crystalline precipitate when hydrogen chloride is led into a solution of the fluoran in methylal or ether.

Bisazo-derivatives (formula given above) were prepared in which R = C_6H_5, *p*-$CH_3 \cdot C_6H_4$, *p*-$NO_2 \cdot C_6H_4$ and *p*-$Cl \cdot C_6H_4$.

CHAPTER XVI.

CONSTITUTION OF RHODAMINES.

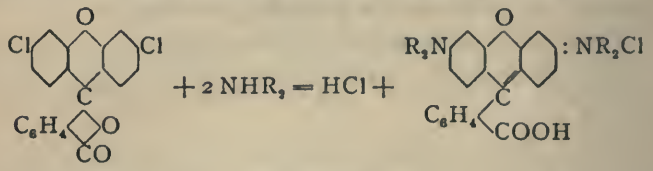
The rhodamines form a class of dyestuffs very nearly related to fluorescein and its derivatives. Whilst fluorescein is 3:6-dihydroxyfluoran, *Rhodamine B* is the corresponding tetraethyl-3:6-diaminofluoran. It was discovered by Ceresole in 1887, phthalic anhydride being fused with two molecular proportions of diethyl-*m*-aminophenol.



It will be seen that the reaction is analogous to that which takes place when phthalic anhydride and resorcin are fused together; the dye proved to be of considerable value and the method of preparation was protected by the Badische Anilin- und Soda-Fabrik (Brit. P. 15374/1887; D. R. P. 44002/1887).

An alternative method of preparation was discovered by

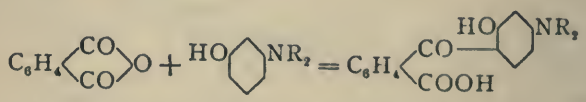
Homolka and Bödeker in the following year and patented by Meister, Lucius and Brüning (Brit. P. 9600/1888; D. R. P. 48 367/1888). The reactivity of the chlorine atoms in 3:6-dichlorofluoran (fluorescein chloride) is so considerable that dialkylamino groups replace the chlorine atoms when the substance is heated with secondary dialkylamines.



Following on these two chief patents, a number of additional patents were taken out by the two firms (the Badische Co. and Meister, Lucius and Brüning) chiefly concerned.

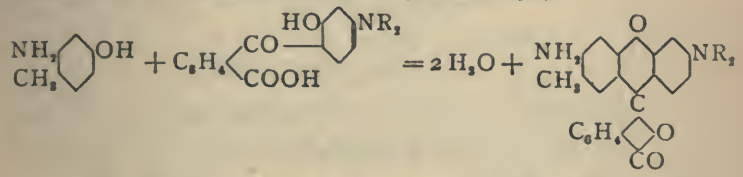
The behaviour of dichlorofluoran is evidently not unique but shared by other esters of fluorescein. It has, for instance, been found that rhodamines are produced by the action of secondary amines on the arylsulphonic esters of fluorescein (Meister, Lucius and Brüning, D. R. P. 116 415/1899).

A few years later, the Baseler chemische Fabrik, Bindschedler obtained patents (D. R. PP. 85 931/1894, 87 068/1894, 132 066/1901) for the condensation of equimolecular quantities of phthalic anhydride and dialkylaminophenols; in this case the intermediate dialkylaminohydroxybenzoylbenzoic acid were isolated.



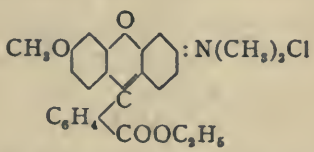
When these compounds were condensed with a further molecular quantity of dialkylaminophenol, rhodamines identical with those produced by the methods already mentioned were obtained. Applications (B. 16 962, Kl. 22 of 3. Dec. 1894 and B. 17 374, Kl. 22 of 13. Mar. 1895) made by the Bindschedler firm for the protection of this second reaction were refused by the German Patent Office. It is fairly evident that the formation of a symmetrical tetraalkyl substituted rhod-

amine must be preceded by the intermediate formation of the substituted benzoylbenzoic acid, so that D. R. P. 44 002 covers the combination. D. R. P. 85 931 relating to the production of dialkylaminohydroxybenzoylbenzoic acids was allowed and the reaction was subsequently made use of. Thus when dimethyl- and diethyl-*m*-aminohydroxybenzoylbenzoic acids are condensed with 2-amino-4-cresol an asymmetric rhodamine is obtained (D. R. P. 96 108/1896).



The corresponding ethyl ester of the dimethylhomorhodamine is known as Rhodamine 3 G, 3 G extra (Badische) or Irisamine G, G extra (Cassella) (Brit. P. 4985/1895; U. S. P. 584 119; F. P. 245 593).

It is also possible to use resorcin or its monoalkyl ethers in place of *m*-aminophenols for condensations of this type. For example, Brack condensed monomethylresorcin with dimethylaminohydroxybenzoylbenzoic acid and esterified the resulting compound. The ester prepared in this way

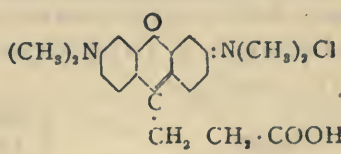


forms the dyestuff *Rhodine 12 GM* of the Gesellschaft für chemische Industrie in Basel.

As far as the condensation of *m*-aminophenols with the aminohydroxybenzoylbenzoic acids is concerned, D. R. P. 106 720/1898 states that ammonia is also liberated so that not only a rhodamine but also a rhodaminol or rhodol is formed at the same time, the amino group of the amino-*p*-cresol being replaced by hydroxyl.

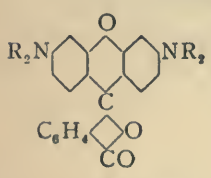
Whilst fluoresceins produced by the condensation of aliphatic acid anhydrides with resorcin have received no

technical application, the rhodamines derived from succinic anhydride proved to be very useful compounds. The dyestuff known as *Rhodamine S* was discovered by Kahn and Majert in 1888; it is the product of the condensation of succinic anhydride and dimethyl- (or diethyl-) aminophenol and is usually marketed as the zinc double salt of the chloride

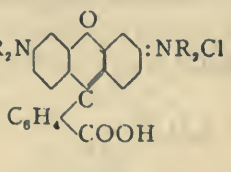


An alternative method for the preparation of this rhodamine consists in heating succinfluorescein with dimethylamine to 170—200°.

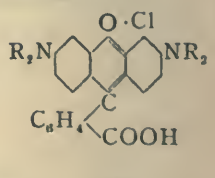
It will have been noticed that the rhodamines themselves are represented as alkylated 3:6-diaminofluorans (I); in fact, for a tetralkylated product any other constitution seems improbable. For the salts of such a base one might assume that the acid merely added itself to one of the tertiary nitrogen atoms or, alternatively, a paraquinonoid structure (II) such as has already been used, or even an orthoquinonoid formula (III) representing the salt as an oxonium compound.



I



II



III

Taking Rhodamine B as an example, it must be noted that the hydrochloride is coloured and dissolves easily in water forming a bluish red solution which, if dilute, exhibits a strong fluorescence. The salt shows a similar behaviour in alcohol; the fluorescence of the dilute solution disappears however on heating but reappears on cooling.

When a small amount of caustic soda is added to a cold solution of the hydrochloride, no change is noticed, but if the solution is hot and much caustic soda is added, a pink

flocculent precipitate is produced which dissolves in ether giving a colourless solution. There is thus some reason for assigning different constitutions to the base itself and the salts which it forms with acids, to the former that of a fluoran compound, to the latter a quinonoid constitution. Whether the quinonoid structure of the salts is para (II) or ortho (III) is a matter of speculation, it seems more reasonable to prefer an ammonium to an oxonium structure since the salts are stable and show no signs of hydrolysis.

But that the salts are really quinonoid and contain a free carboxyl group and are not formed by mere addition of acid to a dimethylamino group rests on more secure evidence than that afforded by the production of a coloured salt from a colourless base.

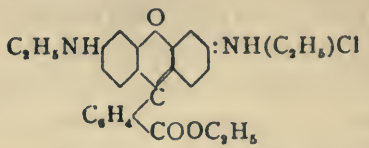
Monnet discovered in 1891 that ethyl chloride reacted with the base of Rhodamine B yielding a compound which was hydrolysed on warming with caustic soda giving once more the base of Rhodamine B. Monnet interpreted his results incorrectly, assuming that alkylation of the hydroxyl groups of the dialkylaminophenol residues had been effected; owing to this misinterpretation he called the new compound "anisoline".

Bernthsen explained the alkylation in a different manner, either alkyl halide adds on to a tertiary dialkylamino group, or else the halogen attaches itself to the dialkylamino group whilst the alkyl enters into carboxylic ester union. The latter is evidently the correct interpretation for rhodamines (as hydrochlorides) are converted into anisolines by treating their alcoholic solutions with hydrochloric acid gas (Bernthsen, *Chem. Zeit.*, 1892, *16*, 1956; D. R. PP. of the Badische Co. 66 238/1891 and 73 451/1892).

Thus the salts of rhodamines and anisolines show the usual relationships of organic acids and their esters; the former are converted into the latter by the usual means, and the latter are hydrolysed if subjected to the action of alkalies.

Normal esterification of Rhodamines may be effected even when the amino groups are not fully alkylated; thus

Bernthsen found that the reaction might be applied to the rhodamine obtained by condensing monoethyl-*m*-aminophenol with phthalic anhydride. The resulting ethyl ester possessing the constitution



forms the dyestuff known as *Rhodamine 6G, 6G extra* (Brit. P. 9633/1892; U. S. P. 516 584; F. P. 225 341; D. R PP. 73 573/1892, 73 880/1892).

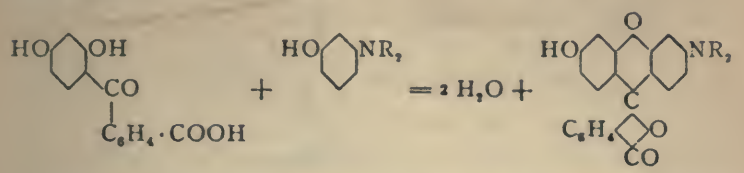
Esters can also be formed in which aryl take the place of alkyl groups. Meister, Lucius and Brüning (D. R. P. 84 656/1893) effect the esterification by means of phosphorus oxychloride and phenol, cresol, naphthol, nitrophenol or resorcin. The Badische Co. carry out a similar esterification using pyrogallol, in virtue of the neighbouring hydroxyl groups in the resulting product, it is a mordant dyestuff (Brit. P. 10 194/1894; F. P. 237 757; D. R. P. 87 174/1894).

Various methods for introducing alkyl groups into rhodamines have been used; thus Meister, Lucius and Brüning have employed the esters of *p*-toluenesulphonic acid (D.R.PP. 121 200/1899, 133 474/1901) and dimethyl sulphate (D. R. P. 121 201/1899).

The *Rhodaminols* or *Rhodols* form a class intermediate between the rhodamines and fluorescein. Of the positions 3 and 6 in the fluoran nucleus, one is substituted by an amino group (which may itself be alkylated or arylated), the other by hydroxyl: as has been pointed out in the case of Rhodine 12 GM, it is also possible to have compounds in which alkyloxyl is present in place of hydroxyl.

As seen above, rhodols are produced by the condensation of 4-dialkylamino-2-hydroxybenzoylbenzoic acids with resorcin and its derivatives; they were first prepared by the complimentary reaction in which dihydroxybenzoylbenzoic acid was condensed with alkyl-*m*-aminophenols (Bayer and

Co., D. R. P. 54085/1889; compare Badische Co., D. R. P. 54684/1890).



Cassella and Co. described a third method in which fluorescein was condensed with secondary amines, one of the hydroxyls being replaced by a dialkylamino group.

The rhodols, like the rhodamines, may be esterified; numerous patents were taken to protect the processes employed (Meister, Lucius and Brüning, D. R. PP. 116057/1899, 119061/1899, 115991/1899; Cassella and Co., D. R. P. 122289/1900).

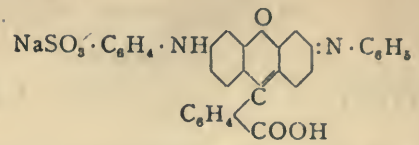
A distinct variation in the employment of rhodols consists in their nitration whereby mordant dyestuffs are obtained (Durand, Huguenin and Co., D. R. P. 245231/1911).

The rhodamine and anisoline are usually employed as basic dyestuffs, but acid dyestuffs may be obtained from them by sulphonation (Meister, Lucius and Brüning, D. R. PP. 79856/1892, 80777/1892, 84773/1895, 85885/1895, 87977/1895, 94398/1895, 119757/1897; Fritsch, D. R. P. 91604/1896; Badische Co., D. R. PP. 96668/1896, 98971/1896, 98972/1897).

Sulphonic acids of rhodamines can also be obtained by using as components compounds which are already sulphonated. Reference may be made to the use of sulphonic acids of *m*-hydroxydiphenylamine by the A. G. f. Anilin-Fabrikation (see D. R. P. 76415).

Amongst sulphonic acids of rhodamines, the *Violamines* of Meister, Lucius and Brüning call for first mention. These dyes were discovered by Bödeker in 1888; 3:6-dichlorofluoran was acted on by aniline and its homologues (D. R. PP. 49057/1888, 53300/1889; F. P. 201660) and the resulting diaryldiaminofluorans (diarylrhodamines) sulphonated and

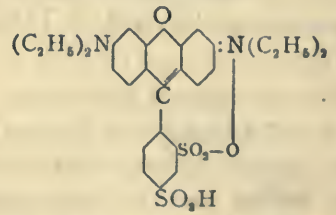
converted into sodium salts. Thus *Violamine B* or *Fast Acid Violet B* is obtained by using aniline or *p*-toluidine; its structure is represented by the formula



Fast Acid Violet A 2R is similarly prepared with the aid of *o*-toluidine, whilst in the case of *Acid Rosamine A* or *Violamine G*, mesidine is employed as primary arylamine (D. R. P. 63 844; F. P. 201 660). When 3:6:3':6'-tetrachlorofluoran reacts with primary bases, the chlorine atoms in positions 3 and 6 are replaced in the usual way; if *p*-phenetidine be the base employed and the resulting rhodamine be sulphonated, a dyestuff known as *Fast Acid Blue R* is obtained. This dyestuff, discovered by Bödeker in 1889, was introduced by Meister, Lucius and Brüning either alone or as a mixture under the name of *Violamine 3B*.

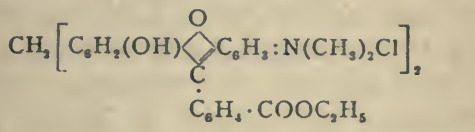
Fast Acid Eosine G and *Fast Acid Phloxine A* of Meister, Lucius and Brüning are obtained by sulphonating Rhodamine with fuming sulphuric acid (Brit. P. 2999/1896; F. P. 253 812; U. S. P. 642 893; D. R. P. 87 977).

The so-called *Sulphorhodamine* (*Brilliant Kiton Red* or *Xylene Red*) is properly a rosamine, it was discovered by Steiner in 1903. For its preparation, benzaldehyde-disulphonic acid is condensed with two molecules of diethyl-*m*-aminophenol and the product oxidised (D. R. P. 205 758). The dyestuff has the constitution



All rhodamines so far considered have contained only one fluoran residue; it is possible to link two such residues

together by the action of formaldehyde. A dyestuff of this description is the *Rhodamine 12 GF* of the Gesellschaft für chemische Industrie, Basel, discovered by Brack in 1898 (Brit. P. 18477/1898; F. P. 280915; U. S. P. 613113; D. R. P. 106720). The rhodol formed by condensing dimethylaminohydroxybenzoylbenzoic acid and resorcin is esterified and then acted on by formaldehyde; the constitution of the dye is probably given by the formula



In preparing rhodamines, 1 : 2-dicarboxylic acids are not essential; other acids which yield anhydrides may be employed. Two patents of the Badische Co. relate to the preparation of rhodamines using phthalonic acid (D. R. PP. 87028 and 89092 of 1895); they are not of technical importance.

If the rhodamines are carboxylic acids, they should correspond to both amides and nitriles. This appears to be the case and Meister, Lucius and Brüning have prepared a number of amides by acting on rhodamines with phosphorus oxychloride and secondary bases in succession (D. R. PP. 94237/1896, 94854/1896, 116416/1900, 118074/1897).

Nitriles of the Rhodamines formed the subject matter of a patent of the Badische Co. (D. R. P. 81264/1893).

Reference has been made to the production of compounds containing the xanthene group by condensing aminophenols with benzaldehyde-sulphonic acids and subsequent oxidation. The compounds described by the Société chimique des Usines du Rhône (D. R. PP. 100779/1896, 100780/1897) and obtained by condensing saccharin with aminophenols (or resorcin) must evidently be nearly related.

Complicated rhodamines containing more than one xanthyl residue have been described by O. Silberrad and C. S. Roy (*J. Amer. Chem. Soc.*, 1910, *33*, 189). Reference has

already been made to the condensation products of mellitic acid with resorcin (See P. 334). By using *m*-aminophenol and its dimethyl and diethyl derivatives, polyxanthyl-rhodamines were prepared. Thus from two molecules of dimethylaminophenol and one of mellitic acid a compound was obtained which contained one xanthyl group and might be regarded as tetramethylphthalrhodamine-tetracarboxylic acid.

When four molecules of dimethyl-*m*-aminophenol were condensed with one molecule of mellitic acid by heating for 8 hours at 160°, a rhodamine with two xanthyl residues was obtained (*loc. cit.*, 203). This compound differed from an isomeride which was prepared by heating 6.84 parts of mellitic acid, 11 parts of dimethyl-*m*-aminophenol and 4 parts of concentrated sulphuric acid for 6 hours to 165—170°. When sulphuric acid is absent, the second xanthyl group is formed in the para position to the first; in presence of sulphuric acid, the second xanthyl group occupies the meta position. This was demonstrated by converting the dixanthyl compound formed in presence of sulphuric acid into the corresponding trixanthyl compound (*Dodecamethyl-3, 3', 3'', 6, 6', 6''-hexamino-9, 9', 9''-trihydroxy-symtrixanthylbenzene-2, 4, 6-tricarboxylactone*) by condensing it with two further molecules of dimethyl-*m*-aminophenol. The trixanthyl compound can also be directly produced from an intimate mixture of 25 parts of mellitic acid, 62 parts of dimethyl-*m*-aminophenol and 100 parts of concentrated sulphuric acid by heating gradually to 180° and maintaining at that temperature for 8 hours.

The nomenclature used above is that of the authors who assign lactonoid constitutions to their compounds. They also arrive at the conclusion "that it may be regarded as fairly proved that the presence of quinoidal grouping is not an essential integral part of a coloured or fluorescent compound" (*loc. cit.*, 197).

CHAPTER XVII.

MANUFACTURE OF RHODAMINES.

Condensation of *m*-aminophenols with Anhydrides.

The first description of the formation of 3:6-diaminofluorans was given by the Badische Anilin und Soda Fabrik (Brit. P. 15374/1887; D. R. P. 44002/1887; U. S. P. 377350 of M. Ceresole; F. PP. 186697, 198173).

According to the specification, the simplest rhodamine, 3:6-diaminofluoran, is prepared by dissolving 1.4 kilos of *m*-aminophenol hydrochloride in 10 kilos of sulphuric acid (66° Bé.), adding 2 kilos of phthalic anhydride and heating for 3 or 4 hours at 180—190°. After cooling, the melt is dissolved in 80 litres of water, the solution filtered and the dyestuff salted out with sodium chloride; it may be purified by repeated crystallisation from hot acidified water.

The salt forms green metallic crystalline leaflets, easily soluble in alcohol, difficultly in cold but easily in hot water. Dilute solutions show a vivid green fluorescence which persists on addition of acid but disappears with alkali. Solutions in concentrated sulphuric acid are yellow and non-fluorescent. Addition of alkali to the aqueous solution liberates the base which is easily soluble in organic solvents. Addition of hydrochloric acid to the colourless solutions in ether or benzene causes the separation of the hydrochloride in scales showing a characteristic purple colour by transmitted light.

The dyestuff is reduced by zinc dust and ammonia to a leuco-compound; the colour is restored by addition of ferricyanide.

When an aqueous acidified solution of the simplest rhodamine is treated with sodium nitrite solution, the colour disappears; on boiling, fluorescein is formed.

An alcoholic solution acquires an eosine red shade on addition of bromine; water then gives a scarlet precipitate, soluble in alkalies.

Colour changes are also observed on heating the dyestuff with alkyl halides, whereby, according to the patent, alkyl derivatives are obtained identical with those formed from dialkylaminophenols and phthalic anhydride. In order to effect such alkylation one part of the rhodamine hydrochloride is heated to 150° for 3 or 4 hours with 3 parts of methyl iodide or ethyl bromide and 6 parts of methyl or ethyl alcohol respectively. According to the degree of alkylation so the shade alters, being more inclined to blue the more complete the alkylation.

D. R. P. 44002 gives methods for preparing rhodamines from dialkylated *m*-aminophenols as well as directions for the preparation of the latter compounds. For the preparation of tetramethylrhodamine, 10 kilos of dimethyl-*m*-aminophenol and 12 kilos of phthalic anhydride are heated for 4 to 5 hours at 170—175°. The operation is carried out in an enamelled vessel provided with stirrer, heating being effected with an oil-bath and air excluded as much as possible.

In this way, a melt consisting of the phthalate of the rhodamine is obtained; this is finely powdered, digested for some hours with dilute ammonia, the base extracted with benzene and the benzene solution treated with hot dilute hydrochloric acid. From the latter, the rhodamine hydrochloride separates on cooling in green crystals showing a bronze lustre.

The preparation of tetraethylrhodamine is carried out in a similar manner.

Rhodamine B, B extra, O, is usually the tetraethylrhodamine obtained from diethyl-*m*-aminophenol and occurs either as green crystals or as a reddish violet powder. It is easily soluble in water with a bluish red shade; dilute solutions are strongly fluorescent. Spectrum $\lambda = 555.0$ and 517.0.

Addition of a small amount of hydrochloric acid to the aqueous solution causes separation of the hydrochloride, larger amounts give a scarlet solution which turns bluish red on dilution. Caustic soda in small amount produces no change in the cold but an excess causes the separation of

reddish pink flocks on warming. Concentrated sulphuric acid gives a yellowish brown solution showing a strong green fluorescence; the colour goes through scarlet to bluish red on dilution with water.

Rhodamine dyes wool and silk from a neutral bath giving a bluish red with strong fluorescence; tannined cotton is dyed violet red without fluorescence.

Tetraalkylrhodamines may be de-alkylated; it is possible in this way to make yellower dyestuffs. The preparation of *Rhodamine G*, essentially consisting of triethylrhodamine, may be taken as an example (Badische Co., Brit. P. 14723/1891; U.S. PP. 516588, 516599 of M. Ceresole; D.R.P. 63325/1891; F.P. 215700).

Thus 3 kilos of tetraethylrhodamine are heated slowly in a capacious enamelled vessel to 230—235° and kept for $2^1/_2$ to 3 hours at this temperature until the crystals are converted into a pasty mass with a bronze—like lustre. After cooling, the mass is broken up, dissolved in hot dilute hydrochloric acid and salted out.

In another example the de-alkylation is effected by heating the hydrochloride of the tetraethylrhodamine with its own weight of aniline hydrochloride for $1^3/_4$ hours to 185—190°. Besides the *Rhodamine G* or *G extra* of the Badische Co., Cassella and Co. marketed triethylrhodamine as *Brilliant Rose G*.

The dyestuff occurs as crystals with a green glance, soluble in water with reddish violet colour and considerable fluorescence. $\lambda = 554.1$ and 516.8.

The alcoholic solution is reddish violet and fluorescent, hydrochloric and sulphuric acids give yellow solutions which become red on dilution. The aqueous solution is unaltered by cold caustic soda, but on warming it is decolourised, separation of the base taking place. The dye gives yellower shades than Rhodamine B.

D.R.P. 44002 was followed by several additional patents taken out by the Badische Co.; variations were made firstly with regard to the *m*-aminophenols employed and

secondly, the phthalic anhydride was replaced by its substitution derivatives.

D. R. P. 45263/1888 (Badische) gives the following examples.

(a) Condensation of 15 kilos of *m*-hydroxydiphenylamine and 10 kilos of phthalic anhydride by heating with 10 kilos of zinc chloride for 4 to 5 hours at 160—170°.

(b) Condensation of 10 kilos of *m*-hydroxydiphenylamine with 10 kilos of *β*-hydroxyphthalic anhydride. 5 to 6 hours at 160—170°.

(c) Condensation of 10 kilos of dichlorophthalic anhydride with 12.5 kilos of dimethyl-*m*-aminophenol (or 15 kilos of diethyl-*m*-aminophenol) by heating with 6 kilos of zinc chloride for 5 to 6 hours at 160°.

D. R. P. 46354/1888 (Badische) describes the condensation of 16 kilos of phenylethyl-*m*-aminophenol with 6 kilos of phthalic anhydride by heating with 10 kilos of zinc chloride for 5 hours at 175—185°.

Similar condensations are described in D. R. P. 47451/1888, viz. — those of dimethyl- and diethyl-*m*-aminophenols with tetrachlorophthalic anhydride, of *m*-hydroxydiphenylamine with di- and tetra-chlorophthalic anhydrides and of *m*-hydroxyphenyl-*p*-tolylamine with phthalic and di- and tetra-chlorophthalic anhydrides. The dyestuff from *m*-hydroxyphenyl-*p*-tolyamine is spirit soluble and gives redder shades than the corresponding dyes obtained from *m*-hydroxydiphenylamine.

D. R. P. 48731/1899 (Badische) describes the condensation of monomethyl-*m*-aminophenol (10 kilos) with phthalic anhydride (10 kilos) by heating with zinc chloride (5 kilos) to 170—180° until the melt shows a disposition to solidify. Dialkyrhodamines dye yellowish red shades on wool and silk, on the latter fibre the fluorescence is specially noticeable.

The dyestuffs from *m*-hydroxydiphenylamine are sparingly soluble; they give rise to soluble acid dyestuffs on sulphonation (Badische Co., D. R. P. 46807/1888). Thus 1 part of diphenylrhodamine may be sulphonated with 3 to 4 parts

of fuming acid (20—30 % SO_3) at 20—30° until soluble in dilute alkali; the mass is then poured into water, neutralised with milk of lime and converted into the sodium salt.

The preparation of sulphonated rhodamines by condensing sulphonic acids of *m*-hydroxydiphenylamine with phthalic anhydride was carried out by the A. G. f. Anilinfabr. Presumably the process was of little value for the patent, D. R. P. 80065/1893 was allowed to lapse in 1896.

We shall find many cases in which substituted rhodamines are converted into acid dyestuffs by sulphonation, a considerable advantage being derived from the fact that such sulphonated compounds can be used in a weak acid bath.

Benzyl groups are sulphonated easily; the Badische Co. (Brit. P. 7258/1891; D. R. P. 59996/1891; F. P. 186697) made use of this property. 45 kilos of ethylbenzyl-*m*-aminophenol and 30 kilos of phthalic anhydride are heated together for about 8 hours to 175—180°. The diethyldibenzylrhodamine base is isolated and sulphonated by adding it to 5 times its weight of fuming sulphuric acid (30 % SO_3) at 5—10°. As soon as it has all dissolved, the solution is poured on to ice, the precipitated sulphonic acid filtered off, dissolved in boiling water, filtered and salted out.

Meister, Lucius and Brüning (Brit. P. 2999/1896; U. S. P. 642893; F. P. 253812; D. R. P. 87977/1895) sulphonated symmetrical diethylrhodamine by adding it to 6 parts of fuming sulphuric acid (10 to 30 % SO_3), not allowing the temperature to exceed 30°. The mixture was then stirred until a sample when treated with alkali gave no free rhodamine base; it was then poured into water, salted out, dissolved in sodium carbonate solution and either evaporated or salted out.

Fast Acid Eosine G and *Fast Acid Phloxine A* (Meister, Lucius and Brüning) are obtained according to the patents just mentioned. Fast Acid Eosine G forms a cinnabar red powder, soluble in water with yellowish red colour and green fluorescence. For Fast Acid Eosine G $\lambda = 523.1$ and 487.1; for Fast Acid Phloxine A $\lambda = 535.3$ and 497.0.

Hydrochloric acid gives a yellowish red, soluble precipitate, caustic soda, a dark red solution with dark green fluorescence. Concentrated sulphuric acid gives a yellow solution with feeble green fluorescence; the colour turns pink on dilution.

Both dyes give a pink on wool when dyed from an acid bath; Fast Acid Eosine G gives a yellowish, Fast Phloxine A, a bluish shade. The fastness to light is greater than in the case of the non-sulphonated dyes.

In a somewhat modified form, the process of sulphonation may be extended to 3':6'-dichlorodiethylrhodamine, 25 kilos of which are dissolved in 150 kilos of monohydrate at 40°, and 150 kilos of fuming sulphuric acid (20% SO_3) added. Sulphonation is completed by stirring for about 5 hours (Meister, Lucius and Brüning, Brit. P. 10054/1899; D. R. P. 108347/1898; U. S. P. of Bödeker, 718408).

Paul Fritsch (D. R. P. 91604/1896) patented the sulphonation of rhodamines made with the help of 4-methoxyphthalic acid.

Rhodamines derived from the simple aminocresols are technically uninteresting. The Soc. Gilliard, P. Monnet et Cartier (F. P. 216256) have used dialkylaminocresols, $C_6H_3(CH_3)(N \cdot Alkyl_2)(OH)$, whilst the employment of ethyl- and methyl-aminocresols, $C_6H_3(CH_3)(NHR)(OH)$, 1:2:4, has been patented by the Badische Co. (Brit. P. 23397/1893; U. S. P. 516585 of A. Bernthsen; D. R. P. 69074/1892; F. P. 225341).

Rhodamines from 3:6-Dichlorofluoran.

The success of the rhodamines as dyestuffs led to a search for other methods of preparation. Meister, Lucius and Brüning (Brit. P. 9600/1888; F. P. 192589; D. R. P. 48367/1888) found that 3:6-dichlorofluoran (the "fluoresceinchlorid" of Baeyer, *Annalen*, 1876, *183*, 18) reacted with diethylamine giving tetraethylrhodamine. The reaction was carried out by heating 5 parts of fluorescein chloride, 4 parts of diethylamine hydrochloride, 5 parts of crystallised sodium

acetate and 8 parts of alcohol for 12 hours at 200—220°. The patent states that another substance is also formed at the same time, this is insoluble in aqueous acids but is converted into rhodamine by boiling with alcohol containing hydrochloric acid. Consequently, the reaction product is boiled for 5 hours with alcohol mixed with 10 per cent of concentrated hydrochloric acid, the alcohol distilled off, the residue boiled up with acidified water and rhodamine separated from the solution by the addition of salt.

In place of sodium acetate, other reagents such as sodium phosphate, lime, caustic soda etc. can be used to liberate the diethylamine from its hydrochloride.

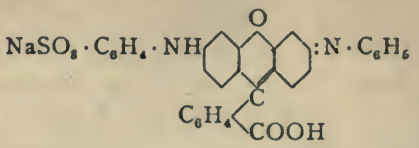
It is remarkable that when "fluorescein chloride" is heated with concentrated aqueous ammonia ($1^1/_2$ parts) for 6 hours at 190—200°, an imide compound, $C_{20}H_{11}O_2NCl_2$, is produced without the chlorine atoms being replaced. This compound is colourless, melts at 235° and is insoluble in aqueous acids and alkalies; it is soluble however in organic solvents and can be crystallised from benzene. By heating it with aliphatic or aromatic bases in presence of zinc chloride at 250—270°, chlorine is replaced and spirit soluble, red to bluish violet dyestuffs are formed which may be rendered water soluble by sulphonation (Meister, Lucius and Brüning, D. R. P. 48980/1889; F. P. 197489).

Additional patents were taken for modifications of the reaction. Thus D. R. P. 49057/1888 (M. L. B.) describes the use of the substituted 3:6-dichlorofluorans which are obtained by the action of phosphorus pentachloride on 3':6'-di- and 3':4':5':6'-tetra-chlorofluoresceins. These were caused to react with various aliphatic and aromatic amines as well as phenylhydrazine, whilst the dichlorotetrabromofluoran obtained from eosine was condensed with aniline.

By sulphonation of the diarylrhodamines obtained from dichlorofluoran and primary aromatic bases, a number of acid dyes may be prepared.

Fast Acid Violet or *Violamine B* (M. L. B.) is made from diphenyl- (or ditolyl-) rhodamine, the product of the action

of aniline (or *p*-toluidine) on fluorescein chloride; its constitution may be represented by a formula such as



It forms a dark bluish violet powder, soluble in water with violet colour, $\lambda = 526.5$. The aqueous solution gives a blue precipitate with hydrochloric acid, caustic soda gives a cherry red solution. Concentrated sulphuric acid dissolves the dye to a reddish yellow solution which on dilution with water first turns violet and then gives a blue precipitate.

Fast Acid Violet A2R (M. L. B.) or *Violamine R* is obtained by sulphonating di-*o*-tolylrhodamine. It is a violet powder giving a violet solution; hydrochloric acid throws out a bluish red precipitate but caustic soda produces no alteration. The solution in concentrated sulphuric acid is reddish yellow, water gives a bluish red precipitate.

Acid Rosamine R, Violamine R (M. L. B., D. R. P. 63 844; F. P. 201 660) is obtained from fluorescein chloride and mesidine, the product being sulphonated. The following directions for bringing about the reaction between fluorescein chloride and mesidine are given in D. R. P. 67 844/1891. Heat 37 kilos of fluorescein chloride, 30 kilos of mesidine and 10 kilos of zinc chloride for 2 hours at 200—220°. Powder the melt, extract zinc chloride with hot dilute hydrochloric acid and sulphonate the dried product with 6 times its weight of monohydrate at 20—25°.

In a second additional patent (D. R. P. 53 300/1889), Meister, Lucius and Brüning claimed the condensation of "fluorescein chloride" and dichlorofluorescein chloride" with ortho- and para- anisidines and phenetidines as well as with amino-*p*-cresol methyl ether and *p*-aminophenyl benzyl ether. Paraanisidine and paraphenetidine give dyestuffs of bluer shade than do their ortho isomerides; introduction of chlorine into the phthalic residue also has the effect of producing a

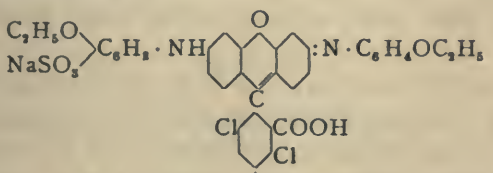
bluer tone. Thus the ortho-bases, when condensed with "fluorescein chloride" give reddish violet dyes but blue dyes are obtained by the condensation of "Dichlorofluorescein chloride" with *p*-anisidine and *p*-phenetidine.

The method of condensation is illustrated by the example of heating 5 kilos of *p*-anisidine with 7.4 kilos of fluorescein chloride and 4 kilos of zinc chloride for $^1/_2$ to 1 hour at 200 to 220°.

The melt is subsequently powdered, boiled with dilute hydrochloric acid, filtered off, pressed and dried. Whilst insoluble in water, the dyestuff is easily soluble in alcohol with a bluish violet colour.

In order to utilise these insoluble dyes, they are sulphonated (8 times the weight of monohydrate) until soluble in dilute alkali, then poured into water, filtered off, dissolved in sodium carbonate solution and salted out.

Fast Acid Blue R (Meister, Lucius and Brüning, D. R. P. 85 805/1895) is prepared by sulphonating the product from *p*-phenetidine and dichlorofluorescein chloride; its structure may be represented by



It forms a dark bluish violet powder, easily soluble in water with a blue colour; $\lambda = 533.9$. Hydrochloric acid gives a blue precipitate, caustic soda colours the solution violet; this shade goes redder on heating. With concentrated sulphuric acid, a dark bordeaux red solution is formed; from this water throws down a blue precipitate. Silk and wool are dyed from an acid bath.

In admixture, this dyestuff is also found as *Violamine 3B*.

Meister, Lucius and Brüning modified the reaction between 3:6-dichlorofluoran and bases in several respects and attention will be paid firstly to additions to D. R. P. 48 367.

D. R. P. 81 056/1894 states that the hydrochlorides may be employed in place of the free aromatic bases; thus diphenylrhodamine is obtained when 37 kilos of fluorescein chloride are heated with 32 kilos of aniline hydrochloride. The mass begins to get pasty at 180° hydrogen chloride being evolved; at 220° a homogeneous melt is produced and the temperature is kept at 220° for an hour. After cooling, the melt is powdered, boiled out with acidified water and the dyestuff filtered off and dried.

D. R. P. 84 773/1895 aims at the production of acid dyestuffs. For this purpose, β-sulphophthalic acid[1] is condensed with resorcin and the resulting fluoresceinsulphonic acid converted into "sulfofluoresceinchlorid". The preparation and structure of this compound are not described; the hydroxyl groups in positions 3 and 6 must be replaced by chlorine, but whether the sulphonic acid group is acted on is not mentioned. Presumably it is unaltered, for by heating 10 parts of "sulfofluoresceinchlorid" with 6 parts of diethylamine hydrochloride, 1.3 parts of lime and 4 parts of zinc chloride to 180—190°, or with 10 parts of aniline hydrochloride to 190—200°, sulphonic acids of the rhodamines are obtained.

The rhodamines prepared from 3:6-dichlorofluoran and primary aromatic bases are at best but sparingly soluble but can be converted into water soluble dyes by heating them with alkyl halides in alkaline solution; the resulting spirit soluble dyes are then sulphonated by means of monohydrate or a weakly fuming sulphuric acid (Meister, Lucius and Brüning, D. R. PP. 79 856, 80 777/1892).

D. R. P. 85 885/1895 shows how it is possible to use 3:6-dichlorofluoran for the preparation of asymmetrically substituted rhodamines, the chlorine atoms being successively

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1 Sulphonated rhodamines may be obtained by condensing the sulphophthalic acids with *m*-aminophenols. This course was followed by W. Majert (D. R. P. 61 690/1890). Friedländer describes the process as being without technical interest. The patent was allowed to lapse in 1892.

replaced by the residues of different bases. Thus, by the regulated action of aniline on "fluorescein chloride", it is possible to obtain the almost colourless 3-phenylamino-6-chlorofluoran (m. p. 211°) and then to cause this to react with another base, e. g. *p*-toluidine. The method of carrying out these reactions is described as follows.

36 kilos of fluorescein chloride are dissolved in a suitable solvent, e. g. 40 kilos of phenol, and 15 kilos of aniline hydrochloride added to the warm solution. The mixture soon turns red and is kept boiling for 4 to 5 hours. The cooled melt is boiled out with water and then washed with dilute alcohol; the compound may be obtained as concentrically grouped needles by crystallisation from benzene.

15 kilos of phenylaminochlorofluoran, 10 kilos of *p*-toluidine, 6 kilos of zinc chloride and 3 kilos of lime are intimately mixed and heated to 190—200° for about half-an-hour. After cooling, powdering and boiling out with dilute hydrochloric acid, the dark violet powder—phenyl-*p*-tolyl-rhodamine—is rendered useful by sulphonation. This is effected by warming for a short time with 8 litres of sulphuric acid (66° Bé.) to 40—50°.

The reactions described in the patent may be illustrated by the scheme

$$C_{20}H_{10}Cl_2O_3 \xrightarrow{(NH_2R)} C_{20}H_{10}Cl(NHR)O_3 \xrightarrow{(NHR'R'')} C_{20}H_{10}(NHR)(NR'R'')O_3$$

the sulphonic groups ultimatly entering one of the aryl groups. Of the compounds $C_{20}H_{10}Cl(NHR)O_3$, melting points are given where R is C_6H_5 (186°), *o*-$CH_3 \cdot C_6H_4$ (192°), *p*-$CH_3 \cdot C_6H_4$ (194°), *p*-$C_2H_5O \cdot C_6H_4$ (192°), 2:4:6-$C_6H_2(CH_3)_3$ (160°), *α*-$C_{10}H_7$ (196°) and *β*-$C_{10}H_7$ (216°).

Meister, Lucius and Brüning (D. R. P. 139727/1902) further describe a process for the preparation of alkylated or arylated aminochlorofluorans, "fluorescein chloride" (or dichlorofluorescein chloride) being heated with the hydrochlorides of fatty or aromatic amins in presence of zinc chloride.

Thus 3-dimethylamino-6-chlorofluoran is prepared by

melting 30 kilos of diethylamine hydrochloride with 42 kilos of solid zinc chloride in an open cast iron vessel provided with a stirrer and adding 10.2 kilos of zinc oxide to the melt at 100—140°. The temperature is raised to 160—165° and a mixture of 60 kilos of fluorescein chloride and 11 kilos of zinc oxide gradually introduced. Stirring and heating to 160 to 165° are continued until fluorescein chloride is no longer present in the mixture; this may be recognised by taking a sample and treating with alcohol, in which solvent the dichlorofluoran is very sparingly, the other substance easily, soluble. The reaction usually takes 18 hours for completion; the product is then broken up and extracted repeatedly with water to which some hydrochloric acid has been added. The residue is suitable for further use; if purified by crystallisation from alcohol it may be obtained in reddish crystals of m. p. 148°. Other examples are given in the patent.

Other fluorescein esters may be used in addition to dichlorofluoran for the preparation of rhodamines. Thus, Meister, Lucius and Brüning (D. R. P. 116415/1899) prepared the toluenesulphonate (m. p. 163—165°) by heating 376 parts of fluorescein with 382 parts of *p*-toluenesulphonyl chloride to 140°. By heating 128 parts each of the resulting ester and of dimethylamine hydrochloride with 80 parts of zinc chloride and 60 parts of lime to 220°, rhodamine was produced.

Rhodamines from Succinic Anhydride.

Succinic anhydride behaves similarly to phthalic anhydride in its reactions with pyrogallol (Baeyer, *Ber.*, 1873, *6*, 664) and resorcin (Damm and Schreiner, *Ber.*, 1882, *15*, 555); the products have no technical value. It is, under the circumstances, somewhat remarkable that the rhodamine obtained from succinic anhydride and diethyl-*m*-aminophenol should possess properties which, in some respects, make it superior to the corresponding phthalein and led to it being placed on the market as *Rhodamine S*.

Bayer and Co. (D. R. P. 51983/1888) state that 5 kilos

of succinic anhydride, 12 kilos of dimethyl-*m*-aminophenol and 2 kilos of zinc chloride are heated for 3 hours at 170°. The melt is subsequently finely powdered and dissolved in hot hydrochloric acid, the rhodamine salt crystallising out in beautiful brown needles on cooling.

Rhodamine S occurs as a dark green crystalline powder soluble in water with red colour and yellow fluorescence. Spectrum $\lambda = 545.1$ and 509.0. Caustic soda decolourises the solution and gives a precipitate of the base. Concentrated sulphuric acid dissolves the dye; the solution is brownish and strongly fluorescent; on dilution with water it becomes rose red.

Though the shade is so similar to that of the ordinary rhodamines, the colouring power is greater, and unmordanted cotton can be dyed directly from a dilute acetic bath at 40 to 50°. The dye is not very suitable for wool but useful for silk and mixtures of silk and cotton.

According to the Gesellschaft für chemische Industrie, Basel (D. R. P. 54997/1890), a mixture of succinrhodamine and the corresponding rhodol is obtained when 13.2 parts of succinfluorescein, 13.8 parts of 40 per cent dimethylamine solution and 70 parts of alcohol are heated for 14 hours to 170—200°.

Rhodamines with modified Carboxyl Groups.

If phosphorus oxychloride be allowed to react with a rhodamine [1] in presence of an amine or phenol, the carboxyl group is attacked and other substances are formed. It would appear at first sight that the hydroxyl of the carboxyl group is replaced by chlorine and the resulting substance of acid chloride structure then reacts in the usual manner. If we

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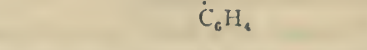
1 The action of phosphorus oxychloride or phosphorus pentachloride on alkylated rhodamines, in presence or absence of a solvent, forms the subject matter of a separate patent. (Meister, Lucius and Brüning, D. R. P. 118074/1897.) The products are stated to dye vegetable fibres bluer and faster than the rhodamines from which they are obtained.

represent a rhodamine by the general formula $X \cdot COOH$ where



and assume that the reactions follow the normal course when an acid chloride acts on a phenol or a primary, secondary or tertiary amine, we arrive at the following equations. (R', R'' $= CH_3$, &c.)

$$R \cdot COCl + C_6H_5OH = R \cdot COOC_6H_5 + HCl$$
$$R \cdot COCl + NH_2R' = R \cdot CONHR' + HCl$$
$$R \cdot COCl + NHR'R'' = R \cdot CONR'R'' + HCl$$
$$R \cdot COCl + C_6H_5NR'R'' = R \cdot CO \cdot C_6H_4 \cdot NR'R'' + HCl$$

How far such simple equations represent the reactions involved is very doubtful, as, for example, where quinoline is used amongst the tertiary bases.

Meister, Lucius and Brüning (Brit. P. 14 207/1893; F. P. 231 700; D. R. P. 75 500/1893) first used the reaction with tetraethyl- and diethyl-rhodamines[1] one or other of which was allowed to react with phosphoryl chloride and one of the following, bases, viz., dimethylaniline, diethylaniline, ethyl-*o*-toluidine, ethylbenzylaniline, quinoline or dimethyl-α-naphthylamine. The compounds made from tetraethylrhodamine dye tannined cotton red to reddish violet, those made from diethylrhodamine give yellowish pink shades. An additional patent (D. R. P. 81 957/1893) extends the reactions to the use of *m*-nitrodimethylaniline.

Shortly afterwards, it was found that the hydrochlorides of the rhodamines react with primary bases either in presence or absence of phosphoryl chloride.

Meister, Lucius and Brüning embodied the results in the same British and French patents as those relating to the

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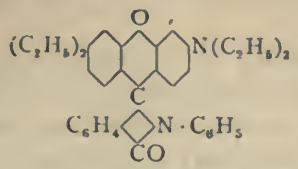
1 According to D. R. P. 116 416/1900, addition of aluminium or ferric chloride has an advantage, in that when the melt is treated with hydrochloric acid, it dissolves more readily without the separation of resinous material.

action of secondary and tertiary bases, but took a separate German patent, 80 153, which is dated only four days later than D. R. P. 75 500.

To prepare the rhodamine anilide (m. p. 222°)



the rhodamine (base or salt) may be boiled for 8 hours with 2 to 3 times its weight of aniline, or the reaction may be brought about at 80—100° in a shorter time by adding 4 parts of phosphoryl chloride to 10 parts of rhodamine base or salt dissolved in 20 parts of aniline. In either case, the product is dissolved in dilute hydrochloric acid, precipitated by sodium acetate and crystallised from alcohol or benzene; it separates from the former in colourless leaflets, from the latter in groups of needles.

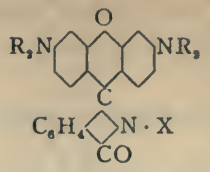
Corresponding compounds are obtained by the use of *o*- and *p*-toluidines, the melting points of which are 179° and 196° respectively.

Whilst solutions in alcohol and benzene are colourless, acetic acid gives a pale bluish red solution exhibiting a yellowish red fluorescence.

Meister, Lucius and Brüning took additional patents. D. R. P. 85 242/1895 describes products obtained by heating rhodamines with primary hydrazines to 150—160°; the products from tetraethyl- and diethyl-rhodamines and phenylhydrazine melt at 214° and 235° respectively, that from tetraethylrhodamine and *p*-tolylhydrazine at 150°.

D. R. P. 88 675/1895 describes the products obtained from tetraethylrhodamine and *o*-, *m*- and *p*-nitranilines which crystallise in yellow to pink needles and melt at 194°, 145° and 200° respectively.

The substances mentioned above possess the general structure



and, except where the aryl group X is nitro-substituted, are colourless. This also holds when X = H, but if the nitrogen atom is linked in a manner which prevents the closing of a phthalimide ring, dyestuffs are obtained.

This result may be achieved in various ways,

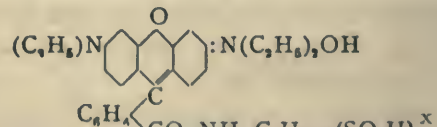
(a) By sulphonation.

(b) By formation of a nitrile group.

(c) By formation of a carboxydialkylamide group.

(a) *Sulphonation.* The Badische Co. (D. R. P. 81 958/1893) produced a difficultly soluble sulphonic acid of rhodamine-anilide (m. p. 222°) by warming with 5 parts of fuming sulphuric acid (23 per cent anhydride) on the water-bath until the sample dissolved completely in warm dilute sodium carbonate solution. A more soluble sulphonic acid was produced by stirring the anilide with 4 parts of fuming sulphuric acid (23 per cent), then heating for $1^1/_2$ hours on the water-bath and pouring the melt on to ice. The sodium salt of the latter acid forms a red powder, the aqueous solution is bluish red and has a yellowish red fluorescence; the solution is nearly decolourised by soda or ammonia but the colour is intensified by acetic acid. Wool is dyed red from an acid bath and shows strong fluorescence; the shade is somewhat bluer and distinctly cleaner than that given by Rhodamine B.

Disregarding internal salt formation, the patentees ascribe the constitution (I) to their products; this is equivalent to a structure (II) for the sodium salts.



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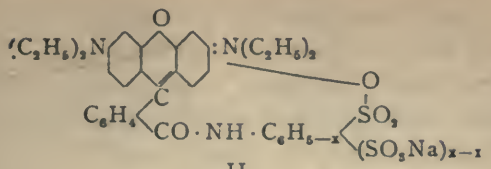
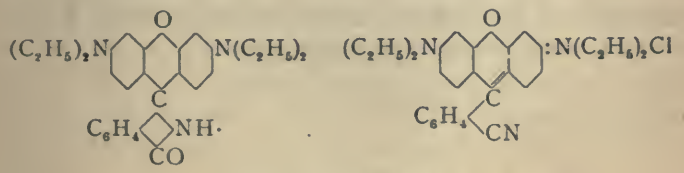


II

(b) *Formation of Nitrile Group.*—In this case the Badische Co. (D. R. P. 81 264/1893) dissolve Rhodamine B extra in 5 times its weight of alcohol, saturate with ammonia gas and heat for 10 hours at 180°. On recrystallisation from alcohol, the product (I, below) is obtained as colourless crystals, m. p. 229°.

On heating the imide (5 parts) with phosphoryl chloride (2 parts) in presence or absence of a diluent, e. g. toluene, the elements of water are removed at water-bath temperature. The dye (II) is obtained by solution and salting out.



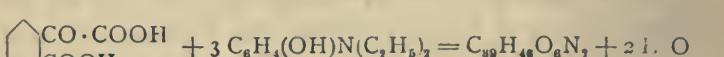
I II

Alkalies precipitate a base as reddish flocks, this has the same percentage composition as the original imide. The colouring matter dyes wool and silk violet red; with tannined cotton an intense fluorescence is observed.

(c) *Dialkylamides.* Meister, Lucius and Brüning (Brit. P. 1592/1897; F.P. 263318; D.R.PP. 94237/1896, 94854/1897) treated rhodamine salts with phosphoryl chloride (3 parts at temperatures up to 80°) and then with secondary aliphatic amines. In this way the carboxyl group became a disubstituted carboxylamide group, $CONR_2$, and formation of a colourless derivative of phthalimide was inhibited.

Phthalonic acid Rhodamines. The Badische Co. discovered (Brit. P. 14 135/1895; F. P. 249 009; D. R. PP. 87 028, 89 092/1895) that dialkyl-*m*-aminophenols could be condensed with phthalonic acid to dyestuffs. If the constituents are made to

react at a high temperature (e. g. 10 kilos of diethyl-*m*-aminophenol, 12 kilos of phthalonic acid for 4 hours at 180°) a dye is obtained, but if 194 parts of phthalonic acid (1 mol.) be well mixed with 495 parts of diethylaminophenol (3 mols,) and stirred and heated for some hours at 100°, a colourless compound is obtained according to the equation



$$\text{CO·COOH / COOH} + 3\,C_6H_4(OH)N(C_2H_5)_2 = C_{39}H_{46}O_6N_2 + 2\,H_2O$$

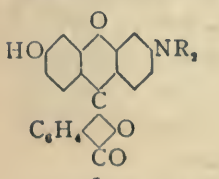
This melts about 175° and is easily soluble in dilute acids and alkalies; on oxidation it gives a rhodamine.

50 parts of the intermediate compound are dissolved in 750 parts of 30 per cent acetic acid (or dilute sulphuric or hydrochloric acid) and 21 parts of potassium persulphate added slowly. The solution is warmed on the water-bath until a test portion treated with excess of dilute caustic soda no longer gives a blue colour turning red on warming. It is then allowed to cool and the dye salted out.

CHAPTER XVIII.

RHODOLS AND UNSYMMETRICAL RHODAMINES.

Intermediate between fluorescein with its two hydroxyl groups and the rhodamines with their two (usually substituted) amino-groups exists a class of compounds, 3:6-amino-hydroxy-derivatives of fluoran (I)



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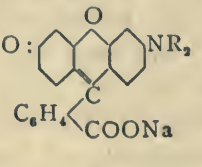
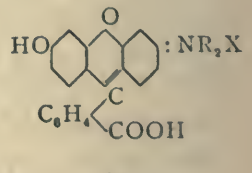


II



III

As to the constitution of their salts, those with alkalies may have the structure (II), those with acids almost certainly structure (III). Compounds of this type may be produced

either by condensing 2:4-dihydroxybenzoylbenzoic acid with a metaaminophenol (Bayer and Co. D. R. P. 54 085/1889) or a derivative of 2-hydroxy-4-aminobenzoylbenzoic acid with resorcin or a homologue (Basler chemische Fabrik, D. R. PP. 85 931/1894, 87 068/1894, 132 066/1901; Badische Co. D. R. P. 96 668/1896).

In Bayer's earliest patent, the dihydroxybenzoylbenzoic acid was condensed with dimethyl-, diethyl- and monophenyl-*m*-aminophenols; the mono- and di-bromo derivatives of dihydroxybenzoylbenzoic acid were also employed in conjunction with alkylated *m*-aminophenols. Zinc chloride was used as condensing agent at 140—160°.

The products obtained were of no particular value and the process was complicated (See comments in Friedländer, II, 86).

The Badische Anilin und Soda Fabrik (D. R. P. 54 684/1890) patented the conversion of rhodols (or rhodaminols) obtained in this manner with 3-chlorodialkylaminofluorans, and the reaction between the latter and dialkylamines whereby rhodamines are formed; this was probably a blocking patent.

Two other processes for the preparation of rhodols may be noticed.

Dialkylrhodols may be obtained by the alkylation of rhodols which the St. Denis Co. (304 773; D. R. P. 56 506/1890) proposed to manufacture by heating fluorescein (10 kilos) with saturated aqueous ammonia (15 kilos) for 8 hours at 160—180°. From the patent, it would appear that some diaminoacridylbenzoic acid (Meyer and Oppelt, *Ber.*, 1888, *21*, 3376) is formed at the same time.

Meister, Lucius and Brüning (D. R. P. 65 195/1892) obtain alkali soluble rhodamine dyes by heating rhodamine with free alkalies or alkaline earths, in presence or absence of calcium or zinc chloride, to 220—240°. Alternatively, fluorescein chloride (10 kilos), diethylamine hydrochloride (10 kilos), zinc chloride (8 kilos) and sodium acetate (15 kilos) are heated for 4 hours to 220—240°. The nature of the products obtained is not very obvious.

The patents of the Basler chemische Fabrik give directions for the preparation of 2-hydroxy-4-dialkylaminobenzoylbenzoic acids; the methods employed are illustrated by examples.

D. R. P. 85931/1894. Example 1. 30 kilos each of phthalic anhydride and dimethyl-*m*-aminophenol are dissolved in 150 kilos of benzene, filtered hot and boiled for 8 to 10 hours. After cooling, the precipitate is collected and crystallised repeatedly from dilute alcohol.

D. R. P. 87068/1895. Example 2. Melt 17 kilos of diethyl-*m*-aminophenol and stir in 15 kilos of finely powdered phthalic anhydride. Keep the melt at 100° until no further increase in solidification can be observed. Then powder, boil up with alcohol, cool, collect the residue and purify by recrystallisation from alcohol. Neither compound shows a sharp melting point; they liquefy and decompose over 180° becoming red at the same time.

The Badische Co. (D. R. P. 96668/1896) adopted a process involving a very similar principle with the object of making rhodamines containing one *o*-tolylamino group. It was stated that the object in producing these compounds was to obtain rhodamines which when sulphonated gave colouring matters dyeing beautiful fiery shades.

By heating equimolecular proportions of *m*-hydroxyphenyl-*o*-tolylamine and phthalic anhydride to 120—130° until the mixture is thick and then extracting the melt with spirit or other solvent, 2-hydroxy-4-*o*-tolylaminobenzoylbenzoic acid is obtained in a pale green, finely crystalline condition. This compound becomes violet above 180° and melts above 200° with complete decomposition.

If this compound is condensed with a second molecule of a *m*-aminophenol, a rhodamine is produced, but with resorcin, *o*-tolylaminorhodol is formed.

Example 1. 17.5 parts of the above mentioned acid, 5.5 parts of resorcin and 15 parts of potassium bisulphate are well mixed, stirred and heated to 170—175° for about an hour; the end of the reaction is denoted by the mixture

becoming so viscous that it can scarcely be stirred. After cooling, the mass is powdered, boiled out several times with water, dried at 100° and extracted with toluene. The residue consists of the sulphate of the rhodol.

Example 2. 17.5 parts of the acid, 6.2 parts of amino-*p*-cresol ($CH_3 : NH_2 : OH = 1 : 2 : 4$) and 15 parts of potassium bisulphate are heated at 190°.

Example 3. 1 part of *o*-tolylrhodol sulphate is dissolved in 5 parts of sulphuric acid (66° Bé.) at the ordinary temperature. The yellowish brown solution is then heated to 45 to 50° until the product is completely soluble in dilute sodium carbonate solution.

Example 4. 1 part of dimethyl-*o*-tolylrhodamine sulphate (prepared from the acid and dimethylaminophenol) and 10 parts of 80 per cent sulphuric acid are heated some hours on the water-bath until the sulphonation is complete.

Example 5. Dissolve 10 parts of *o*-tolylhomorhodamine sulphate in 4 parts of concentrated sulphuric acid, cool to 0—5° and add fuming sulphuric acid (24 per cent anhydride) drop by drop until the product is completely soluble in dilute sodium carbonate solution.

The patent describes the properties of several rhodamines and rhodols obtained, also of the sulphonic acids produced from them. The components; other than the tolylamino-hydroxybenzoylbenzoic acid are, in addition to those mentioned in examples 1 and 2, mono- and di-methyl-*m*-aminophenols and a homologue of resorcin.

D. R. P. 98971/1896 of the same firm (Brit. P. 2655/1897; U. S. P. 609998; 4th. Addition to F. P. 186697) describes a very similar procedure starting with *p*-ethylbenzylamino-*o*-hydroxybenzoylbenzoic acid which it is not necessary to isolate.

Example 1 gives the following directions for preparing 3-ethylbenzyl-6-ethylrhodamine. 5.8 parts of ethylbenzyl-*m*-aminophenol and 3.8 parts of phthalic anhydride are melted

together without allowing the temperature to exceed 120 or 130°. When the liquid mass has solidified, 3.5 parts of ethyl-*m*-aminophenol are added and an uniform melt obtained at 130°; 8 parts of potassium bisulphate are next introduced and the temperature raised and kept at 175° for one hour, stirring well all the time. After cooling, the melt is powdered, boiled out several times with water, dried and again powdered.

In place of ethylbenzyl-*m*-aminophenol, the methylbenzyl-derivative may be used and a number of *m*-aminophenols are described as second components.

The rhodamines and rhodols obtained in this manner are distinguished by the ease with which they are sulphonated. Two processes of sulphonation are employed, viz. the use of hot concentrated sulphuric acid and of cold fuming sulphuric acid. The sulphonic acids obtained by the two processes appear to be different, those by the latter process being usually far more soluble and frequently different in shade.

D. R. P. 98 972/1897 (Brit. P. 2655/1897; 5th addition to F. P. 186 697) describes the sulphonation of the rhodamines obtained by condensing hydroxydiethylaminobenzoylbenzoic acid with benzyl-*m*-aminophenol.

Meanwhile, patents for the production of rhodols or asymmetric rhodamines from dialkylaminophenols were applied for by the Basler chemische Fabrik (Bindschedler).

D. R. P. 96 108/1896 (transferred to Cassella and Co., see also Brit. P. 12 180/1897; F. P. 266 985/1897) describes the preparation of a rhodamine by dissolving 31 kilos of hydroxydimethylaminobenzoylbenzoic acid and 15 kilos of aminocresol ($CH_3 : OH : NH_2 = 1 : 2 : 4$) in 180 kilos of sulphuric acid and 40 kilos of water and heating at 140—160° until the product is soluble in warm water.

D. R. P. 108 419/1897 (Cassella and Co.; applied for by the Basler chemische Fabrik; Brit. P. 12 181/1897) describes the formation of a rhodol from 28 kilos of dimethyl- (or diethyl-) aminohydroxybenzoylbenzoic acid and 14 kilos of

resorcin in 180 parts each of sulphuric acid and water at water-bath temperature. The product can be esterified.

D. R. P. 106720/1898 (Basler chemische Fabrik, transferred to Cassella and Co., see also Brit. P. 18477/1898; U. S. PP. 613131/1898 and 625536/1899 of J. J. Brack; F. P. 280925/1898) deals with the formation of rhodols from hydroxydialkylaminobenzoylbenzoic acids and resorcin or *p*-amino-*o*-cresol (in which case, ammonia is eliminated), their esterification and condensation by means of formaldehyde to dyestuffs such a *Rhodamine 12 GF*; these are distinguished by several useful properties. The esters of the rhodols give zinc ferrocyanide lakes which alter their colour on steaming from yellowish red to bluish violet. Treatment of the esters with formaldehyde produces well defined compounds which give as stable zinc ferrocyanide lakes as other rhodamines and, at the same time, of a much yellower shade.

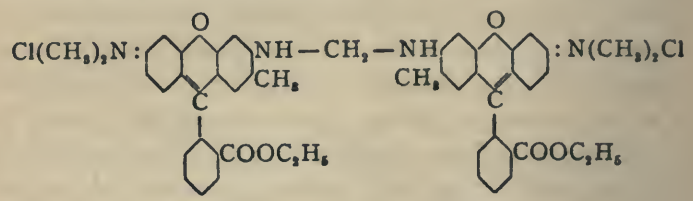
A solution of 42 kilos of esterified dimethylrhodol in 200 kilos of concentrated sulphuric acid is treated with a mixture of 8 kilos of 40 per cent formaldehyde in 100 kilos of concentrated sulphuric acid. Temperature rises as the reaction sets in; for its completion, the mixture is left for some days at the ordinary temperature and then poured on to ice.

The sulphate of the condensation product remains in solution; addition of brine throws out a resinous precipitate, said to consist of the sulphate.

To obtain the hydrochloride, the sulphate is dissolved in 60 kilos of alcohol and 70 kilos of water, and 70 kilos of hydrochloric acid (20° Bé.) added to the hot solution. After standing some time, brine is stirred in whereby the hydrochloride is precipitated as a resin; the supernatant liquor is decanted and the resin dried and ground.

Rhodamine 12 GF forms a bright red powder giving yellowish red aqueous and alcoholic solutions. Spectrum, $\lambda = 526.7$, 489.2 and 458.4. The aqueous solution is unaltered by hydrochloric acid, caustic soda gives a bright red precipitate. Concentrated sulphuric acid gives a yellow solution turning yellowish red on dilution.

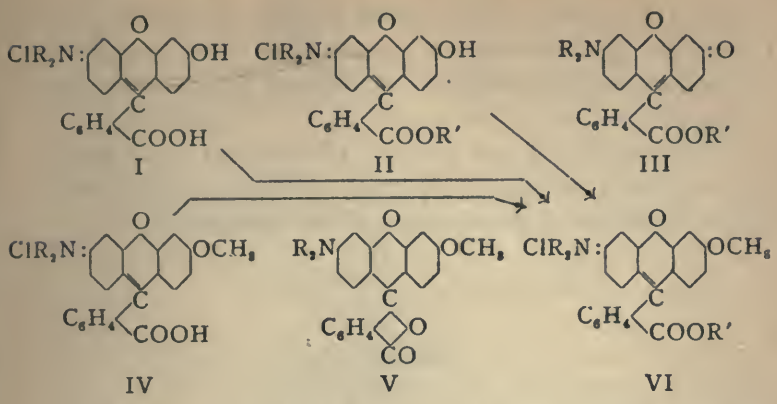
Cassella and Co. (D. R. P. 109 883/1899) also obtained a condensation product by adding a solution of $2^1/_2$ kilos of 40 per cent formaldehyde in 30 kilos of concentrated sulphuric acid to 30 kilos of the esterified condensation product obtained from dimethylaminohydroxybenzoylbenzoic acid and *o*-amino-*p*-cresol dissolved in 200 kilos of concentrated sulphuric acid. The constitution



is assigned to the compound which dyes cotton a fiery red. (Bluer shade than that given by the uncondensed ester.)

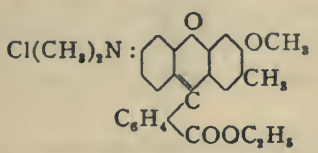
When a dialkylaminohydroxybenzoylbenzoic acid is condensed with a *m*-aminophenol, it should be remembered that water may be split off between a hydroxyl and an amino group (formation of an acridylbenzoic acid) so that there is no guarantee of the production of a chemical individual. To obviate this difficulty Meister, Lucius and Brüning (Brit. P. 12 272/1901; U. S. P. 694 149 of Hoffmann; F P. 371 805; D. R. P. 128 574/1901) added $2^1/_2$ parts of *m*-acetaminophenol to 5 parts of diethylaminohydroxybenzoylbenzoic acid dissolved in 40 parts of concentrated sulphuric acid at 20—30°, allowed the mixture to stand for some hours and poured out on to ice. It was claimed that the process yielded an acetyldiethylrhodamine as sole product.

For some time, the rhodols found little application, largely on account of their lack of fastness to soap. In this case, esterification with production of compounds of type II was of no avail (see D. R. P. 108 419); the colours thus obtained are also not fast to soap and solutions of the salts are precipitated by sodium carbonate. It may be noted in this connection that there is the possibility of quinonoid anhydrobases (III) being produced.



If, however, the hydroxyl and carboxyl groups are both alkylated, compounds of type VI are produced; tannined cotton is dyed by them in shades which are quite fast to soap. Patents for the production of such compounds were obtained by Meister, Lucius and Brüning (Brit. P. 15983/1899; U.S.P. 656426/1899 of Schmidt; F. P. 291621; D. R. P. 116057/1899) and Cassella and Co. (D. R. P. 122289/1900;[1] additional to D. R. P. 108419 which was transferred from the Basler chemische Fabrik, see Brit. P. 12181/1897). One of the dyestuffs of this class has found application under the name of *Rhodine*.

Rhodine 12 GM (Ges. f. chem. Ind. Basel)

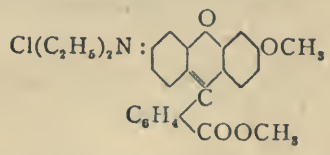


forms a reddish brown powder, soluble in water and alcohol with yellowish red colour ($\lambda = 525.8, 488.5, 457.8$). Hydro-

1 D. R. P. 122289 protects the formation of rhodol alkyl ethers from mono- or di-methylrescorcin, water or methyl alcohol being eliminated as the case may be. Thus 28.5 parts of dimethylamino-hydroxybenzoylbenzoic acid are dissolved in 180 parts of sulphuric acid and 90 parts of water, a solution of 12.4 parts of mono- or 13.8 parts of di-methylresorcin in 50 parts of methyl alcohol added and the mixture warmed for 6 hours on the water-bath.

chloric acid produces no alteration, caustic soda, a bright red precipitate. The solution in concentrated sulphuric acid is yellow becoming yellowish red on dilution. Silk and tannined cotton are dyed yellowish red.

Meister, Lucius and Brüning give several methods for the preparation of these compounds which may be illustrated by the formation of the substance of the constitution



(a) From Diethylrhodol (Formula I, p. 373).

An intimate mixture of 120 parts each of diethylrhodol hydrochloride and soda-ash is stirred and treated with 190 parts of dimethyl sulphate. Temperature rises to about 85°, the mass becomes viscous and finally hard; it is either allowed to stand for some time at the ordinary temperature or else warmed for half-an-hour to 90°. On extraction with hydrochloric acid, dilution with water until solution is complete and salting out, the dyestuff is precipitated as an oil which solidifies to a crystalline crust.

(b) From Diethylrhodolcarboxylic ester (Formula II, p. 373).

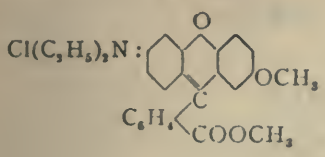
An intimate mixture of 41 parts of the hydrochloride of diethylrhodolcarboxylic ester and 20 parts of soda-ash are treated with 30 parts of dimethyl sulphate as in the last example.

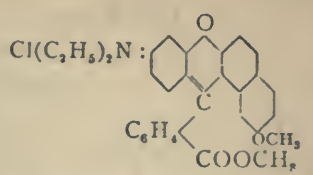
(c) *From Diethylrhodol methyl ether* (Formulae IV and V, p. 373).

38 parts of diethylrhodol methyl ether, preferably with addition of soda-ash, are heated for some time to 80—90° with 25 parts of dimethyl sulphate.

In addition to other compounds of the same type, but containing different alkyl groups, e. g. benzyl, condensation products from quinol and 2:7-dihydroxynaphthalene are also described. These are produced by heating the respective

phenols in 50 per cent sulphuric acid solution with diethyl-*m*-aminohydroxybenzoylbenzoic acid to 140° and subsequent alkylation. The corresponding hydrochlorides must possess the constitutions





An additional patent of the same firm (D. R. P. 119061/1899) describes the esterification of rhodol ethers by means of alcohols and hydrochloric acid.

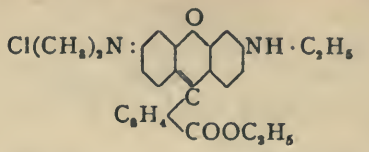
The compounds obtained by condensation of diethylaminohydroxybenzoylbenzoic acid with phenol and either of the naphthols and subsequent esterification appear to have been of little importance, as the patent (D. R. P. 115991/1899) was allowed to lapse in 1901.

A number of similar dyestuffs were made by condensing dialkylaminohydroxybenzoylbenzoic acids (and their di- and tetra-chloro-substitution products made with the aid of di- and tetra-chlorophthalic acids) with naphthol-sulphonic acids and chromotrope acid (Meister, Lucius and Brüning, D. R. P. 118077/1899; F. P. 299176/1900). The following acids are mentioned; 1-naphthol-4- and 5-mono- and 3:8- and 4:8-disulphonic acids; 2-naphthol-6-mono-, 3:6-, and 6:8-di- and 3:6:8-tri-sulphonic acids.

The colours obtained with these monohydroxynaphthalene derivatives give reddish shades and are weaker in dyeing properties than the colours produced with chromotrope acid. Thus the dyestuff obtained by heating (140° for 10 hours) 100 parts of diethylaminohydroxybenzoylbenzoic acid with 200 parts of chromotrope salt and 2700 parts of 50 per cent sulphuric acid without replacing water lost by evaporation, produces a bluish violet shade on wool which, on treatment with chromate, gives a greenish blue, fast to milling.

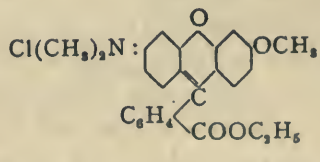
The name *rhodine* has also been applied to certain unsymmetrical rhodamines.

Rhodine 2 G (Ges. f. chem. Ind., Basel).



This dye was discovered by Müller (Brit. P. 4985/1895; U. S. P. 584 119; F. P. 245 593); it is obtained by condensing dimethylaminohydroxybenzoylbenzoic acid with ethyl-*m*-aminophenol and esterifying the product. It forms a green crystalline powder which dissolves in water with a carmine shade; the alcoholic solution is scarlet with green fluorescence. Hydrochloric acid produces no alteration, with caustic soda a scarlet red precipitate is formed. Silk and tannined cotton are dyed bright red.

Rhodamine 3 G, 3 G extra (Badische) or *Irisamine G, G extra* (Cassella)



is a very similar dye; its colour reactions are much the same as those of Rhodamine 2 G. $\lambda = 535.3$ and 498.8.

The methods described hitherto depend on the condensation of dialkylaminohydroxybenzoylbenzoic acids with another component and subsequant esterification. The operation may however be modified by introducing diethylaminohydroxybenzoylbenzoic acid (56 kilos) into a mixture of sulphuric acid (360 kilos of monohydrate) and methyl alcohol (80 kilos). By warming for some time at 100°, esterification is completed and the other component, e. g. *o*-amino-*p*-cresol (24 kilos), can then be added and condensation effected at 100° (Basler chemische Fabrik, U. S. P. 695 441/1902 of Brack; F. P. 317 891/1902; D. R. P. 132 066/1901).

The sulphonation of asymmetric rhodamines is stated to give valuable dyestuffs; the shades produced are similar to those given by non-sulphonated tetraalkyl compounds but the exhaustion of the dye-bath is better (Meister, Lucius and Brüning, Brit. P. 14879/1900; U.S.P. 675216/1900 of Hoffmann; F.P. 303177/1900; D.R.P. 119757/1900).

Example 1. Add slowly, with stirring, 10 kilos of asymmetric diethylrhodamine hydrochloride to 60 kilos of oleum (20 to 30% SO_3) taking care that the temperature does not exceed 35—40°. Allow to stand for 12 hours, pour into ice water and filter off the sulphonic acid.

Example 2 decribes a similar sulphonation of the rhodamine obtained by condensing diethylaminohydroxybenzoylbenzoic acid with *o*-amino-*p*-cresol.

It will have been noticed that in all the above cases, trialkylated rhodamines are produced by condensing dialkylaminohydroxybenzoylbenzoic acids with monoalkylaminophenols. The reason for this procedure is that monoalkylaminohydroxybenzoylbenzoic acids are not obtainable by direct condensation of phthalic acid with a monoalkylaminophenol; there result, instead, phthalamic acids of the constitution

$$C_6H_4\begin{cases}CO\cdot NR\cdot C_6H_4OH\\COOH\end{cases}$$

The Badische Co. (Brit. P. 23198/1904; U.S.P. 821452/1904 of H. A. Bernthsen; F.P. 347546/1904; D.R.P. 162034/1903) succeeded however in preparing the isomeric acids. Thus if 147 parts of phthalimide, 137 parts of ethyl-*m*-aminophenol and 130 parts of crystallised boric acid are heated to 150—160°, the reaction follows the course indicated by the equation

$$C_6H_4\begin{cases}CO\\CO\end{cases}NH + C_6H_4\begin{cases}OH\\NHC_2H_5\end{cases} = C_6H_4\begin{cases}CO\cdot C_6H_3(OH)(NHC_2H_5)\\CONH_2\end{cases}$$

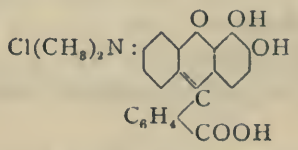
The amide is readily hydrolysed by boiling with dilute caustic soda; the resulting acid melts at 152—153°. The corresponding acid from methyl-*m*-aminophenol melts at 178—179°.

By condensing these acids with *m*-aminophenol and *p*-cresol, dyestuffs are obtained which can be esterified. The products give yellowish shades.

Mordant Dyestuffs of Rhodol Type.

Condensation of substituted aminohydroxybenzoylbenzoic acids may also be carried out with polyhydroxy-derivatives of benzene. Using compounds such as pyrogallol, gallic acid &c., products are obtained containing two hydroxyl groups in the ortho position. These dye mordanted wool and cotton in dark violet or blue shades, very fast to milling and light; their solubility in acid baths is claimed as an advantage over alizarine colours.[1]

Cassella and Co. (Brit. P. 14220/1900; F. P. 302725; D. R. P. 122352/1900) give examples of how such condensations may be effected. Thus in order to obtain the dyestuff having the constitution



28.5 kilos of dimethylaminohydroxybenzoylbenzoic acid are dissolved at 90° in a mixture of 120 kilos of sulphuric acid and 30 kilos of water. The temperature is then raised to 100°, 15 kilos of pyrogallol are added and the mixture kept at 110° for 4 or 5 hours. The melt is then poured into 200 litres of hot water; the dyestuff crystallises on cooling. It is somewhat difficultly soluble in cold water; the solution in dilute acetic acid is red, that in alkalies is bluish violet. Chromed wool is dyed bluish violet.

Very similar dyestuffs are obtained when the pyrogallol is replaced by gallic or gallamic acids or tannin; it is advisable in these cases to carry out the reaction at 125°.

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1 These dyes are stated not to be sufficiently soluble for printing. Durand, Huguenin and Co., D. R. P. 244652/1910.)

Other substituted acids may be employed, e. g. 4,*o*-tolylamino-2-hydroxybenzoylbenzoic acid which is prepared by carefully condensing phthalic acid with *o*-tolyl-*m*-hydroxyphenylamine.

Mordant dyes often contain a hydroxyl and a carboxyl group in the ortho position to one another. In an additional patent (D. R. P. 123077/1900), Cassella and Co. describe products obtained by condensation of phthalic anhydride with one molecule of an alkylated aminophenol and subsequently with one molecule of *β*-resorcylic acid; the second stage is effected in concentrated sulphuric acid solution at temperatures ranging from 55 to 80°.

Durand, Huguenin and Co. (Brit. P. 10523/1911; U. S. PP. 1002825 and 1003257/1911 of de la Harpe and Bodmer; D. R. P. 244652/1910) follow a different course in producing mordant dyes of the rhodol series. If, for example, a sulphonic group be introduced in the ortho position to the hydroxyl of a simple rhodol obtained from resorcin (or pyrogallol), the resulting compound may be fixed on mordants. This property is also shared by rhodols produced from dialkylaminohydroxybenzoylpropionic acids which are prepared from a *m*-aminophenol and succinic anhydride.

In order to obtain such compounds, resorcin mono- or di-sulphonic acid may be used; in the latter case one of the sulphonic groups is eliminated during the condensation which is effected by means of sulphuric acid or a bisulphate. The acid concentration can be varied between fairly wide limits, it is desirable not to have it too dilute otherwise complete desulphonation may result.

The simplest way is to sulphonate the resorcin or pyrogallol and add the aminohydroxybenzoylbenzoic acid to the mixture, so combining the two operations.

Example 1. 14 kilos of dimethyl-*m*-aminohydroxybenzoylbenzoic acid are stirred into a solution of 10 kilos of resorcinmonosulphonic acid in 60 kilos of 70 per cent sulphuric acid and heated to 90° until no further formation of dyestuff is observed. On cooling, the melt is poured into ice water, the

dyestuff filtered off, pressed, dissolved in sodium acetate solution, filtered and reprecipitated by hydrochloric acid. Finally the sulphonic acid is converted into an alkaline salt.

Example 2. 14 kilos of dimethylaminohydroxybenzoylbenzoic acid are condensed at 90° with 14 kilos of resorcin disulphonic acid dissolved in 60 kilos of sulphuric acid (66° Bé.).

Dyes obtained in this way from resorcinsulphonic acids give red shades on chromed wool; if prepared from pyrogallolsulphonic acids, violet to brownish violet shades are obtained. Fastness to chlorine and light are stated to be remarkable.

Similar dyes may also be prepared by the sulphonation of rhodols. (Durand, Huguenin and Co., D. R. P. 246653/1911.) Thus 10 parts of dimethylrhodol (from dimethylaminohydroxybenzoylbenzoic acid and resorcin) are sulphonated by warming with 40 parts of 26 per cent oleum to 90—95°; after pouring into ice water, unsulphonated material is separated by dissolving the sulphonic acid in sodium acetate solution and reprecipitation by hydrochloric acid.

The presence of a nitro group alters the properties of rhodolsulphonic acid dyestuffs in certain respects. The shades produced on fibres are yellower and, on chromed wool, the fastness to light is greater. Further, non-sulphonated rhodols containing a carboxyl group, such as those obtained from resorcylic acid, yield more soluble alkali salts if nitrated.

Durand, Huguenin and Co. (D. R. P. 245231/1911) obtain nitrated rhodols either by condensing an aminohydroxybenzoylbenzoic acid with a nitro derivative of resorcin or by nitration of the rhodols themselves.

Example 1. 43.9 parts of dimethylrhodolsulphonic acid are dissolved in the fourfold weight of concentrated sulphuric acid at ordinary temperature, cooled, stirred and nitrated by addition of 14.3 parts of a mixed acid with 44 per cent HNO_3. The nitration is completed by standing for some days at ordinary temperature or warming for a short time to 70°. The mixture is then poured into ice water and the precipitated

dyestuff collected and converted into an easily soluble alkali salt.

Example 2. 40.3 parts of dimethylrhodolcarboxylic acid (from dimethylaminohydroxybenzoylbenzoic acid and β-resorcylic acid) are dissolved in four times the weight of sulphuric acid and nitrated with mixed acid containing 6.3 parts of HNO_3.

Example 3. Nitration of 49.3 parts of the dyestuff from ethylbenzylaminohydroxybenzoylbenzoic acid dissolved in 4 times its weight of sulphuric acid is effected with a mixed acid containing 12.6 parts of nitric acid; say with 36 parts of mixed acid with 35 per cent HNO_3.

Example 4. 11 parts of resorcin are dissolved in 120 parts of concentrated sulphuric acid and sulphonated; then nitrated with 14.3 parts of mixed acid containing 44 per cent HNO_3. 28.5 parts of dimethylaminohydroxylbenzoylbenzoic acid are then added and the mixture heated to 90° until no further dyestuff formation is observed.

Example 5. 18 parts of mixed acid (35 per cent HNO_3) containing 6.3 parts of nitric acid are added to a solution of sulphonated β-resorcylic acid obtained from 16 parts of β-resorcylic acid and 64 parts of sulphuric acid (monohydrate). After standing some time at ordinary temperature and finally warming for a short time to 70°, 28.5 parts of dimethylaminohydroxybenzoylbenzoic acid are added and the condensation carried out at 90°.

CHAPTER XIX.

ANISOLINES.

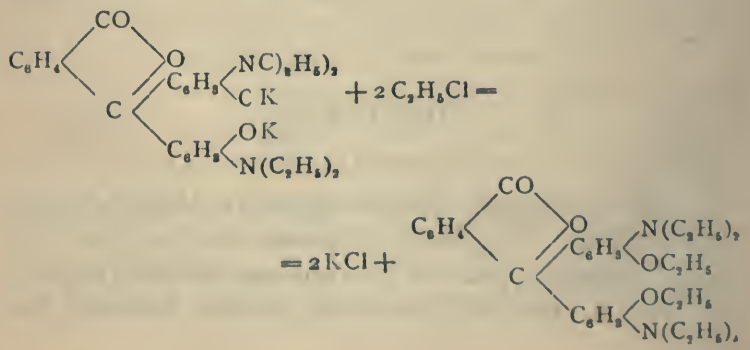
The earliest observation respecting the further alkylation of rhodamines was made by P. Monnet (*Bull. soc. chim.*, 1892, III, 7, 523) who appears to have obtained the first rhodamine as early as 1882 by condensing phthalic anhydride with

m-hydroxydiphenylamine. Impressed by Baeyer's production of hydrated fluorescein ($C_{20}H_{14}O_6$) under the influence of excess of alkali, Monnet acted on rhodamine with alkali and subjected the material obtained in this manner to the action of an alkyl halide. A new product was formed which Monnet supposed owed its formation to the rupture of the pyrone ring and alkylation of the two hydroxyl groups. He described the production of the first "anisoline" as follows.

100 grams of rhodamine hydrochloride (product from diethyl-*m*-aminophenol and phthalic acid) are dissolved in 500 grams of water; to the boiling solution another boiling solution of 50 grams of caustic potash in 200 grams of water is added. The potassium salt in thus precipitated; if filtered and dried at 100° it forms a red powder, but if dried in the cold, crystals containing two molecules of water are obtained.

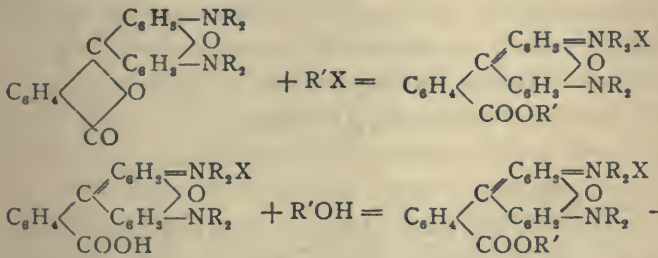
To convert the potassium salt (dried at 100°), into an anisoline, 10 grams are dissolved in 30 grams of strong alcohol, cooled, and 5 grams of ethyl chloride added. The mixture is then heated in a sealed tube for 4 hours at 120° and the product dissolved in 300 grams of water. After expelling alcohol and ethyl chloride by boiling, the solution is treated with 5 grams of hydrochloric acid, filtered and salted out.

Monnet interpreted these results by supposing that the rhodamine gives a dipotassium salt on rupture of the pyrone ring and that the two potassium atoms are then replaced by ethyl groups.



The new dyestuffs obtained in this manner were found to dye fibres, cotton included, without the help of a mordant, the shades produced being of a "rouge violacé magnifique". Patents were applied for, the value of the new dyestuffs being evident (Brit. P. 4677/1892; F. P. 216256; Friedländer, III, 178).

Monnet's interpretation of his results was wrong and Bernthsen (*Chem. Zeit.*, 1892, *16*, 1956) showed that alkylation had really taken place on the carboxyl group. Acting on this knowledge, the Badische Anilin- und Sodafabrik obtained patents for the conversion of rhodamines into anisolines by acting on free rhodamine bases with alkyl halides or by digesting rhodamines with an alcohol and a mineral acid, so effecting esterification.



Both Monnet and the Badische Co. obtained British patents (4677/1892 and 7298/1892 respectively), litigation ensued, and Monnet's specification, as amended, shows the errors made in his earlier interpretation of his results.

The Badische Co. took out a series of patents protecting the conversion of rhodamines into higher alkylated (ester) colouring matters.

D. R. P. 66238/1891 deals with direct addition of alkyl halide to the rhodamine base; it is mentioned that by heating the resulting compound to 140—170°, the alkyl halide is again split off and the original colouring matter regenerated; the reaction is therefore reversible. This behaviour would equally agree with the compounds being of ammonium type, but their formation by other methods shows that they are really esters.

The following example is given.

Free tetraethylrhodamine base (tetraethyldiaminofluoran) is obtained by the action of caustic potash solution at the boiling point on a solution of the colouring matter (hydrochloride). 6 kilos of the base prepared in this manner, 3 to 6 kilos of ethyl chloride and 20 kilos of ethyl alcohol of 92 per cent are heated for 4 to 10 hours at 120° under pressure or until the colour shows no further increase in blue shade. After cooling, the reaction product is diluted with water, excess of ethyl chloride and alcohol distilled off and the hot solution salted out. The hydrochloride separates as a syrup on cooling; for purification it is again dissolved in water, the solution filtered and salted out.

After drying and powdering, the anisoline is thus obtained as a powder with greenish yellow metallic glance; it is easily soluble in water and dyes wool, cotton and silk in beautiful red shades without the help of mordants.

Other alkyl halides may be employed in place of ethyl chloride; it is alo possible to use a rhodamine salt with the equivalent amount of alkali instead of the free base.

D. R. P. 72 576/1892 (Addit. P. to 66 238) refers to the alkylation of succineins. Thus 1 kilo of tetramethylsuccinrhodamine hydrochloride is heated with a solution of 1 kilo of methyl chloride in 4 kilos of methyl alcohol and 250 cc. of caustic soda lye of 32° Bé. in an enamelled autoclave by means of a boiling brine bath for 12 hours. The product is freed from methyl alcohol, dissolved in hot water and salted out by sodium chloride and, if necessary, zinc chloride in addition. This operation is repeated.

For further purification, fractional addition of hydrochloric acid to the aqueous solution may be employed or the substance can be fractionally crystallised from hydrochloric acid, the less soluble succinrhodamine separating first.

D. R. P. 71 490/1892 of the Badische Co. (see Brit. P. 7298/1892) first describes the conversion of rhodamines into anisolines by esterification with an alcohol and a mineral

acid. Examples are given showing that not only monatomic but also polyatomic alcohols may be employed.

Example 1. 1 kilo of the tetraethylphthalrhodamine base (or a salt) is stirred with 2 kilos of ethyl alcohol and $1^1/_2$ kilos of concentrated sulphuric acid added gradually to the mixture which is then heated on the water-bath for 6 hours. After pouring into 20 litres of water, the acid is neutralised with sodium carbonate and the dyestuff salted out in a syrupy state. It is again dissolved and salted out; after drying at 50° it solidifies and can then be powdered.

If it is desired to remove any non-esterified rhodamine, the solution is made alkaline by addition of sodium carbonate and the less basic rhodamine extracted by benzene.

Example 2. 1 kilo of tetramethylsuccinrhodamine (zinc chloride double salt) is added to 5 kilos of methyl alcohol saturated with hydrogen chloride and allowed to stand for one or two days; the greater amount of the hydrogen chloride and alcohol are then removed by heating on the water bath. The residue is dissolved in hot water and salted out by sodium and zinc chlorides.

Example 3. 1 kilo of tetraethylphthalrhodamine is dissolved in 10 kilos of glycerine by warming and saturated at water bath temperature with hydrogen chloride which is led in until no further increase of blue shade is observed. The product is poured into water, neutralised with sodium carbonate and salted out.

D. R. P. 73 457/1892 (Badische Co., additional to 71 490) describes the alkylation of rhodamine salts by heating with alcohols to 150—180°. Two examples are given.

Exampe 1. 1 kilo of tetraethylsuccinrhodamine and 3 kilos of methyl alcohol are heated for 8 hours in an autoclave to 150—160°.

Example 2. Tetraethylphthalrhodamine sulphate is heated for 12 hours with 5 times its weight of ethyl alcohol to 170°.

The Badische Co. found that the comparatively useless dialkylrhodamines of D. R. P. 48 731 might be converted into

useful dyestuffs by esterification; in this way, symmetrical diethyldiaminofluoran gives *Rhodamine 6G*. (Brit. P. 9633/1892; U. S. P. 516 584 of A. Bernthsen; F. P. 225 341; D. R. P. 73 573/1892).

In the example given, 5 kilos of the rhodamine hydrochloride are dissolved in 25 kilos of ethyl alcohol (96 per cent) and saturated with dry hydrogen chloride. Although the formation of the new dyestuff begins in the cold mixture, it is advisable to pass the acid gas through the solution for 4 to 5 hours whilst it is heated on the water-bath under reflux, the heating being continued until a test portion dissolved in hot water no longer gives a precipitate on addition of sodium acetate. At this stage the solution is filtered if necessary and allowed to cool, the dyestuff crystallising on cooling.

The rhodamine (1 part) may also be alkylated by heating with ethyl alcohol (2 parts) and sulphuric acid ($1^1/_2$ parts) on the water-bath or by heating one of its salts for some time, say 10 hours, with alcohol to 150°.

The British Patent (9633/1892) further describes the alkylation of diethylrhodamine base (40 parts) by heating it with methyl or ethyl alcohol (200 parts) and methyl or ethyl chloride (50 parts) for 8 hours in an autoclave placed in a boiling brine-bath. This process forms the subject matter of a separate German Patent (D. R. P. 73 880/1892).

In D. R. PP. 75 528, 75 529/1892, the Badische Co. extend the process of D. R. P. 73 573 to higher homologues, e. g. to the phthaleins obtained from methyl- and ethyl-aminocresols.

Meister, Lucius and Brüning (Brit. P. 16 067/1899; F. P. 291 453; D. R. P. 121 200/1899) describe a variation in the method of obtaining alkyl esters from dialkylrhodamines, the use of alcohol and an acid or of an alkyl halide being replaced by the employment of alkyl esters of *p*-toluenesulphonic acid.

Example 1. 40 parts of diethylrhodamine base and 20 parts of methyl *p*-toluenesulphonate are heated for 2 hours at 100°, the cold reaction product powdered and stirred with cold caustic soda solution. The base is converted into hydro-

chloride and unaltered dimethylrhodamine removed by sodium acetate.

Example 2. A similar process employing ethyl-*p*-toluenesulphonate.

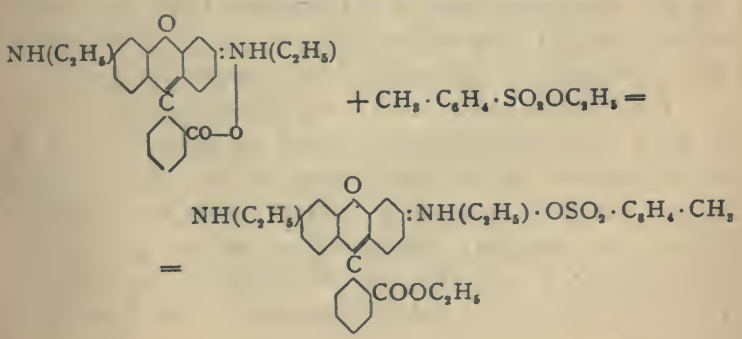
Example 3. 36 parts of dimethylrhodamine base and 20 parts of ethyl-*p*-toluenesulphonate are treated analogously.

In further patents (Brit. P. 16068/1899; F. P. 291690; D. R. P. 121201/1899) the use of methyl sulphate as an alkylating agent is described.

Example 1. An intimate mixture of 40 parts of dimethylrhodamine base, 5 parts of solid sodium carbonate and 20 parts of methyl sulphate is allowed to stand for 48 hours at the ordinary temperature. The mass is powdered, extracted with water containing hydrochloric acid and the hydrochloride completely separated by the addition of sodium chloride. The colour salt is then dissolved in water, unaltered rhodamine base precipitated by means of sodium acetate and the colouring matter separated from the filtered solution by addition of hydrochloric acid and salt.

Example 2. 40 parts of diethylrhodamine base and 20 parts of methyl sulphate are warmed for some hours to 60°; the resulting dye is worked up as in Example 1.

In the foregoing patents, the rhodamine base is evidently taken in a hydrated condition, for subsequently (D. R. P. 133474/1901) Meister, Lucius and Brüning describe a process for alkylating the anhydrous form of the dialkylrhodamine bases; they formulate the reaction in the following way.



386 parts of anhydrous dialkylrhodamine base (prepared at 170°) are introduced into 240 parts of molten ethyl *p*-toluenesulphonate. The mixture is now heated slowly with stirring to 105° and kept for half-an-hour at this temperature. The cooled and powdered product may be used as such or converted into the easily soluble chloride.

Sulphonation of Anisolines.

The anisolines may be sulphonated but the conditions must be such that hydrolysis of the alkyl carboxylate group is avoided. The direct sulphonation of symmetrical diethylphthalrhodamine is described by Meister, Lucius and Brüning (Brit. P. 2999/1896; D. R. P. 87 977). An additional patent of the same firm (D. R. P. 94 398/1896) describes the sulphonation of the corresponding anisoline (ethyl ester of the above rhodamine) by treating its hydrochloride with 6 times its weight of oleum (20 to 30 per cent SO_3). After allowing to stand for 12 hours in the cold, the mixture is poured into ice water, salted out and the sulphonic acid converted into sodium salt.

Aryl esters of rhodamines.

Anisolines containing aryl carboxylate in place of alkyl carboxylate groups can be prepared. The result was achieved in the first instance by using halogenated aromatic compounds containing a reactive halogen atom.

Meister, Lucius and Brüning (D. R. P. 75 071/1892) describe the preparation of red dyestuffs from rhodamines, substituting 2:4-dinitrochlorobenzene for the alkyl halides mentioned in D. R. P. 66 238. Two examples are given.

Example 1. 44 kilos of tetraethylphthalrhodamine (base), 20 kilos of dinitrochlorobenzene and 100 litres of spirit are boiled together for 10 hours under reflux. After distilling off the spirit, the dyestuff is extracted from the residue by boiling out repeatedly with water and salting out.

Example 2. 48 kilos of the rhodamine salt (hydrochloride), 5.3 kilos of soda-ash dissolved in 20 litres of hot

water, 20 kilos of dinitrochlorobenzene and 100 litres of spirit are boiled together for 10 hours under reflux.

In D. R. P. 79673/1893, Meister, Lucius and Brüning describe the preparation of "nitrorosamines" from phthalrhodamines.

Example 1. 21 kilos of diethylrhodamine hydrochloride, 8.6 kilos of *p*-nitrobenzyl chloride, 10 kilos of soda-ash, 265 kilos of water and 50 kilos of alcohol (97 %) are boiled for 6 hours under reflux. The alcohol is distilled off, the solution filtered and salted out.

Example 2. 19.3 kilos of the above rhodamine base, 10.1 kilos of chlorodinitrobenzene and 54 litres of spirit are boiled for 6 hours under reflux.

The constitution of these dyes is not given by the patentees, but when a rhodamine is treated successively with phosphoryl chloride and a phenol there can be little doubt but that an anisoline containing an aryl carboxylate group is produced. In carrying out an esterification of this sort, Meister, Lucius and Brüning (D. R. P. 84656/1893) allow equal weights of rhodamine and phosphoryl chloride to interact and then remove the excess of the latter compound by distillation. Phenol ($^1/_2$ part) is then added and the mixture heated for 1 to 2 hours at 100—120°.

If a rhodamine is converted into an ester of a polyatomic phenol, the resulting dyestuff may have the property of dyeing mordants (Badische Co., Brit. P. 10194/1894; F. P. 237757; D. R. P. 87174/1894). Such a dye can be obtained by heating a mixture of 2 parts of diethylrhodamine and 1 part of pyrogallol to 110—120° and adding 1 part of phosphoryl chloride. Liquefaction takes place at first but the material then becomes viscous; the heating is continued until the mass is solid.

After cooling, the mass is powdered and any unaltered pyrogallol and rhodamine extracted with very dilute acid, the residue is best used in paste form. Cotton mordanted with tin or alum is dyed red (blue shade), chromed wool takes a yellower shade.

NAME INDEX.

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E.

Q.

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