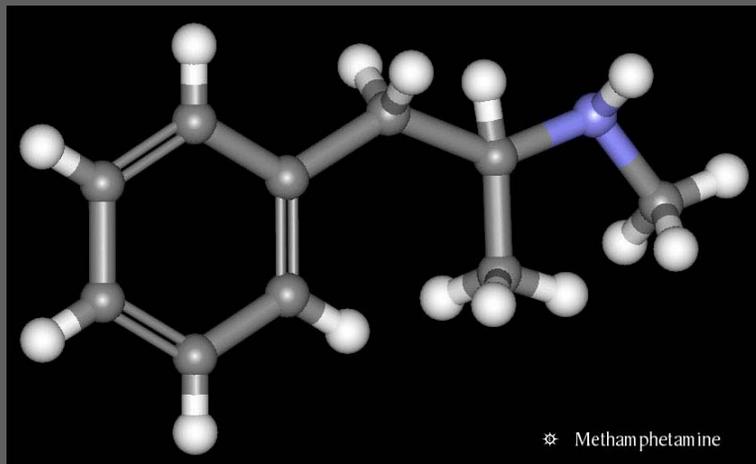


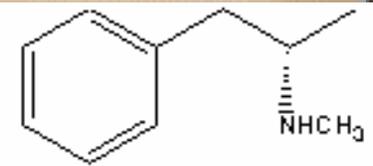
# Meth Chemistry

## "What's Cookin'?"

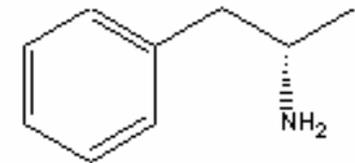


# Methamphetamine History

- Amphetamine synthesized 1887 by German chemist, L. Edeleano
- Methamphetamine was first produced by Dr. Nagayoshi Nagai of Tokyo Imperial University in 1888 by reducing ephedrine with HI & Red Phosphorus
- Methamphetamine synthesized from methylamine and phenyl-2-propanone 1919 by Japanese researcher, A. Ogata
- Early 1900s: Western civilization discovers benefits of ephedrine and pseudoephedrine as bronchodilators and nasal decongestants. Fear that ma huang plants will run out (source for the herb ephedra).
- 1927 (USA): Researcher Gordon Alles discovers that amphetamine works as a substitute for ephedrine. Amphetamine starts being synthesized as substitute for *ma huang*.
- 1930: Amphetamine discovered to increase blood pressure. Marketed in 1932 as "benzedrine" in an over-the-counter inhaler to treat nasal congestion
- 1935: Amphetamine's stimulant effect first recognized and used to treat narcolepsy (compulsion to sleep)



(+)-methamphetamine



(+)-amphetamine

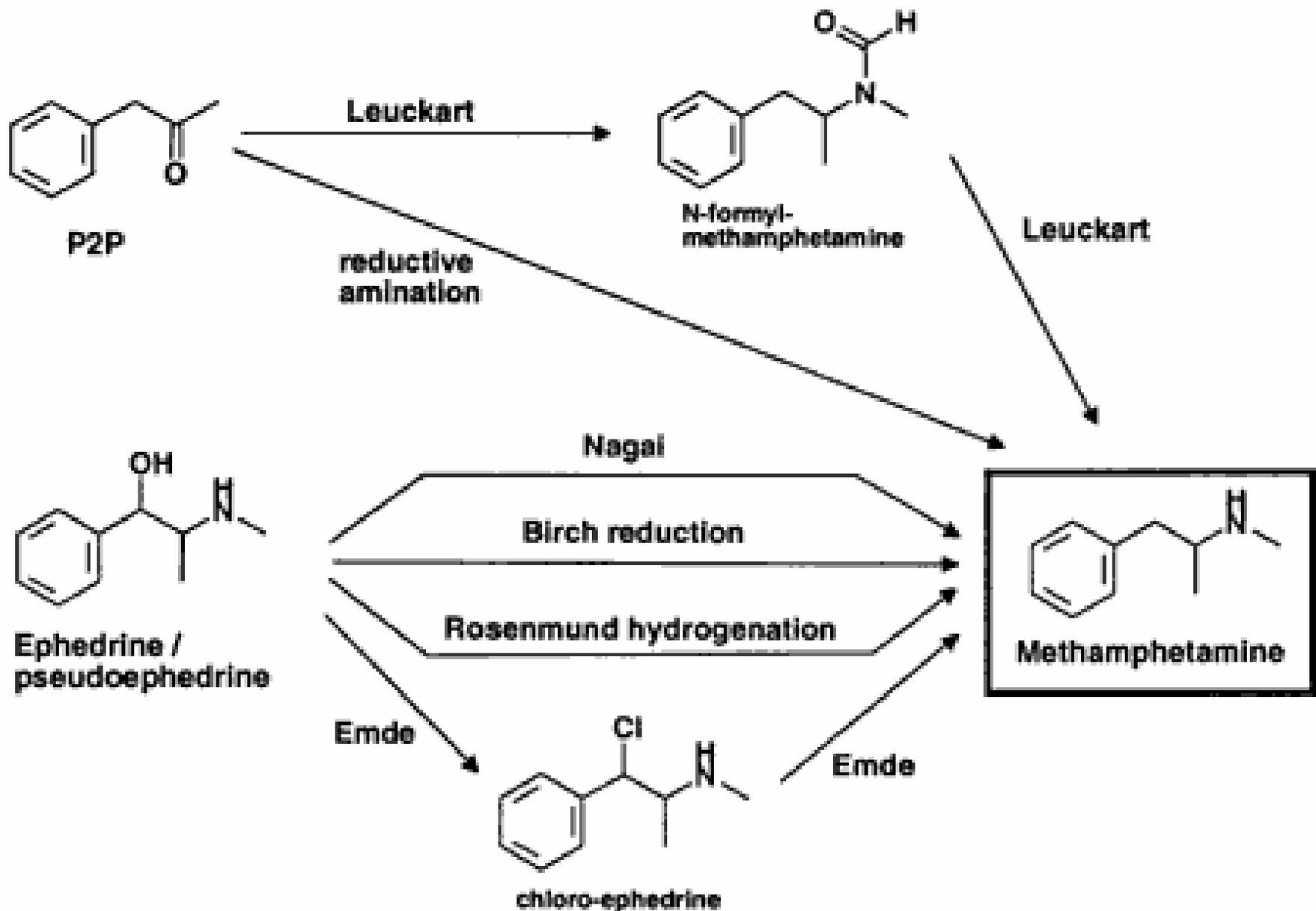
# Meth History Cont.

- 1938: First published report of amphetamine addition and psychosis
- 1940: "Methedrine" commercial trade name for methamphetamine
- Both amphetamine and methamphetamine used as performance enhancer by Japanese, German and Americans in WWII. Led to addiction problems in Japanese after the war.
- 1950-53: amphetamine distributed to US troops in Korean war
- 1951: U.S. Congress passes a law requiring prescriptions for all oral and injectable amphetamines used commonly to treat obesity, narcolepsy and depression.
- 1954: Height of Japanese addiction: 2 million users in 88.5 million population
- 1959: first report of IV injection of contents of benzedrine inhaler. OTC Benzedrine Inhalers within drawn from market. OTC Methedrine inhalers offered.

# Meth History, cont.

- 1962: early reports of illicit domestic production by biker gangs
- 1965: OTC Methedrine inhalers withdrawn from market. 31 million prescriptions written: mostly to women.
- Amphetamine and methamphetamine become Schedule II drugs in 1971
- 1970-80s cocaine drug of choice until it gets too pricey. People turn to speed as a substitute
- Motorcycle gangs synthesized drug using phenyl-2-propanone until late 1980's. P2P became restricted substance, so chemistry shifted to making P2P from phenyl acetic acid or other ways
- 1987, DEA busts first HI/Red Phosphorus lab in the country in California. This method has a higher yield and more potent methamphetamine. Mexican nationals take over the market from biker gangs with this method.
- 1990s: Mexican "Super labs" produce pounds of meth from chemicals obtained overseas and smuggled across border. Illegal aliens make the meth in well-organized discreet segments in the Central Valley of CA.
- Current methods (Iodine/Red P or Lithium/Ammonia) using pseudoephedrine became popular as other chemicals became illegal

# Most common synthesis routes of clandestinely manufactured methamphetamine



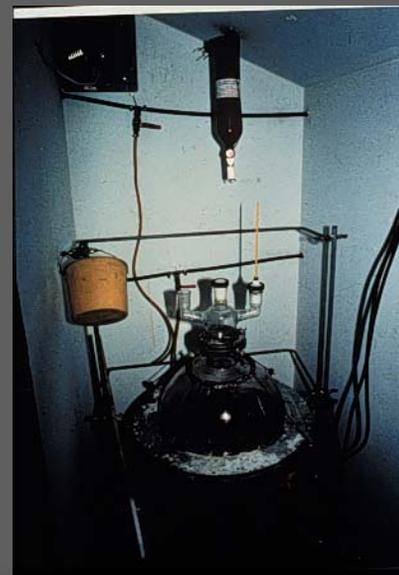
# Current Methods

- ⇒ Reducing ephedrine/pseudoephedrine to methamphetamine
  - Iodine-red phosphorus
  - Ammonia-lithium (Nazi method)

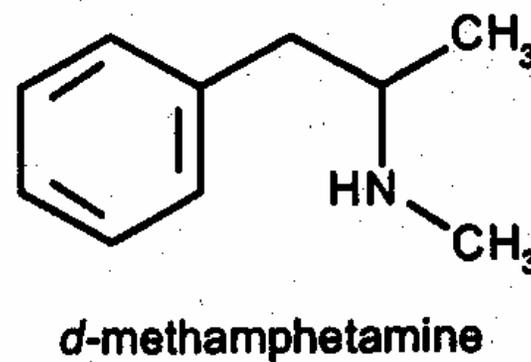
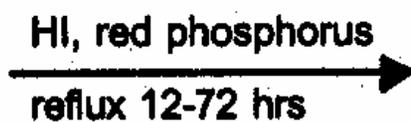
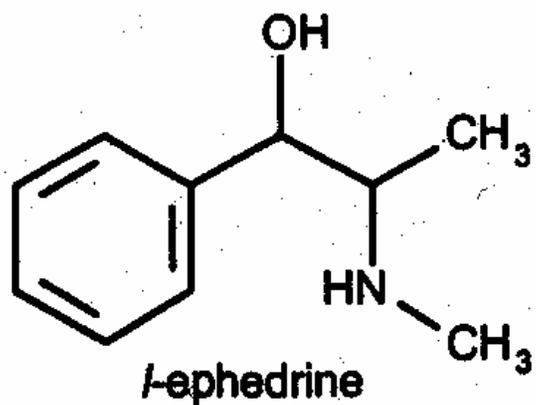


# Old Methods

- ➔ Reductive Amination of Phenyl-2-propanone with Aluminum amalgam
- ➔ Reducing ephedrine/pseudoephedrine to methamphetamine via Catalytic hydrogenation



# I. HI/Red Phosphorus Reduction



# Ephedrine

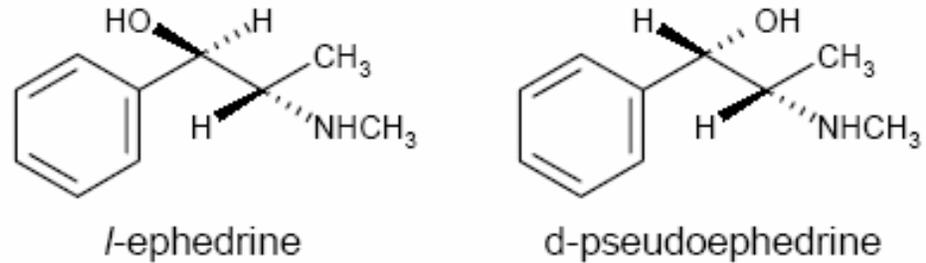
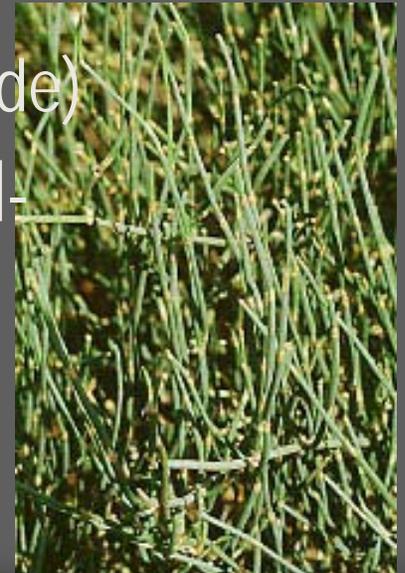
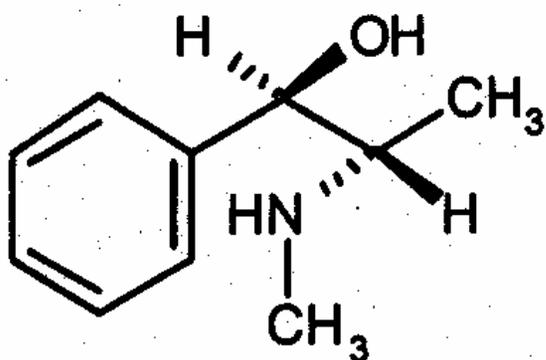


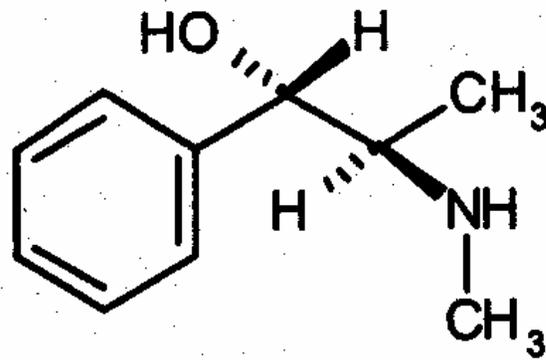
Figure 1. *l*-Ephedrine and *d*-pseudoephedrine chemical structures

- ⇒ Natural source: ephedra sinica (source: dried stem)
- ⇒ Stereochemistry: 2 chiral center= 4 forms
  - d,l ephedrine
  - d,l pseudoephedrine (OH and NH on same side)
- ⇒ *l*-ephedrine, *d*-pseudoephedrine produce *d*-methamphetamine
- ⇒ Ephedrine used as bronchodilator; pseudoephedrine used as decongestant



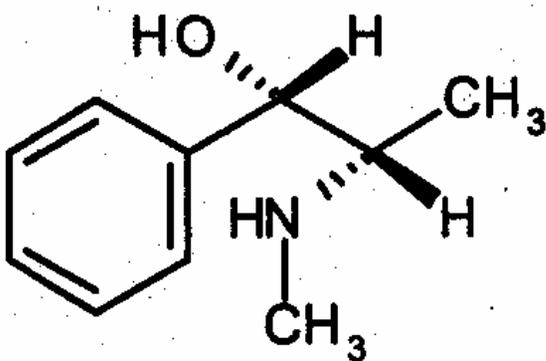


*l*-(1R, 2S)-ephedrine

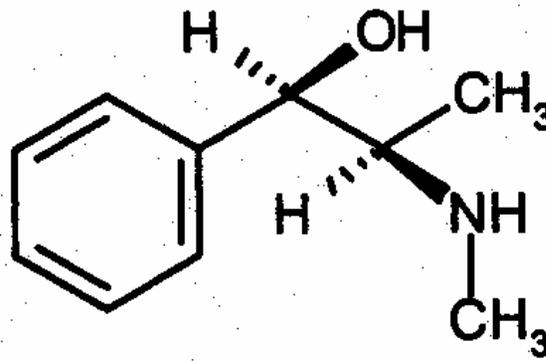


*d*-(1S, 2R)-ephedrine

enantiomers



*d*-(1S, 2S)-pseudoephedrine



*l*-(1R, 2R)-pseudoephedrine

ephedrine and pseudoephedrine are diastereomers

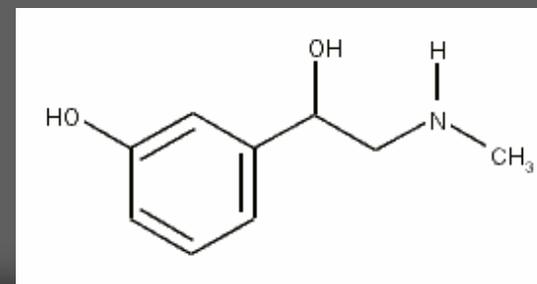
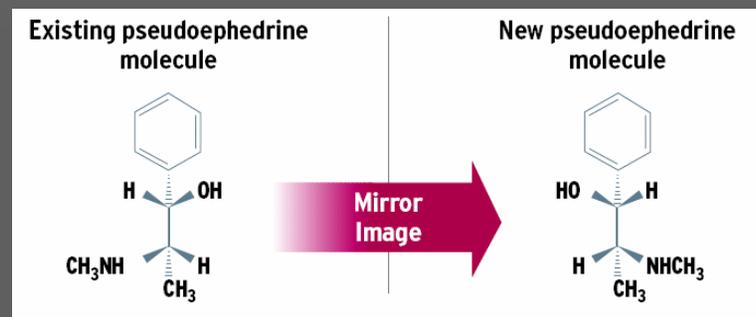
# Efforts to prevent/limit access to Ephedrine and Pseudo

⇒ Place behind counter

- Ask for id
- Limit purchases

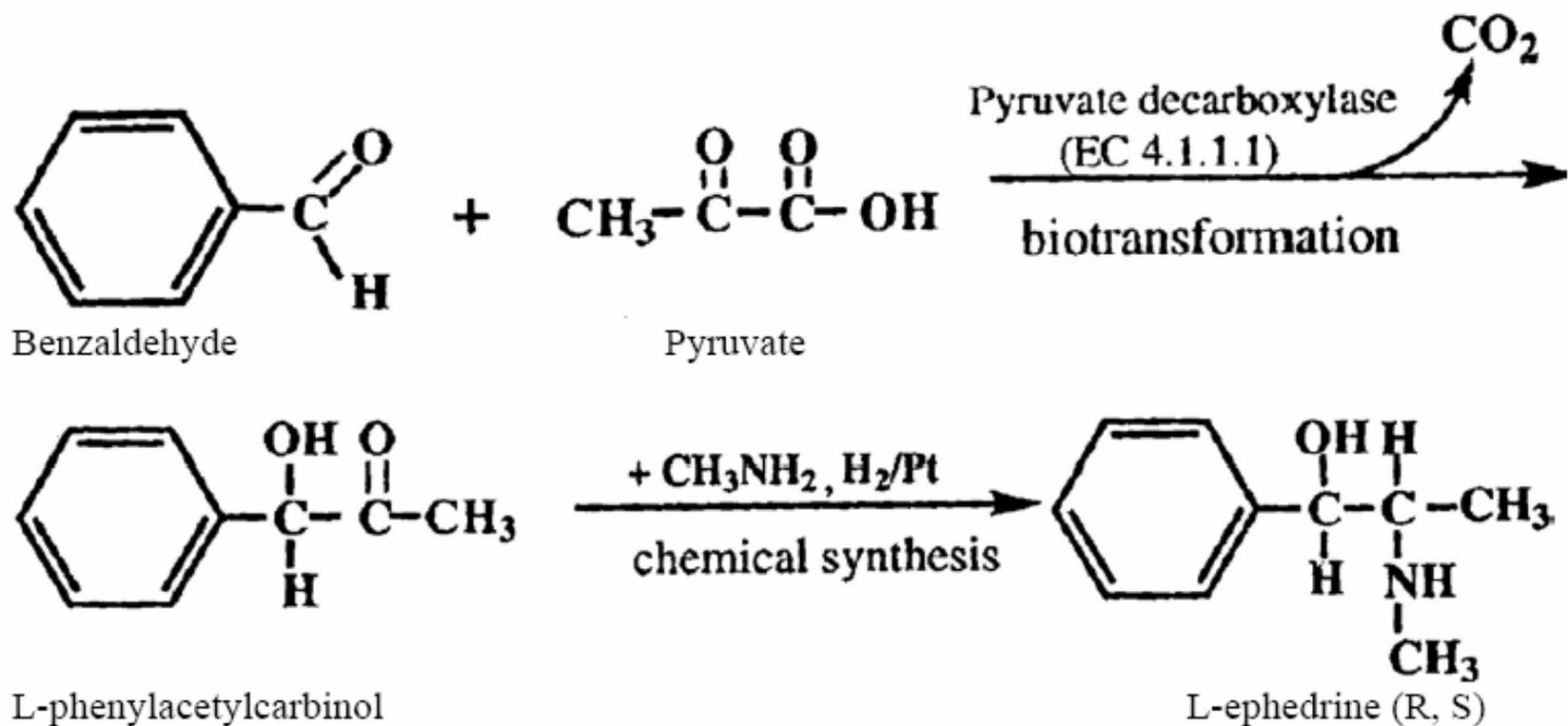
⇒ Modify the Pseudo to make it unavailable to convert

- Use l-pseudo instead of d-pseudo
  - 1/10<sup>th</sup> psychoactive power
- Modify the molecule (ex: phenylephrine) and prevent methamphetamine from being formed. Still works as decongestant



# So make your own...?

- ⇒ On-line recipe for Brewer's yeast, molasses and benzaldehyde
  - Industrial processes use "special" yeast
  - Benzaldehyde toxicity reduces output
  - Product produced is l-phenylacetylcarbinol
    - Still needs to go through reductive amination to become l-ephedrine
      - ◆ Methyl amine, aluminum amalgam
      - ◆ Then you would have to do it again to make meth



**Fig.2.** Mechanism of L-PAC and ephedrine production

from <http://designer-drugs.com/pte/12.162.180.114/dcd/pdf/biotransformation.ephedrine.pdf>

“Biotransformation for L-Ephedrine Production”, P.L. Rogers, H.S. Shin, and B. Wang, Univ. of New South Wales, Sidney, Australia

# Phosphorus

⇒ Red P can only be ordered out-of-country except as a reagent

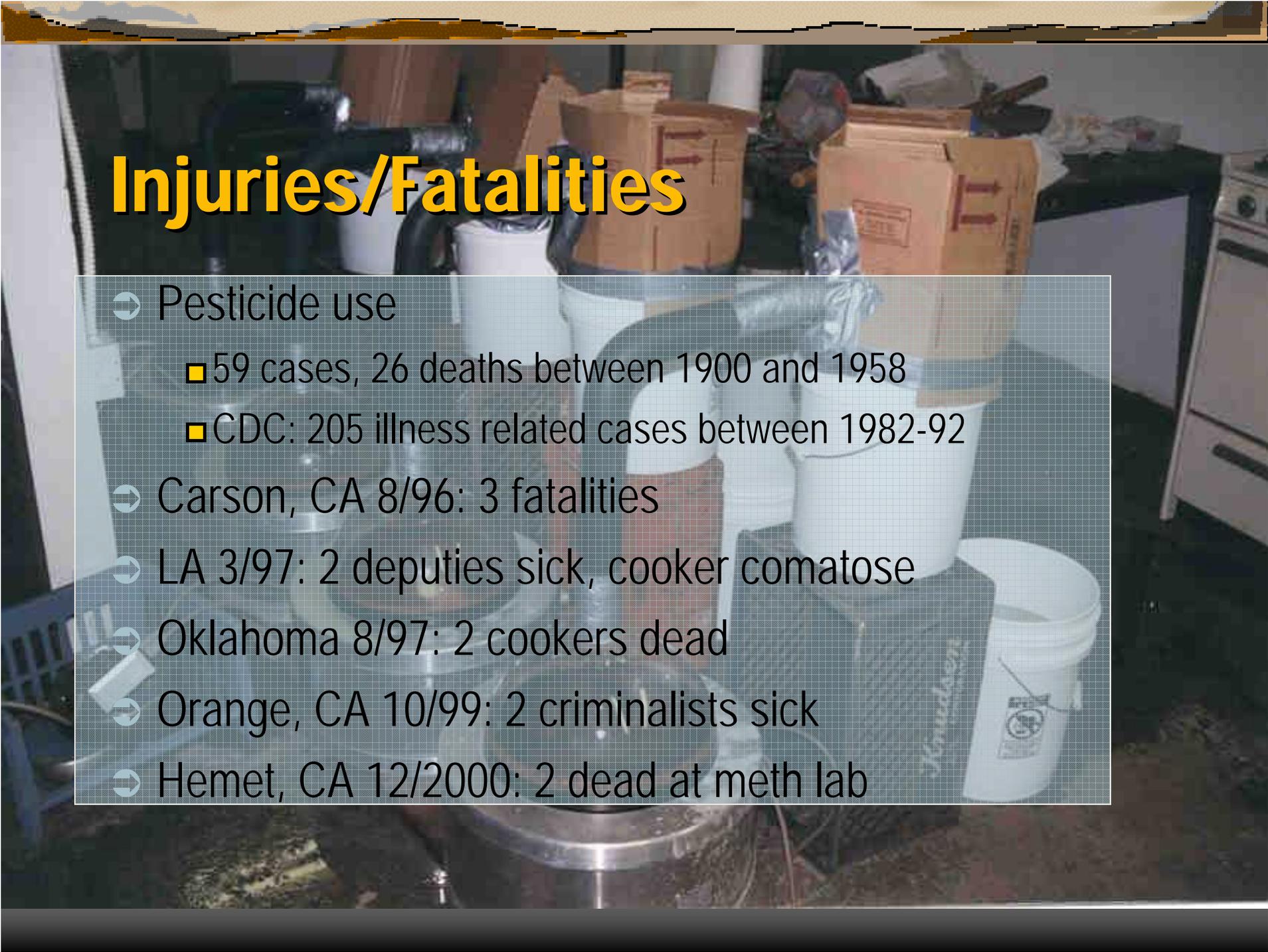
- Get from match box strike plates
  - 40% red P, 30% antimony sulfate
- Use white phosphorus
- Use hypophosphorous or phosphorous acid



⇒ Hazards

- Flammable solid (friction)
- If heated, converts to white phosphorus
  - Air reactive flammable solid
- Off-gasses phosphine, especially when heated





# Injuries/Fatalities

- Pesticide use
  - 59 cases, 26 deaths between 1900 and 1958
  - CDC: 205 illness related cases between 1982-92
- Carson, CA 8/96: 3 fatalities
- LA 3/97: 2 deputies sick, cooker comatose
- Oklahoma 8/97: 2 cookers dead
- Orange, CA 10/99: 2 criminalists sick
- Hemet, CA 12/2000: 2 dead at meth lab

# Phosphine



- ⇒ PEL = 0.3 ppm, IDLH = 50 ppm
- ⇒ LEL = 1.8%, auto-ignition @ 38°C
- ⇒ Examples of levels measured in controlled cook situations
  - Open container of red phosphorus = 1.4 ppm
  - HI/RP cook: 0-13 ppm at sample port
  - Making HI by mixing I<sub>2</sub> and water, then adding RP: 0-42 ppm
  - Hypophosphorous acid cook: 0-85 ppm
- ⇒ Levels measured at clan labs: 23 ppm at opening of 22 liter
- ⇒ Levels measured opening evidence containers
  - 1-28 ppm opening kaypak
  - 5-7.5 ppm opening evidence bucket



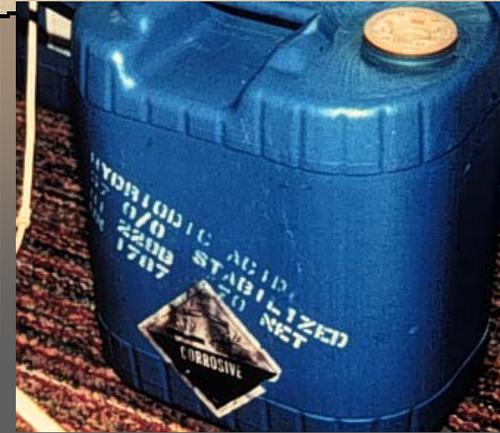
# Iodine

## ➔ Sources

- Hydriodic acid
- Iodine crystals/prills from commercial sources
- Feed supply (antibiotic, supplement)
- Make from iodine tincture

## ➔ Hazards

- Severe respiratory irritant
  - PEL= 0.1 ppm
  - IDLH = 2 ppm
- Corrosive
- Oxidizer



# HI/Red Phosphorus

## Step 1: Tablet Extraction



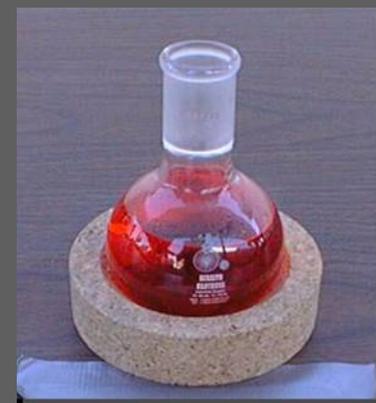
- ⇒ Pseudoephedrine tablets ground up using any type of grinder
- ⇒ Tablets extracted with water or polar solvent (MeOH, denatured alcohol)
- ⇒ Filter off pill binder material
- ⇒ Evaporate off solvent to leave pseudoephedrine solid
  - Fire hazard!!



# HI/Red Phosphorus

## Step 2: Convert to Meth

- ➔ Mix red phosphorus, water, pseudo and iodine
  - Heat generated by reaction alone; splatter if not added slowly or in order
- ➔ Boil for extended period of time
  - Phosphine gas (deadly) and iodine vapor emitted during cook (deadly). Attach hose to top of reaction vessel and run into water, kitty litter.



4 hr cook yields 76-79% conversion

1 hr cook with hypo yields 83%

# HI/Red Phosphorus

## Step 3: Isolate

- ⇒ Filter off red phosphorus
  - Waste flammable solid
- ⇒ Make solution basic ( $> \text{pH } 12$ )
  - Lot of heat generated, volatilizing meth base into the air
- ⇒ Add non-polar solvent to extract meth
  - Coleman fuel, naphtha, lighter fluid, toluene, diethyl ether, freon 11, carbon tetrachloride
    - Except for freons and heavily chlorinated solvents, all are very flammable.
  - Biphasic solution (meth in top layer if solvent lighter than water)



# HI/Red Phosphorus

## Step 4: Salt out

- ⇒ Separate off solvent phase
- ⇒ Bubble HCl through solvent mixture to make methamphetamine-hydrochloride
  - Used to use commercial HCl cylinders
  - Make own by mixing coarse salt and sulfuric acid, or muriatic acid and aluminum strips in a closed container with a hose
    - Levels measured during controlled cooks exceed IDLH
- ⇒ Evaporate off solvent to have meth powder
  - Flammability issue again!!



# Wastes



- ⇒ Red P/iodine mixtures: corrosive, off-gassing irritating or toxic gases
- ⇒ Sodium hydroxide mixture: corrosive, some meth by-products
- ⇒ Waste solvents
  - Alcohols with binder material
  - Non-polar solvents with meth



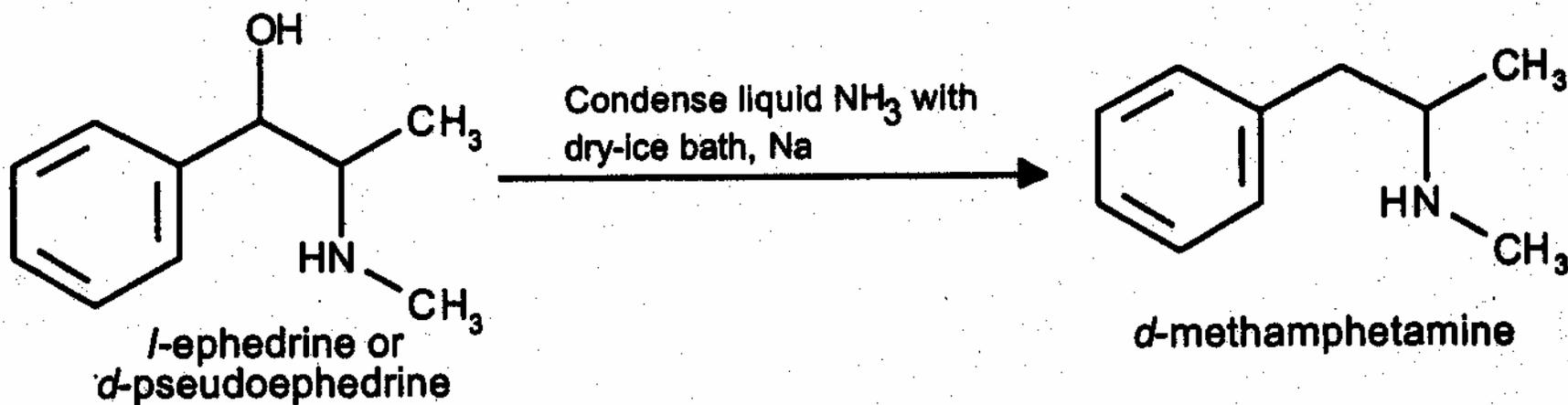
# Contamination

- ⇒ Iodine
- ⇒ Methamphetamine
- ⇒ HCl residual
- ⇒ Acidic/basic spills
- ⇒ Flammable solid residual
- ⇒ Solvent residuals



## II. Birch Reduction

aka: "Nazi Method"



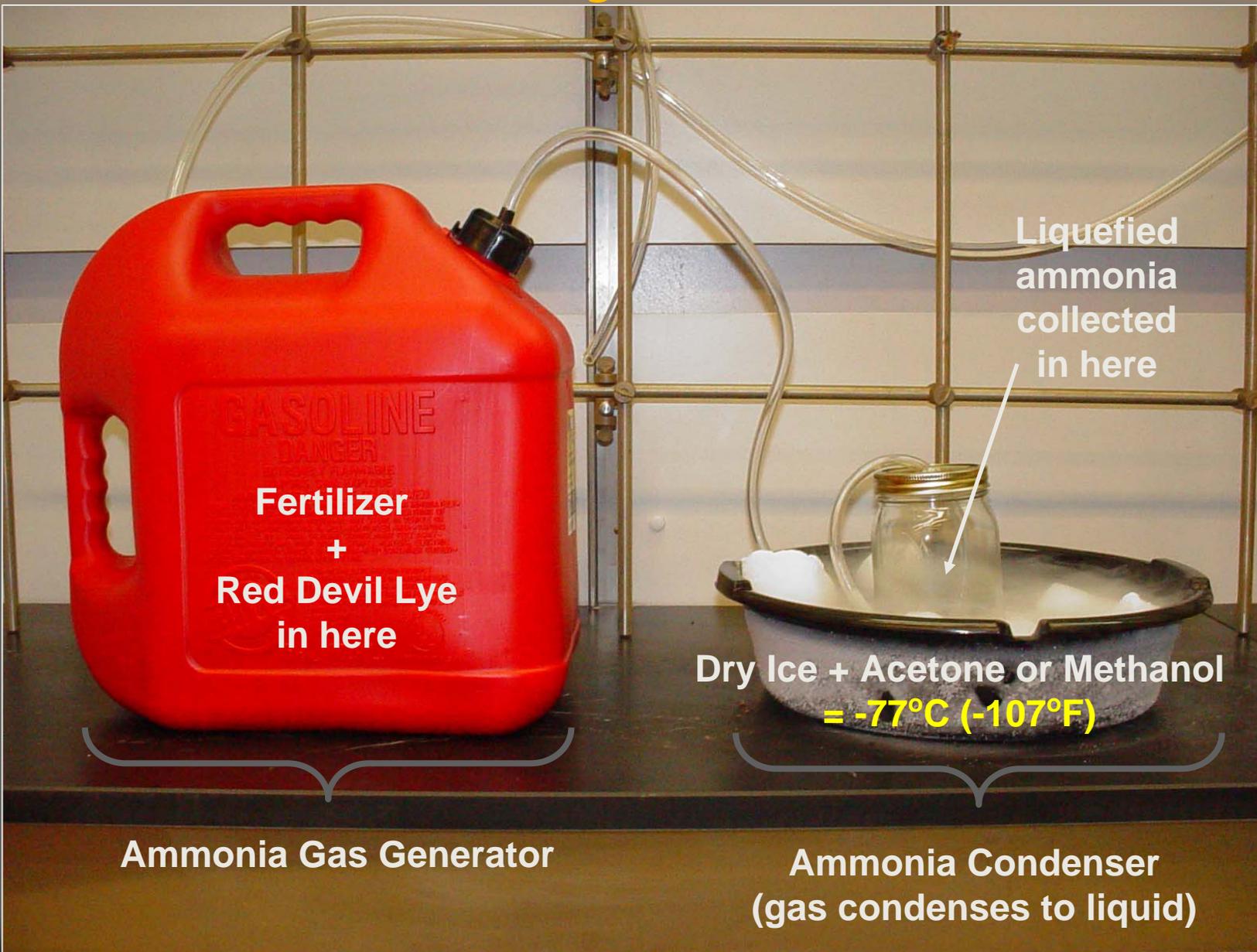
Benkeser used THF and lithium instead of sodium.  
Lithium is commonly substituted for sodium

# Birch Reduction

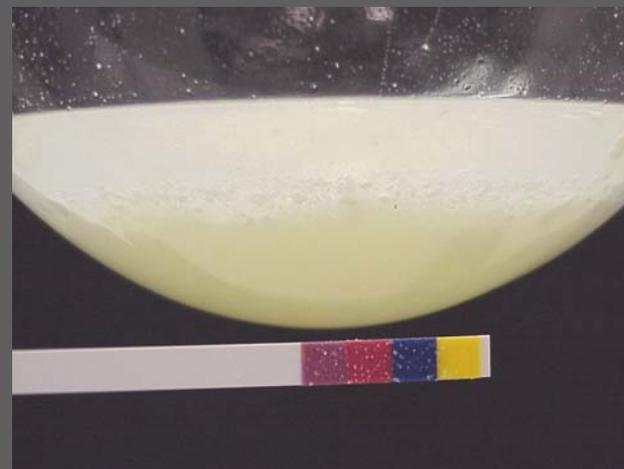
- ⇒ Mix ground-up pseudoephedrine (no extraction needed) and dry lithium (from batteries)
- ⇒ Add anhydrous ammonia until all lithium reacts



# Homemade Anhydrous Ammonia



- ⇒ Allow to warm to room temperature
  - Blue color disappears
- ⇒ Add water to react remaining lithium
  - Meth "oil" collects on surface
- ⇒ Add non-polar solvent to remove methamphetamine base
- ⇒ Salt-out as previously described



# Chemical Hazards

## ⇒ Ammonia

- Corrosive, toxic, cryogenic, combustible

## ⇒ Lithium

- Corrosive, flammable solid, water reactive

## ⇒ Non-polar solvents

- Flammable, toxic

# Wastes from Birch Reduction

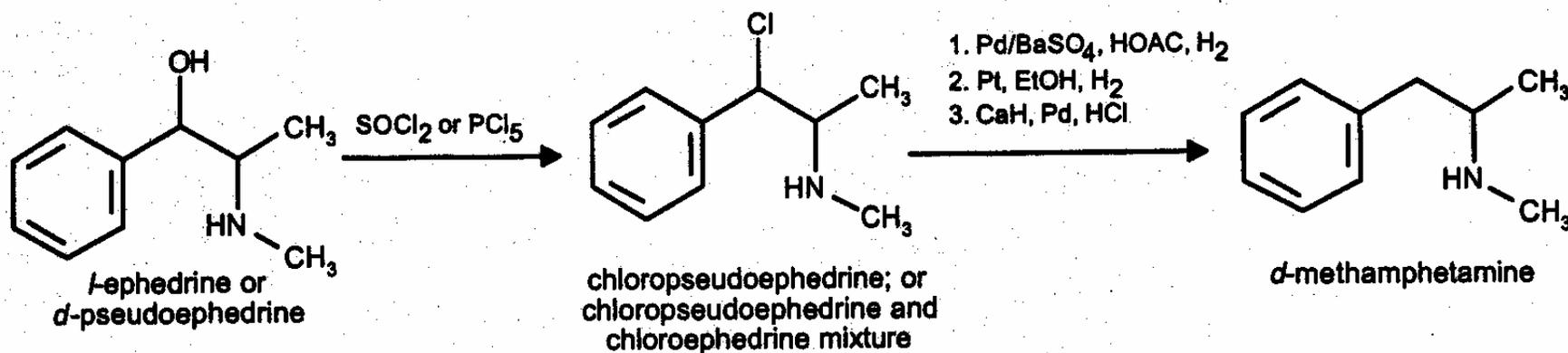
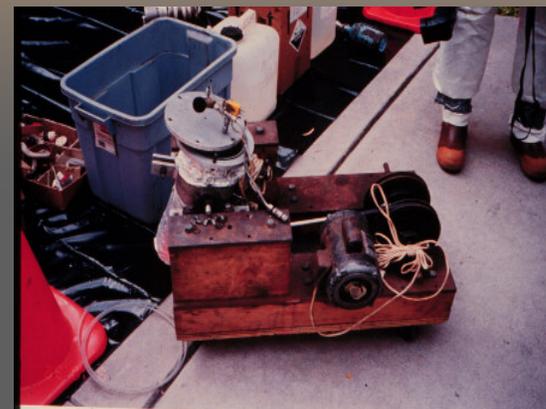
- ⇒ Basic sludge from ammonia/lithium reaction
- ⇒ Solvent wastes from salting-out
- ⇒ Salt/sulfuric acid wastes

# Contamination from Birch Reduction

- ⇒ Methamphetamine residuals
- ⇒ Basic residuals on surfaces from ammonia
- ⇒ Solvents
- ⇒ Hydrogen chloride contamination on surfaces from gassing-out

# III. Catalytic reduction

- ⇒ Pseudo added to chloroform
- ⇒ Add thionyl chloride and stir 1-4 hrs
- ⇒ Add diethyl ether until precipitates
- ⇒ Filter and dry intermediate
- ⇒ Add methanol, palladium to hydrogenator (pressure vessel)
- ⇒ Add hydrogen under pressure until reaction stops absorbing hydrogen



# Catalytic reduction hazards

- ⇒ Thionyl chloride
  - Water reactive, off-gasses sulfur dioxide, HCl
- ⇒ Flammable solvents: methanol, diethyl ether
- ⇒ Flammable gas under pressure: hydrogen
- ⇒ Flammable solid: palladium

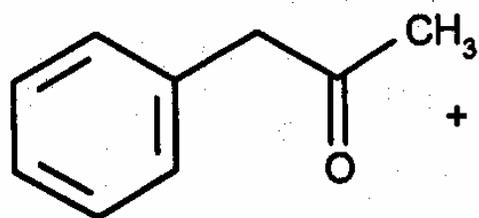
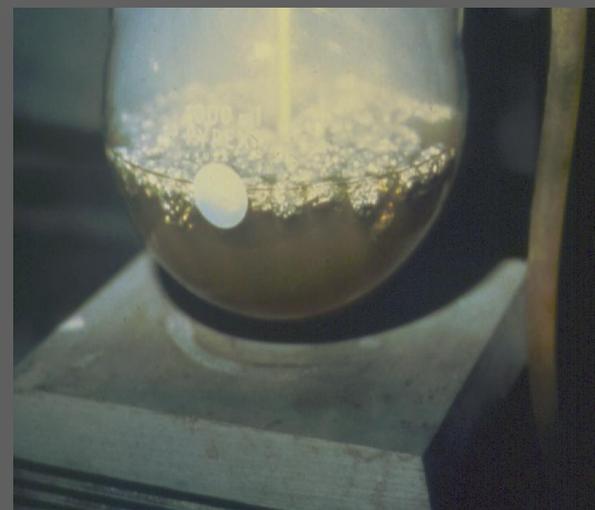


# IV. Chemicals in older methods

## ⇒ Reductive Amination

### ■ Biker dope (aluminum amalgam)

- Phenyl-2-propanone (P2P)
- Methyl amine: smells bad!!
- Mercuric chloride: contamination issue
- Aluminum foil

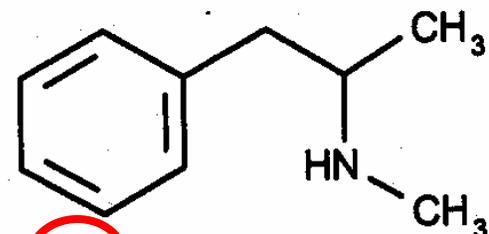


phenylacetone (P2P)



methylamine

1. aluminum amalgam, or  
2. catalytic hydrogenation



d,l-methamphetamine

- ⇒ Combine P2P, methylamine, mercuric chloride, alcohol, and aluminum foil
  - Rinse foil with mercuric chloride first
- ⇒ Exothermic; react 12-18 hrs. Mixture will separate and form oil layer on top. Cool reaction
- ⇒ Separate to keep oil layer. Titrate with aqueous HCl to pH 6
- ⇒ Evaporate to recover crystals. Wash with acetone.
  - Mixture of d,l methamphetamine (less potent)
  - Poorer yields; more subject to ability of chemist and quality of reagents

## ⇒ Catalytic Hydrogenation (shake 'n bake)

- P2P, methylamine then reacted under pressure with hydrogen, palladium/carbon, platinum or Raney nickel



# V. Make your own P2P

- Phenyl acetic acid (PAA) + acetic anhydride + sodium acetate or pyridine → P2P
- PAA + lead (II) acetate + dry distillation → P2P
- Benzaldehyde + nitroethane → 1-phenyl-2-nitropropene.  
Reflux w/ HCl, Fe, FeCl<sub>3</sub> → P2P
- Benzyl cyanide, sodium ethoxide, ethyl acetate produce intermediate. Mix with acetic acid and sulfuric → P2P
- PAA, acetic acid reacted in thorium furnace (>400°C) → P2P

