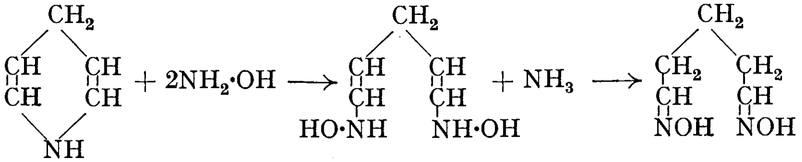
# 61. *The Preparation of* 1 : 5-*Dioximes from Pyridine Bases.*

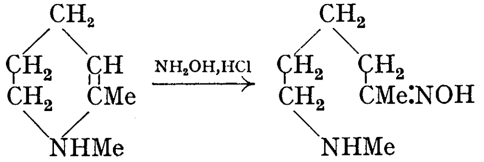
By Brian Duncan Shaw.

In a previous communication (J., 1925, **127**, 215) it was shown that glutardialdoxime may be prepared from pyridine by treatment with hydroxylamine after reduction of the base to the dihydro-stage. This reaction is now shown to be a general one for the pyridine series, dioximes having been obtained from the following bases : pyridine, α-picoline, nicotine, 2-styrylpyridine, 4-styrylpyridine, 2 : 4 : 6-trimethylpyridine, 2-methyl-5-ethylpyridine, 2-benzylpyridine, and 2-β-phenylethylpyridine.

The course of the reaction is believed to be as follows :



(I.)



(II.)

This view is supported by the known conversion of 1-methyl-$\Delta^1$-pipecoleine (I) into the oxime of methyl δ-methylaminobutyl ketone by the action of hydroxylamine hydrochloride (Lipp and Widnmann, *Ber.*, 1905, **38**, 2473).

None of the oximes other than glutardialdoxime have been obtained as solids except at low temperature; they are thick, almost colourless glues which yield glass-like solids which can be powdered when cooled in solid carbon dioxide–acetone, but revert to the semi-liquid state at room temperature and fail to crystallise on standing during several years. As this failure to crystallise might be due to impurity in the original bases, a simple but effective method was developed for the purification of 2 : 4 : 6-trimethylpyridine, the oxime was distilled in a vacuum, converted into the diketone, and the dioxime regenerated from this; the product was still a glue. The bis-2 : 4-dinitrophenylhydrazones, however, are solids which can be crystallised from alcohol, although very sparingly soluble. They are formed slowly from the oximes by treatment with 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid, or more rapidly from the free 1 : 5-dicarbonyl compounds. The latter are readily obtained by treating the dioximes with sodium nitrite in cold acid solution. Those from bases having an unsubstituted 2-position give colours with Schiff's reagent and reduce Fehling's solution.

Glutardialdoxime regenerates pyridine when boiled with concentrated hydrochloric acid, but in poor yield and with formation of much tar. The mechanism of the reaction is obscure, but the first stage is undoubtedly elimination of one molecule of hydroxylamine. In the cold the reaction ceases at this stage; the resulting red fluorescent solution turns yellow with alkali in the cold. The alkaline solution slowly turns red when heated, but reverts to yellow when cooled. These changes can be repeated indefinitely.

The pyridine nucleus in 2-styrylpyridine is more easily reduced than the ethylenic linkage in the side chain when sodium and ethyl alcohol are used. With amyl alcohol and with acid reducing agents the reverse is the case.

## EXPERIMENTAL.

*Drying of Alcohol.*—A small percentage of water in the alcohol seriously reduces the yield owing to hydrolysis of the dihydropyridine (J., 1924, **125**, 3041). Boiling with calcium carbide is the most effective and economical process, but necessitates pulverisation of the drying agent, and the product has a highly unpleasant odour. These disadvantages are avoided by using a simple apparatus which the author has found satisfactory during the past eleven years. Its efficiency is due to the greater volatility, as compared with anhydrous alcohol, of the constant-boiling mixture of alcohol and water, as a result of which the moisture is concentrated on the surface of the drying agent.

A metal boiler is surmounted by a glass tube, 1 m. long and 3 cm. internal diameter, fitted with a double-surface reflux condenser. The tube is packed with calcium carbide broken to the size of Brazil nuts; the finer material obtained in breaking the calcium carbide is put into the boiler. The lime produced is washed down by the refluxing liquid. As the gases are produced in contact with only a small proportion of alcohol, the product has no unpleasant odour. Drying is complete when bubbles can no longer be seen, with a magnifying glass, on the surface of the lumps of calcium carbide. The product is distilled from the lime. By this method 5 l. of 96% alcohol may be completely dried in 12 hours. If the process be prolonged, a yellow solution results from which crystals of calcium ethoxide separate on cooling. Although the azeotropic mixture method of drying alcohol is inconvenient in ordinary laboratory practice, it is valuable for ensuring the dryness of alcohol used in the method described, when the alcohol has been stored in an ordinary bottle for any length of time. For this purpose the alcohol is mixed with 10% by volume of dry benzene and distilled through a fractionating column until 15% of the mixture has been removed. The residue is used for the reduction.

*General Method.*—The pyridine base (1 mol.) is reduced with sodium (1 atom) and boiling, dry ethyl alcohol. The cooled solution is treated with hydroxylamine hydrochloride (0·5 mol.) dissolved in the minimum quantity of warm water, followed as rapidly as possible by concentrated hydrochloric acid (0·5 mol.) diluted with twice its volume of alcohol (96%). The mixture is boiled until the evolution of ammonia slackens (1 hour), filtered, and the alcohol removed. The oxime is extracted from the residue with a 10 or 20% solution of sodium hydroxide, the solution washed with ether and neutralised, the oxime extracted with ether, the solvent removed, and the product dried in a vacuum. The yields, allowing for recovered base, exceed 90% of the theoretical. When the filtered alcoholic solution is allowed to stand overnight, a small quantity of sodium chloride is deposited in well-defined needles, ½—1 cm. in length.

Amyl alcohol may be substituted for ethyl: in this case the quantity of sodium is halved and the hydrochloric acid omitted, since, whereas with ethyl alcohol approximately half the hydrogen escapes, with amyl alcohol it is almost completely absorbed. An alcoholic solution of hydroxylamine hydrochloride is necessary, however, as otherwise the yield is reduced owing to hydrolysis of the dihydropyridine. Details of variations with particular bases are given in the sequel.

*Pyridine.*—The solution from pyridine (80 g.), sodium (23 g.), alcohol (350 c.c.), hydroxylamine hydrochloride (35 g.), and concentrated hydrochloric acid (50 c.c.), after removal of sodium chloride, was distilled until approx. 100 c.c. remained. On standing overnight, glutardialdoxime crystallised; it was pure after washing with water to remove sodium chloride. Yield, 27 g., m. p. 175°. *Glutardialdehydebis*-2 : 4-*dinitrophenylhydrazone* has m. p. 169—172° (Found : N, 24·3. $C_{17}H_{16}O_8N_8$ requires N, 24·35%).

*Action of Hydrochloric Acid on Glutardialdoxime.*—The oxime (26 g.) was warmed with 18% hydrochloric acid (100 c.c.). A vigorous reaction set in and the solution turned dark brown. Basification and distillation yielded pyridine (4 g. ; 20% of the theoretical quantity) and a residue of tar. The purity of the base was established by complete conversion of a sample into the methiodide, m. p. 117° without purification. Modifications failed to improve the yield.

The oxime (13 g.) was added to cold concentrated hydrochloric acid (25 c.c.), and the solution kept in a vacuum over sulphuric acid. Pure hydroxylamine hydrochloride commenced to separate at once, and continued during 7 days ; yield, 6·5 g. (93% of the theoretical for 1 mol.). The viscous filtrate was completely soluble in water and showed the curious colour changes already described ; when heated, it gave pyridine and tar as before.

2-*Picoline.*—The oxime was not readily soluble in ether ; it was therefore washed by decantation and dissolved in alcohol, and the alcohol removed in a vacuum. δ-*Acetobutaldehydebis*-2 : 4-*dinitrophenylhydrazone* has m. p. 129° (Found : N, 23·7. $C_{18}H_{18}O_8N_8$ requires N, 23·6%).

2 : 4 : 6-*Trimethylpyridine.*—The product of condensation of acetone, paraldehyde, and ammonia was fractionated, and the portion, b. p. 169—175°, mixed with the theoretical quantity of nitric acid (*d* 1·42) ; the *nitrate* separated at once on cooling and was recrystallised from alcohol, m. p. 199° (decomp.) (Found : *M* by titration, 185. $C_8H_{11}N,HNO_3$ requires *M*, 184). The base had b. p. 169·2—169·4°/760 mm., $d^{17^\circ}_{17^\circ}$ 0·9166. αγ-*Diacetyl*-β-*methylpropanedioxime* had b. p. 275°/12 mm. (Found : N, 16·1. $C_8H_{16}O_2N_2$ requires N, 16·3%), and the *bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 197—199° (Found : N, 22·5. $C_{20}H_{22}O_8N_8$ requires N, 22·3%).

2-*Styrylpyridine.*—From the base (66 g.), sodium (9 g.), alcohol (135 c.c.), and hydroxylamine hydrochloride (15 g.) there was obtained ω-*aldehydo*-γ-*keto*-α-*phenyl*-$\Delta^{\alpha}$-*hexenedioxime* (9·6 g.) (Found : C, 66·7 ; H, 7·6 ; N, 11·8. $C_{13}H_{16}O_2N_2$ requires C, 66·9 ; H, 7·3 ; N, 12·0%). 57 G. of base were recovered. The *bis*-2 : 4-*dinitrophenylhydrazone* had m. p. 55—59° (Found : N, 19·4. $C_{25}H_{22}O_8N_8$ requires N, 19·9%).

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