132. 1 : 2 : 5 : 6-*Tetrahydropyridine : Isolation from Technical Piperidine by Efficient Fractional Distillation.*

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Technical piperidine has been fractionally distilled and found to contain some water, about 20% of 1 : 2 : 5 : 6-tetrahydropyridine, b. p. 117·4°/771 mm., and only 70% of piperidine, b. p. 106°. The unsaturated base was identified by a series of derivatives. Traces of α-picoline and tetrahydropicolines have also been found in some samples.

For over 40 years, and from different countries, there have been reports that technical piperidine, presumably prepared by reduction of pyridine, usually contains unsaturated impurities. When pure piperidine has been required, it has been obtained by making an *N*-derivative, *e.g.*, the nitroso- (Vorländer and Wallis, *Annalen*, 1906, **345**, 277) or the benzoyl (Ainley and King, *Proc. Roy. Soc.*, 1938, **125**, *B*, 60) derivative, oxidising away the unsaturated material with permanganate in acetone, and hydrolysing off the protecting group.

Reduction of alkyl-substituted pyridines with sodium in alcohol is known to give tetrahydro-derivatives which appear to be Δ^1- or Δ^2-isomers (Tschitschibabin, *J. Russ. Phys. Chem. Soc.*, 1902, **34**, 508 : Koenigs *et al.*, *Ber.*, 1905, **38**, 3042, 3928; 1907, **40**, 3199). Marie and Lejeune (*J. Chim. physique*, 1925, **22**, 59) stated that electrolytic reduction of pyridine gave piperidine in about 65% yield together with about 20% of tetrahydropyridine. The evidence for the latter was that a semi-crystalline mass separated from the distillation residue; this was assumed to be " dipiperidein," the dimer of 2 : 3 : 4 : 5-tetrahydropyridine previously obtained by Lellman and Schwaderer (*Ber.*, 1889, **22**, 1319) by the action of alkali on *N*-chloropiperidine. In a patent (Tech. Res. Works, B. P. 309,300) it is reported that hydrogenation of pyridine over nickel at 180°/300 lb. gives 80% of piperidine and about 10% of tetrahydropyridine, b. p. 93—95°. Again, no evidence was given that the product was a tetrahydropyridine; the low boiling point is surprising and suggests that this fraction may have been the piperidine–water azeotrope, b. p. 92·8° (cf. Horsley, *Ind. Eng. Chem.*, *Anal.*, 1947, **19**, 508). Apart from this work, the compounds responsible for the unsaturation in technical piperidine have not, so far as we are aware, been isolated or characterised.

As we required pure piperidine, we examined several samples of commercially available piperidine. Material sold as 96% piperidine was slightly yellow and a " pure " sample, sold as 98—99% piperidine, was water-white; apart from this yellow impurity, the samples seemed to be identical and the "pure" was probably obtained by total distillation of the 96% material. Samples of both types were found to have b. p. 106° (by direct determination) but by good fractionation gave three main products : (i) 6%, b. p. 92° (piperidine–water azeotrope; cf. Horsley, *loc. cit.*), (ii) 70%, b. p. 106° (pure piperidine), and (iii) 20%, b. p. 117°. (These percentages are roughly corrected for the losses in the intermediate fractions.) A very small and variable amount of higher-boiling bases, mainly b. p. 123°, was also obtained in some cases. The 117° fraction was freed from traces of pipecolines (methylhexahydropyridines) by azeotropic distillation.

The infra-red absorption spectrum of the base of b. p. 117° showed that it was free from pyridine, picolines, and pipecolines. Analysis of the base itself and of its *acetyl* and *benzoyl* derivatives (from which the base could be regenerated) agreed with the empirical formula C_5H_9N, *i.e.*, a tetrahydropyridine. Hydrogenation over Raney nickel resulted in absorption of 1 mole of hydrogen to give piperidine (identified by physical constants and its benzoyl derivative).

The three tetrahydropyridines have previously been reported. The base, b. p. 117°, cannot be the 2 : 3 : 4 : 5-tetrahydro-compound because it forms *N*-acyl derivatives. The 1 : 2 : 3 : 4-tetrahydro-isomer [obtained by caustic fusion of " *N*-oxypiperidine " (Wolffenstein, *Ber.*, 1892, **25**, 2783) or piperidine-2-sulphonic acid (Paal and Hubaleck, *Ber.*, 1901, **34**, 2761)] gives an oily benzoyl derivative and a hydrochloride, m. p. 230° (decomp.); the m. p.s of the corresponding derivatives of the base, b. p. 117°, were 60—62° and 191—193° (decomp.). The 1 : 2 : 5 : 6-tetrahydropyridine has been prepared by Renshaw and Conn (*J. Amer. Chem. Soc.*, 1938, **60**, 745) by treating 4-bromopiperidine with sodium methoxide. They reported m. p.s (or decomposition points) for the hydrochloride, aurichloride, platinichloride, and *N*-methyl methiodide (*i.e.*, 1 : 1-dimethyl-1 : 2 : 5 : 6-tetrahydropyridinium iodide) in close agreement with those of the corresponding derivatives of our base, b. p. 117°, which is therefore, beyond doubt, 1 : 2 : 5 : 6-tetrahydropyridine. Renshaw and Conn did not isolate the free base because of its " ready polymerisation ; " we find, on the other hand, that the free base is stable under ordinary conditions and can be distilled without appreciable polymerisation.

The amount of the higher-boiling fraction, b. p. 123°, varied with different samples of technical piperidine and was in all cases very small. Infra-red absorption spectra indicated the presence of *C*-methyl groups and unsaturation. From chemical evidence, this fraction was clearly a mixture. On conversion into its picrate, a mixture was formed from which α-picoline picrate was isolated in 17% yield. After mild hydrogenation, α-picoline was again isolated as its picrate (in 14% yield) and α-pipecoline as its *benzenesulphonyl* derivative. It is probable, therefore, that the fraction of b. p. 123° is a mixture of α-picoline (about 20%) and one or more of its tetrahydro-derivatives (about 80%), these properties being in agreement with the picoline isolated as picrate and with the hydrogen absorption.

Catalytic hydrogenation of pyridine over Raney nickel and over nickel on kieselguhr was examined but there was no appreciable formation of 1 : 2 : 5 : 6-tetrahydropyridine. Not all samples of commercially available piperidine contained the unsaturated base, and it seems possible that it is only present when the " piperidine " is manufactured by electrolytic reduction of pyridine. It is curious that the mixture in this technical piperidine should have approximately the correct b. p. for pure piperidine (106°) : presumably the water and the tetrahydropyridine balance the b. p. to give this fortuitous result.

EXPERIMENTAL.

Distillation of Technical Piperidine.—The following is a typical batch run. A column (14″ × $\frac{5}{8}$″) packed with $\frac{1}{16}$″ × $\frac{1}{16}$″ stainless-steel gauze rings was used : theoretical plates at total reflux, 46 ; at 10 c.c. per hour take-off rate, 30 (approx.) ; at 20 c.c. per hour take-off, 20 (approx.). Pressure, 756·5 mm. Charge : 200 c.c. of good-quality technical piperidine (sold as 95·5% piperidine).

Fraction no.	Temp.	Vol. (c.c.).	% of total.	Take-off rate (c.c./hr.).	Reflux ratio
1	92°	10	5	10	30 : 1
2	92—106	3·0	1·5	10	30 : 1
3	106	125·0	62·5	20	15 : 1
4	106—117	13·4	6·7	10	30 : 1
5	117	33·5	16·7	20	15 : 1
Residue	—	11·0	—	—	—
Column hold-up	—	5·0	—	—	—

Fraction 1 was the azeotrope of piperidine (65%) and water (cf. Horsley, *loc. cit.*). After this fraction had been dried (KOH), infra-red absorption spectra indicated that it was mainly piperidine and that it was substantially free from pipecolines (azeotrope, b. p. 92—93°). The total piperidine content (fractions 1—3) was about 70%.

Fraction 5 was 1 : 2 : 5 : 6-tetrahydropyridine, the content of which in the technical piperidine must be about 20%.

Purification of 1 : 2 : 5 : 6-*Tetrahydropyridine.*—The base (fraction 5, above; 45 c.c.) and water (10 c.c.) were distilled to give fractions : (i) b. p. 92—93° (3%), (ii) b. p. 95° (26%), and (iii) b. p. 117° (20%). At this point, a further 5 c.c. of water was added and the distillation continued to give the azeotrope of 1 : 2 : 5 : 6-tetrahydropyridine, b. p. 95°, identical with fraction (ii). The azeotrope was dried (KOH) and distilled, to give 1 : 2 : 5 : 6-*tetrahydropyridine*, b. p. 117°, m. p. −48° (Found : C, 71·85; H, 10·65; N, 16·6. C_5H_9N requires C, 72·16; H, 10·8; N, 16·8%).

Fraction (i) was shown to be an azeotrope in which pipecolines were identified by infra-red absorption. Similar results were obtained with other samples of technical piperidine.

B. p. Determinations.—Technical piperidine, 105·6°; pure piperidine, 105·6°; 85% piperidine +15% 1 : 2 : 5 : 6-tetrahydropyridine (water-free), 106·7°.

Derivatives of 1 : 2 : 5 : 6-*Tetrahydropyridine.*—*Acetyl* (by refluxing in acetic anhydride), b. p. 117°/19 mm., n_D^{23} 1·4985, m. p. *ca.* −3° (Found : N, 11·3. $C_7H_{11}ON$ requires N, 11·2%). *Benzoyl* (by Schotten–Baumann method), b. p. 113°/0·15 mm., m. p. 60—62° (from light petroleum) (Found : C, 76·7; H, 6·95; N, 7·65. $C_{12}H_{13}ON$ requires C, 77·0; H, 7·0; N, 7·5%). *Picrate*, m. p. 161—163° (from water) (Found : N, 17·7. $C_5H_9N,C_6H_3O_7N_3$ requires N, 17·9%). Hydrochloride (from ethanol), m. p. 191—193° (Found : Cl′, 29·3. Calc. for C_5H_9N,HCl : Cl′, 29·7%). Aurichloride, m. p. 141—142° (decomp.). Platinichloride, m. p. 187—188° (m. p. depends on rate of heating). Metho-methiodide, m. p. 274—275° (decomp.) (Found : I′, 53·0. Calc. for $C_6H_{11}N,CH_3I$: I′, 53·1%). For the corresponding last four derivatives of 1 : 2 : 5 : 6-tetrahydropyridine, Renshaw and Conn (*loc. cit.*) give m. p. 188—189°, 141° (decomp.), 187—188° (decomp.), and 274—275°, respectively.

Base of B. p. 123°.—This was obtained by fractionating the higher-boiling residues from a number of distillations of technical piperidine. The crude picrate, prepared in water, had m. p. 133—144° and was crystallised from water to give α-picoline picrate (17%), m. p. (alone or mixed with an authentic sample) 164—166° (Found: C, 44·7; H, 3·1; N, 17·3. Calc. for $C_6H_7N,C_6H_3O_7N_3$: C, 44·7; H, 3·1; N, 17·4%); the *benzenesulphonyl* derivative (prepared by the Schotten–Baumann method) had m. p. 67—69° (from methanol) (Found : C, 60·4; H, 6·1; N, 5·7. $C_{12}H_{15}O_2NS$ requires C, 60·8; H, 6·3; N, 5·9%). This is a derivative of a methyltetrahydropyridine but the positions of the methyl group and double bond were not established.

The base of b. p. 123° (2 g.) in dioxan (15 c.c.) was hydrogenated at ordinary temperature and pressure over platinum (0·2 g.) (Hydrogen absorption: 380 c.c. Calc. for $C_6H_{11}N$, 460 c.c. Calc. for 80% $C_6H_{11}N$, 370 c.c.). On conversion of part of the reduced base into its picrate, a mixture was obtained from which α-picoline picrate was isolated in 14% yield. The rest of the reduced base was treated with benzenesulphonyl chloride under Schotten–Baumann conditions to give N-*benzenesulphonyl-α-pipecoline* (30%), m. p. 64—66° (from light petroleum), alone or mixed with an authentic sample (Found: C, 60·25; H, 6·75; N, 5·7. $C_{12}H_{17}O_2NS$ requires C, 60·3; H, 7·1; N, 5·9%).

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[*Received, November* 19*th*. 1949.]