287. *Studies of Coal Tar Bases. Part III.* By-products of the Hydrogenation of Pyridine with Raney Nickel.*

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When pyridine is hydrogenated with a Raney nickel catalyst at about 200° or piperidine is heated with the same catalyst in a hydrogen atmosphere at the same temperature, some hydrogenolysis of the piperidine occurs with the formation of high-boiling bases. High yields of hydrogenolysis products are obtained by increasing the temperature. Prominent constituents of the mixture obtained by heating piperidine with the nickel catalyst at 250° are *N*-*n*-butyl-, *N*-*n*-amyl-, and *N*-*cyclo*pentyl-piperidine and 1 : 5-dipiperidinopentane. The *N*-*n*-amylpiperidine was separated from contaminating bases on an ion-exchange column.

Adkins and his co-workers (*J. Amer. Chem. Soc.*, 1934, **56**, 2425) have shown that pyridine and its substituted derivatives are readily hydrogenated in the liquid phase in presence of Raney nickel. An 83% yield of piperidine was obtained after 7 hours at 200° with an unspecified hydrogen pressure (in the range 150—300 atmospheres) and 25 g. of Raney nickel for 610 g. of product. There is no record of the amount of unchanged pyridine or of examination of the distillation residue. The present investigation was initiated after an observation that, even under optimum conditions for pyridine hydrogenation with Raney nickel, a small amount of high-boiling material accompanies the piperidine in the product. By modifying the conditions of the hydrogenation, notably by use of temperatures above 200°, the yield of piperidine drops while the amount of high-boiling material increases. Thus, when pyridine was hydrogenated for 12 hours with 5% of its weight of catalyst at 200°/200 atmospheres 9% of the liquid product obtained distilled above 125°, *i.e.*, well above the boiling point of piperidine or pyridine. At 250°, 300°, and 330°, but under otherwise comparable conditions, the yields of high-boiling product rose to 29, 33, and 45%, respectively. Liberation of ammonia was particularly noticeable at the higher temperatures. In the absence of hydrogen, only 8% of product boiling above 125° was obtained after heating pyridine at 300° for 12 hours with the same amount of Raney nickel. In this case, but not in those noted above, some di-2-pyridyl was identified in the product (cf. Wibaut, *Rec. Trav. chim.*, 1931, **50**, 287; 1935, **54**, 275). No di-2-piperidyl was found.

Sabatier and Maihle (*Compt. rend.*, 1907, **144**, 784) investigated the vapour-phase hydrogenation of pyridine over nickel at temperatures ranging from 120° to 220°. No piperidine could be found in the product formed at 160—180° but a primary amine, believed to be *n*-amylamine (phenylurethane, m. p. 150°), was present in small amount. At 220° some *n*-pentane and ammonia were formed, a similar rupture of the nucleus having been observed earlier by Hofmann (*Ber.*, 1883, **16**, 590) on heating pyridine to 300° with hydriodic acid. Vapour-phase hydrogenation of pyridine to piperidine is now an established industrial process and recently (B.P. Appl. 7488/1948) Milner claimed that small amounts of high-boiling by-products are formed when nickel is used as catalyst. Dehydrogenation to pyridine was observed by Sabatier and Maihle (*loc. cit.*) when piperidine vapour alone was passed over nickel at 250°. Padoa and Carughi (*Atti R. Accad. Lincei*, 1906, **15**, 113) found that quinoline is transformed into methylindole by the action of finely divided nickel in the presence of hydrogen. Later Padoa (*ibid.*, 1907, **16**, 819), in rather inconclusive attempts to convert pyridine analogously into a pyrrolidine derivative, obtained indications of the formation of pyrrole derivatives. From piperidine and finely divided nickel under various conditions he obtained a mixture including pyridine, products of a pyrrole-like character, and two complex bases $C_{10}H_{21}N$ and $C_{14}H_{28}N_2$. In addition, he claimed that some ammonia was formed together with a mixture of combustible gases of a low carbon content, " probably hydrogen and methane."

In a more recent paper Saadikow and Michailow (*Ber.*, 1928, **61**, 421) described by-products of " an alkaloid-like nature " formed in appreciable amounts during the pressure hydrogenation of pyridine with osmium and osmium–cerium catalysts. Two main fractions boiling at 195—200° and 295—300°, giving crystalline derivatives, were probably $C_9H_{19}N$ and $C_{15}H_{30}N_2$ (approximating in composition to the bases described by Padoa), but the authors merely speculated about their identity.

These observations seem to indicate that during the catalytic hydrogenation of pyridine the piperidine which is first formed suffers hydrogenolysis in amount depending upon the conditions,

* Cf. Part I, *J. Soc. Chem. Ind.*, 1946, **65**, 169; Part II, *ibid.*, in the press.

and that the hydrogenolysis products react further to yield high-boiling by-products. Cleavage of the carbon–nitrogen bonds in quinoline and *iso*quinoline during high-temperature hydrogenation has also been reported (Rapoport, *J. Appl. Chem., U.S.S.R.*, 1936, **9**, 1456; Eru *et al.*, *J. Gen. Chem. Russia*, 1938, **8**, 1563; Yamaguchi, *Bull. Chem. Soc. Japan*, 1934, **9**, 303).

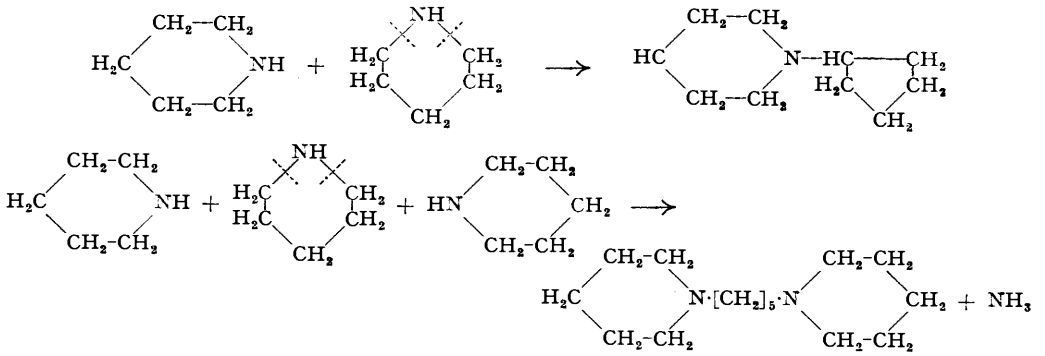
The present paper describes a preliminary investigation of the hydrogenolysis of piperidine with Raney nickel as catalyst. It has been found that in the presence of 10% of this catalyst some hydrogenolysis takes place at temperatures as low as 180°. Increasing the temperature and the time of contact leads to higher yields of hydrogenolysis products. When piperidine was heated at 230—250° for 12 hours with 10% of its weight of Raney nickel, only 9·3% survived; the total yield of liquid product, including unchanged piperidine, was 94%; ammonia, together with smaller amounts of the lower aliphatic amines and some gaseous paraffinic hydrocarbons, was also formed. Distillation the liquid product gave fractions covering a very wide boiling range, 80—300° at atmospheric pressure. Detailed examination of the various fractions is now in progress but already some of the major constituents have been identified. In the main the fractions consist of tertiary bases, but some secondary and primary bases and pyrrole derivatives are also present. The four major constituents are *N*-*n*-butyl-, *N*-*n*-amyl-, and *N*-*cyclo*pentyl-piperidine and 1 : 5-dipiperidinopentane. These have been isolated and characterised as picrates, hydrochlorides, and methiodides; for comparison the corresponding derivatives of the synthetic materials have been prepared. *N*-*n*-Butyl- and *N*-*n*-amyl-piperidine were synthesised from *n*-butyl and *n*-amyl bromide respectively. *N*-*cyclo*Pentylpiperidine was prepared from *cyclo*pentyl chloride and piperidine, and also by heating piperidine with *cyclo*pentanone in the presence of Raney nickel. Direct condensation of piperidine with pentamethylene dibromide or dichloride affords but little 1 : 5-dipiperidinopentane, the bulk of the product being the corresponding bispiperidinium halide (von Braun, *Ber.*, 1906, **39**, 4347; 1916, **49**, 972); however, as reported by von Braun, Kühn, and Goll (*Ber.*, 1926, **59**, 2330), treatment of this quaternary compound with excess of piperidine at a high temperature yields the ditertiary base. Alternatively, 1 : 5-dipiperidinopentane as the dihydrobromide may be obtained by hydrogenation of *NN'*-pentamethylenepyridinium dibromide in acetic acid with Adams's catalyst. Attempts to hydrogenate glutaroylpiperidine by the method of Adkins (*J. Amer. Chem. Soc.*, 1934, **56**, 2419; 1936, **58**, 2487), using copper chromite in dioxan, were not successful, the catalyst itself being reduced under the somewhat drastic conditions (250°/250 atmospheres) and the dioxan used as solvent showing signs of instability.

Some difficulty was experienced in separating and characterising the *N*-*n*-amylpiperidine owing to the co-existence of other bases in the same fraction. However, a clear-cut separation was achieved by selective elution from an ion-exchange column.

In the light of these observations and the measure of agreement between the melting points of some of the derivatives it seems likely that the $C_{15}H_{30}N_2$ base reported by Saadikow and Michailow (*loc. cit.*) was 1 : 5-dipiperidinopentane but in view of their somewhat obscure claims about the behaviour of certain derivatives it is doubtful whether the material they isolated was pure. Similarly, their $C_9H_{19}N$ base was probably *N*-*n*-butylpiperidine contaminated with some *N*-*n*-amyl- and possibly some *N*-*cyclo*pentyl-piperidine.

The formation of these tertiary bases from piperidine may be interpreted in terms of hydrogenolysis of piperidine with subsequent reaction of the primary products with unchanged piperidine. In the case of *N*-*n*-amylpiperidine, the carbon–nitrogen bond is cleaved with formation of *n*-amylamine, which with a mole of piperidine then gives ammonia and the *N*-*n*-amyl derivative (cf. Adkins and Winans, *J. Amer. Chem. Soc.*, 1932, **54**, 306). The formation of *N*-*n*-butylpiperidine is not so easy to explain but here again it seems likely that this has been formed by alkylation of piperidine with *n*-butylamine, another primary product of the reaction. In fact, *n*-butylamine has been identified in one experiment as a by-product of pyridine hydrogenation with Raney nickel, one carbon atom being eliminated. The missing carbon atom is accounted for by the presence of 2- and perhaps 3- and 4-methylpiperidine in the mixture. It is also interesting that *N*-methylpiperidine appears to be absent, which rules out cleavage resulting in methylamine. In one of the experiments starting with pyridine and hydrogen some α-picoline was detected; if the rupture of the piperidine nucleus occurs with formation of a methylene group, this could conceivably react with some of the unhydrogenated pyridine to give α-picoline. Likewise, when only piperidine is present, it reacts to give α-pipecoline. Both the pyridine and piperidine were distilled before the reactions and it is unlikely that either contained more than traces of their methyl homologues. Rupture of both carbon–nitrogen bonds in piperidine accounts for the formation of *N*-*cyclo*pentylpiperidine and

1 : 5-dipiperidinopentane; in both reactions ammonia is liberated by subsequent interaction with one and two moles respectively of uncleaved piperidine, thus:



It is evident from the complexity of the reaction product, which contains, in addition to the compounds mentioned, small amounts of secondary and primary bases, pyrrole derivatives, and gaseous hydrocarbons, that other modes of cleavage of the piperidine nucleus are also operative. The more detailed examination of the final products which is now in progress will, it is hoped, help to throw light on these other breakdown reactions.

Experimental.

(Microanalyses are by Drs. Weiler and Strauss and Miss M. Corner. M. p.s are uncorrected.)

Hydrogenation of Pyridine with Raney Nickel.—When redistilled pyridine, b. p. 115—115·2° (400 g.), was hydrogenated with Raney nickel * (20 g.) (Adkins and Covert, *J. Amer. Chem. Soc.*, 1932, **54**, 4116), at 200°/200 atmospheres for 12 hours in a 1-l. stainless-steel autoclave with stirring, the yield of piperidine obtained by distillation of the product was 83% (354 g.). Further distillation afforded unchanged pyridine (30 g.) and a residue (38 g., 9·0%), b. p. >125°.

When pyridine (400 g.) was heated at 300° in an autoclave with 5% of its weight of Raney nickel but without a hydrogen atmosphere 92% of the pyridine was recovered unchanged. High-boiling material, b. p. 160—180°/40 mm. (10 g.), yielded some di-2-pyridyl, m. p. and mixed m. p. 272°. Pyridine, therefore, apears to be remarkably stable under these conditions.

The liquid products from the four pyridine hydrogenation experiments were combined and were carefully fractionated in a 4-ft. Stedman column (1″ internal diameter). At 150° the pressure was reduced to 20 mm. and distillation was continued again to 150° at which stage decomposition set in. Despite the use of vacuum there remained a fair amount of undistilled material. Although there were some obvious peak fractions among the distillates it did not seem worth while investigating them in detail. It is likely that the reactions taking place at 200° and at 330° are quite different. For this reason, and because of the failure to distil a significant portion of the mixed products little reliance could be placed on the interpretation of the results. However, in some of the fractions in the lower-boiling range of *n*-butylamine [picrate, m. p. 148° (Found: C, 39·5; H, 4·4; N, 18·4. Calc. for $C_{10}H_{14}O_7N_4$: C, 39·7; H, 4·6; N, 18·5%)] and α-picoline [picrate, m. p. 169° [Found: C, 44·5; H, 3·1; N, 17·3. Calc. for $C_{12}H_{10}O_7N_4$: C, 44·7; H, 3·1; N, 17·4%)] were identified. The fraction, b. p. 130—132°, gave a strong colour with Ehrlich's reagent and presumably contained pyrrole. A fraction, b. p. 142—143°, was suspected of containing β- and γ-picoline; the picrate obtained from it, although clearly not homogeneous, gave the correct analysis for methylpyridine picrate.

Treatment of Piperidine with Raney Nickel and Hydrogen at 250°.—Piperidine (1 kg., a close-cut fraction from distillation of commercial piperidine), with freshly prepared Raney nickel (100 g.) which had been washed with piperidine, was stirred in a 2-l. stainless-steel autoclave. Hydrogen was introduced to a pressure of 100 atms. before heating was commenced and the temperature was brought up to 250° and kept thereat for 12 hours. After cooling to room temperature the residual pressure in the autoclave was released, the issuing gases passing through scrubbers containing 1 : 1 hydrochloric acid solution to absorb ammonia or lower amines. The liquid contents of the autoclave were filtered, and the catalyst was washed with fresh piperidine (75 g.). The product was then heated under reflux to expel dissolved gases. An absorption train containing 1 : 1 hydrochloric acid solution removed ammonia or volatile amines; a sample of the scrubbed gas had the composition: CO_2, 0·7; C_nH_m, 1·7; O_2, 10·8; CO, 0·2; H_2, 1·7; C_nH_{2n+2}, 38·0; N_2, 46·9. The value of n in C_nH_{2n+2} was 4·16. The total bases removed in the two scrubbing operations were determined, as ammonia, by making the acid solution up to a known volume, distilling the bases from an aliquot portion into N-hydrochloric acid, and back-titrating. Total bases gave a value of 67·2 g. as ammonia, and of this total 63 g. were ammonia itself (determined by the method of Wagner, Brown, and Peters, *J. Amer. Chem. Soc.*, 1947, **69**, 2612), the remainder presumably being lower amines.

The total yield of liquid product, including 75 g. of piperidine added to wash the catalyst, was 952 g.

* It is customary to store Raney nickel under alcohol. However, if ethyl alcohol is introduced with the catalyst for pyridine hydrogenation it reacts with the piperidine formed to give *N*-ethylpiperidine.

of which 12 g. was lost during the refluxing process. Total bases, as ammonia, made up only 1·7 g. of this loss, with ammonia itself contributing 0·8 g. It is thus clear from the gas analysis that dissolved hydrocarbon gases account for the major proportion. It is also likely that some of these neutral hydrocarbons were lost with the hydrogen on releasing the pressure in the autoclave. A preliminary distillation of the final liquid product yielded 365 g. of material boiling up to 147°. This fraction was fractionally distilled at atmospheric pressure in a 4′ × 1″ Stedman column (see Table I). The portion boiling above 147° (574 g.) was distilled at 5 mm. pressure in a Claisen flask with a 12″ indented side-arm, (see Table II); at 208° there remained only 28·8 g. of residue, which was beginning to decompose.

TABLE I.

Fractional distillation of low-boiling portion (365 *g.*).

Fraction.	Boiling range.	Yield, g.	Fraction.	Boiling range.	Yield, g.	Fraction.	Boiling range.	Yield, g.
1	<80°	11·4	13	102—104°	0·7	25	126—128°	4·8
2	80—82	0·3	14	104—106	3·0	26	128—130	2·9
3	82—84	3·3	15	106—108	93·0	27	130—132	3·0
4	84—86	3·3	16	108—110	5·0	28	132—134	1·7
5	86—88	3·8	17	110—112	2·6	29	134—136	0·25
6	88—90	8·2	18	112—114	3·2	30	136—138	0·8
7	90—92	1·3	19	114—116	2·7	31	138—140	0·25
8	92—94	2·0	20	116—118	3·2	32	140—142	0·6
9	94—96	0·75	21	118—120	5·6	33	142—144	1·0
10	96—98	0·9	22	120—122	4·0	34	144—146	1·8
11	98—100	0·8	23	122—124	2·3	35	146—148	0·8
12	100—102	0·9	24	124—126	3·9	Residue	—	44·0

TABLE II.

Fractional distillation (at 5 mm.) of high-boiling constituents (574 *g.*).

Fraction.	Boiling range.	Yield, g.	Fraction.	Boiling range.	Yield, g.	Fraction.	Boiling range.	Yield, g.
36	45—50°	45·0	43	84—100	13·6	50	135—150°	6·5
37	50—55	61·1	44	100—110	8·6	51	150—155	45·7
38	55—60	44·6	45	110—115	5·6	52	155—160	104·2
39	60—65	24·0	46	115—120	10·2	53	160—165	25·0
40	65—70	43·1	47	120—125	11·4	54	165—208	19·6
41	70—75	22·0	48	125—130	5·8	Residue	—	28·8
42	78—85	9·9	49	130—135	5·4			

Examination of the Liquid Products.—Fraction 15 consisted of almost pure piperidine; *N*-methylpiperidine, which has virtually the same b. p., could be detected by Hinsberg's method using benzenesulphonyl chloride.

Fraction 21 yielded from alcohol an orange-yellow picrate, m. p. 134°, but by repeated recrystallisation from acetone–light petroleum (b. p. 80—100°) (1 : 1) the m. p. was raised to 139° (Found: C, 43·85; H, 4·9; N, 17·3. Calc. for $C_{12}H_{16}O_7N_4$: C, 43·9; H, 4·9; N, 17·1%). A hydrochloride, m. p. 215° (Found: C, 53·05; H, 10·3; N, 10·3; Cl, 25·1. Calc. for $C_6H_{14}NCl$: C, 53·1; H, 10·4; N, 10·3; Cl, 26·1%), and a hydrobromide, m. p. 194—195° (Found: C, 40·2; H, 7·8; N, 7·9; Br, 44·0. Calc. for $C_6H_{14}NBr$: C, 40·0; H, 7·9; N, 7·8; Br, 44·3%), were obtained as colourless needles from acetone–alcohol. These analyses confirm the presence of a methyl homologue of piperidine; the b. p. agrees with that of (±)-α-pipecoline; recorded values of the m. p.s are: picrate, 134—135°; hydrochloride, 210°; hydrobromide, 189°. In view of the small yield of this base the possibility that it was present in the original piperidine cannot be ruled out, but this is considered unlikely. β- and γ-Pipecoline boil at 126—129°; although a small peak occurred in this distillation range, the fractions 24—26 were not homogeneous and gave no derivatives of constant m. p. Analyses of the derivatives, however, yielded values in agreement with those for a methylpiperidine. The slight reddish colour formed during attempts to prepare a hydrochloride from these fractions and the positive colour reaction with Ehrlich's reagent indicated the presence of some pyrrole. Fraction 27 gave a very marked colour with the reagent.

A very pronounced peak occurred at 50—55°/5 mm. This fraction (no. 37) consisted substantially (over 90%) of a tertiary base, but small amounts of primary and secondary bases were also present. The tertiary base, separated by treating a sample with benzenesulphonyl chloride, gave a picrate, m. p. 129·5° (Found: C, 48·9; H, 6·0; N, 14·9. Calc. for $C_{15}H_{22}O_7N_4$: C, 48·7; H, 6·0; N, 15·1%), hydrochloride, m. p. 232° (Found: C, 60·4; H, 11·2; N, 7·4; Cl, 19·6. Calc. for $C_9H_{20}NCl$: C, 60·8; H, 11·3; N, 7·9; Cl, 20·0%), and methiodide, m. p. 203° (Found: C, 42·5; H, 7·4; N, 5·0; I, 44·7. Calc. for $C_{10}H_{22}NI$: C, 42·4; H, 7·8; N, 4·95; I, 44·8%). The base regenerated from recrystallised picrate had b. p. 177° and $n_D^{25\cdot3}$ 1·4456 (Found: C, 76·8; H, 13·3; N, 10·1. Calc. for $C_9H_{19}N$: C, 76·6; H, 13·5; N, 9·9%) and yielded a hydrochloride and methiodide identical with those obtained as above. This base was identical with *N*-*n*-butylpiperidine (obtained from piperidine and *n*-butyl bromide), b. p. 176°, $n^{25\cdot3}$ 1·4446 (picrate, m. p. 130·5°; hydrochloride, m. p. 238·5°; methiodide, m. p. 205°). The small amount of secondary base present in the fraction was not identified, but when the mixed base fraction (1·5 g.) was treated with phenyl *iso*cyanate (1·2 g.) a small amount of crystalline substance

(0·1 g.), m. p. 147° (Found: C, 72·8; H, 4·9; N, 12·5. Calc. for $C_{20}H_{17}O_2N_3$: C, 72·5; H, 5·1; N, 12·7%), was obtained.

By reaction with benzenesulphonyl chloride, fraction 40 was shown to consist principally of tertiary bases and their separation proved to be difficult. The only pure derivative prepared was a ***methiodide***, m. p. 231° (decomp.) (Found: C, 44·6; H, 7·5; N, 4·4; I, 42·8. $C_{11}H_{22}NI$ requires C, 44·7; H, 7·5; N, 4·7; I, 43·0%). The same derivative, m. p. 230—231° (decomp.), was obtained in small amount from fraction 43, but here again its isolation proved somewhat difficult owing to the presence of another tertiary base. In the latter fraction secondary bases preponderated, but attempts to obtain crystalline derivatives therefrom were unsuccessful. The above methiodide corresponds to a base $C_{10}H_{19}N$ and, by synthesis, was shown to be *N-cyclo*pentylpiperidine. A *picrate*, m. p. 170° (Found: C, 49·9; H, 5·4; N, 15·0. $C_{16}H_{22}O_7N_4$ requires C, 50·3; H, 5·7; N, 14·6%), and a hydrochloride, m. p. 270° (Found: C, 63·3; H, 10·5; N, 7·6; Cl, 19·0. Calc. for $C_{10}H_{20}NCl$: C, 63·3; H, 10·55; N, 7·4; Cl, 18·7%), corresponding roughly to the same base, were obtained from fraction 43. Loevenich *et al.* (*Ber.*, 1929, **62**, *B*, 3084) give the analysis of this derivative but state no m. p.

Synthesis of N-cyclo*Pentylpiperidine* (compare Loevenich *et al.*, *loc. cit.*).—Piperidine (8 g.) and *cyclo*pentyl chloride (4 g.) were refluxed for 8 hours and the mixture, after being made acid with hydrochloric acid, was extracted with ether. The bases liberated from the acid portion by addition of alkali were extracted with ether and, after being dried (NaOH), were distilled to give unchanged piperidine and *N-cyclo*pentylpiperidine (1·5 g.), b. p. 210° [methiodide, m. p. 230° (decomp.) (Found: C, 44·65; H, 7·4; N, 4·6; I, 43·0%)]. This derivative did not depress the m. p. of the methiodide obtained as above.

A 74% yield of *N-cyclo*pentylpiperidine, b. p. 210° [picrate, m. p. 174° (Found: C, 50·4; H, 5·8; N, 14·5%); hydrochloride, m. p. 277—278° (Found: C, 63·3; H, 10·5; N, 7·2; Cl, 18·9%)], was obtained by heating piperidine (45 g.) with *cyclo*pentanone (42 g.) and Raney nickel (10 g.) in an autoclave at 125—150° for 5 hours with an initial hydrogen pressure of 100 atms.

Separation of Bases in Fraction 40 (*b. p.* 65—70°/5 *mm.*) *by Ion-exchange*.—In addition to *N-cyclo*pentylpiperidine (see above) this fraction contained another tertiary base in considerable quantity but it was not possible to prepare pure derivatives for its characterisation. However, a fairly clear-cut separation was effected by means of an ion-exchange column consisting of a sulphonated, cross-linked polystyrene–divinylbenzene resin. The mixed base fraction (3 g.) was adsorbed on the column and N-hydrochloric acid in 50% ethyl alcohol was used to elute the bases. The effluent was collected every 40 ml. and by determining its conductivity at short intervals and on plotting of the results against the volume of effluent it was found that two constituents had been removed and that a useful separation had been accomplished. Further treatment of the column with 0·5N-potassium hydroxide in 50% ethyl alcohol removed a third component. The first series of effluent fractions, corresponding to the first minimum in the conductivity curve, yielded, after removal of the solvent under vacuum, the greater part of the original base mixture as a crystalline hydrochloride, m. p. 218° (Found: C, 62·4; H, 11·3; N, 7·9; Cl, 18·3. Calc. for $C_{10}H_{22}NCl$: C, 62·6; H, 11·5; N, 7·3; Cl, 18·5%), from which was also prepared a picrate, m. p. 109—110°. Neither of these derivatives on admixture with the corresponding derivatives of synthetic *N-n*-amylpiperidine (from *n*-amyl bromide and piperidine) caused any depression in the m. p. The other two constituents of the mixture removed from the column were not examined.

Examination of Fraction 52 (*b. p.* 155—160°/5 *mm.*).—This fraction was the most abundant; together with its immediate neighbours it represented 17·5% by weight of the original piperidine. Reaction with benzenesulphonyl chloride indicated that 94% of the bases in this fraction were tertiary. Further examination showed that at least 90% of the fraction could be accounted for as one base. Thus, when 30 g. of the fraction were treated with 65 g. of picric acid, 79·7 g. of an insoluble *dipicrate*, m. p. 197·5° (Found: C, 46·5; H, 5·2; N, 16·0. $C_{27}H_{36}O_{14}N_8$ requires C, 46·5; H, 5·2; N, 16·1%), were eventually obtained after a series of recrystallisations. From the picrate (10 g.) the free base (3·3 g.), b. p. 124—125°/1·5 mm., 142—144°/4·5 mm. (Found: C, 75·3; H, 12·6; N, 11·5. Calc. for $C_{15}H_{30}N_2$: C, 75·55; H, 12·7; N, 11·75%), was regenerated with dilute sodium hydroxide solution followed by steam-distillation. This base was di-tertiary and yielded a dihydrochloride, m. p. 259° (Adkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2487; m. p. 253°), and a *dimethiodide*, m. p. 272° (decomp.) (Found: C, 39·1; H, 6·6; N, 5·0; I, 48·5. $C_{17}H_{36}N_2I_2$ requires C, 39·1; H, 6·9; N, 5·4; I, 48·6%). It was identified as 1 : 5-dipiperidinopentane.

Synthesis of 1 : 5-*Dipiperidinopentane* (cf. von Braun, *loc. cit.*).—Pentamethylene dichloride (10 g.), piperidine (15 g.), and water (10 g.) were heated on the steam-bath for 5½ hours. A further quantity of piperidine (5 g.) was added and heating continued for a further 4½ hours. The mixture was acidified with hydrochloric acid and extracted with ether to remove unchanged pentamethylene dichloride (4·1 g.). Addition of alkali, followed by steam-distillation removed excess of piperidine and any 1 : 5-dipiperidinopentane formed. These were extracted from the steam-distillate with ether, dried (NaOH), and distilled. A small fraction (1 g.) of 1 : 5-dipiperidinopentane remained after complete removal of the piperidine. This yielded a dipicrate, m. p. 197·5°, and a dimethiodide, m. p. 272° (decomp.), which gave no depression in m. p. in admixture with the derivatives described above. The involatile residue from the steam-dstillation was made strongly alkaline with sodium hydroxide, whereupon a crystalline precipitate of the quaternary compound separated. As it was extremely hygroscopic it was necessary to remove water from this compound by azeotropic distillation with benzene. Dissolution in absolute alcohol followed by precipitation in sodium-dried ether yielded the quaternary compound (8 g.) free from sodium chloride. Dipiperidinium dichloride has no definite m. p.; decomposition sets in around 335°. Dipiperidinium picrate, m. p. 208°, crystallised from alcohol as long yellow needles.

Piperidine (213 g.), water (50 g.), and pentamethylene dibromide (115 g.) were heated in an autoclave with stirring for 5½ hours at 180—230°. After cooling, excess of 40% sodium hydroxide solution was added and the free bases were extracted with ether. The ethereal solution was dried (NaOH). From the total bases recovered (185·5 g.), excess of piperidine was distilled off leaving a residue of high-boiling base which yielded on distillation in a vacuum 1 : 5-dipiperidinopentane (81 g.), b. p. 124—125°/1·5 mm.

(Found : C, 75·3; H, 12·6; N, 11·5%) [dipicrate, m. p. 197·5° (Found : C, 46·5; H, 5·3; N, 15·3%); dimethiodide, m. p. 272° (Found : C, 38·9; H, 7·0; N, 5·25; I, 47·9%); *dihydrobromide*, m. p. 243·5° (Found : C, 45·1; H, 8·1; N, 6·3; Br, 40·0. $C_{15}H_{32}N_2Br_2$ requires C, 45·0; H, 8·0; N, 7·0; Br, 40·0%)].

Gautier and Renault (*Compt. rend.*, 1947, **225**, 682) have shown that *NN'*-polymethylene(bispyridinium halides) are obtained in good yield by heating pyridine with Hal·$[CH_2]_n$·Hal in ethyl alcohol. A nearly quantitative yield of pentane-1 : 5-(bispyridinium bromide) was obtained from pyridine and pentamethylene dibromide by this method. When the diquaternary compound (0·25 g.) was hydrogenated in acetic acid (10 g.) with Adams's catalyst (0·1 g.) at room temperature it took up the theoretical amount of hydrogen corresponding to reduction to 1 : 5-dipiperidinopentane dihydrobromide. The dihydrobromide (0·25 g.) was recovered as colourless crystalline needles, m. p. and mixed m. p. with the above dihydrobromide, 243° (Found : C, 45·1; H, 8·1; N, 6·3; Br, 40·0%).

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