

### 623. *Studies of Coal Tar Bases. Part VI.\* Hydrogenation of 2-Methylpyridine.*

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Use of W6 Raney nickel for hydrogenation of 2-methylpyridine at 150° leads to improved yields of 2-methylpiperidine. At higher temperatures hydrogenolysis of 2-methylpiperidine occurs. 1-*n*-Amylpiperidine, *n*-pentane, *cyclopentane*, methyl*cyclopentane*, and *n*-hexane have been identified among the products, and possible structures for other basic products are discussed. The origin of 6-methyl-2-piperidone, which is also formed, is ascribed to the absorption of atmospheric carbon dioxide by the base before the reaction and arises by hydrogenolysis of the intermediate 1-formyl-2-methylpiperidine.

In a study of the catalytic hydrogenation of 2-methylpyridine we have confirmed McElvain and Carney's report (*J. Amer. Chem. Soc.*, 1946, **68**, 2592) that at 200°/150—300 atm. over W2 Raney nickel 2-methylpiperidine is obtained in only 45% yield after careful fractionation of the product. However, by using the more active W6 Raney nickel (Adkins and Billica, *ibid.*, 1948, **70**, 695) hydrogenation proceeds readily at 140—150°/200 atm., giving 70—75% yields of pure 2-methylpiperidine, owing to the smaller amount of hydrogenolysis at the lower temperature. As with pyridine (*J.*, 1950, 1392) considerable hydrogenolysis occurs with Raney nickel at <200° and this paper describes an examination of the hydrogenolysis products. In general, the results indicate that cleavage and condensation reactions similar to those described for pyridine occur but there is an even greater variety of products owing to the dissymmetry of the molecule and the yields of individual compounds are smaller.

Presence, in the products, of 1-*n*-amylpiperidine, previously shown to be a product of hydrogenolysis of piperidine, shows that the methyl group is fairly readily removed. *n*-Pentane and *cyclopentane* are found, presumably resulting by elimination of ammonia from the piperidine, followed by hydrogenation and cyclisation respectively. Similarly, *n*-hexane and methyl*cyclopentane*, also present, are derived by analogous elimination of ammonia from 2-methylpiperidine. One of the high-boiling products was 6-methyl-2-piperidone, the nature of which followed from its dehydrogenation to 6-methyl-2-pyridone and direct comparison with an authentic specimen (Bunzel, *Ber.*, 1889, **22**, 1056).

A likely source of the combined oxygen was atmospheric carbon dioxide previously absorbed by the base, since examination of the hydrogen employed revealed only traces of carbon dioxide: indeed, hydrogenation of 2-methylpyridine in the presence of carbon dioxide gave 6-methyl-2-piperidone, in low yield. Farlow and Adkins (*J. Amer. Chem. Soc.*, 1935, **57**, 2222) have shown that in the presence of amines, carbon dioxide is readily reduced to formic acid and that at >100° formylation of the amine occurs. With 2-methylpiperidine, 1-formyl-2-methylpiperidine is first formed. This then undergoes cleavage with elimination of the  $\alpha$ -carbon atom, followed by recyclisation to 6-methyl-2-piperidone. In support of this view, 1-formyl-2-methylpiperidine on hydrogenolysis under conditions similar to the above affords 6-methyl-2-piperidone in about 5% yield. Hydrogenation of piperidine in presence of carbon dioxide gives 1-formylpiperidine but no piperidone; and hydrogenolysis of 1-formylpiperidine did not lead to detectable amounts of piperidone. It is possible that in this case, where there is no "protecting" methyl group, piperidone is hydrogenated to piperidine as soon as it is formed. Formation of 6-methyl-2-piperidone under the conditions described affords striking confirmation of the cleavage reaction observed in the previous work on piperidine (*loc. cit.*), where similar elimination of the  $\alpha$ -carbon atom of the ring led to the formation of 1-*n*-butylpiperidine in appreciable quantity.

Four tertiary bases, C<sub>7</sub>H<sub>15</sub>N, C<sub>10</sub>H<sub>21</sub>N, C<sub>10</sub>H<sub>21</sub>N, and C<sub>11</sub>H<sub>21</sub>N were also isolated in the experiments with 2-methylpiperidine, but their identities have not been definitely established. The C<sub>7</sub> base, which is neither 1-ethyl- nor 1:2-dimethyl-piperidine, is

\* Part V, *J. Appl. Chem.*, 1952, **2**, 236.

probably (? *trans*-)1 : 2 : 5-trimethylpyrrolidine, as we have found 1 : 2-dimethylpyrrolidine among the low-boiling products of pressure hydrogenolysis of piperidine; comparison of the C<sub>7</sub> base with a synthetic sample of (? *cis*-)1 : 2 : 5-trimethylpyrrolidine was, however, not conclusive. By direct comparisons, the C<sub>10</sub> base (picrate, m. p. 96—97°) was shown not to be identical with 1-*n*-, or 1-*sec*-amyl- or 1-*n*- or 1-*sec*-butyl-2-methylpiperidine. The infra-red absorption spectrum of this base showed an ethylenic bond to be present, which suggests that it may be an alkenyldialkylamine.

Some derivatives of a number of 1-alkylpiperidines, prepared by standard methods during this investigation, are described in the Experimental section. Of these, 1-*sec*-amyl- and 2-methyl-1-cyclopentyl-piperidine appear to be new.

#### EXPERIMENTAL

Microanalyses were carried out by Miss M. Corner of this Laboratory and by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

*Hydrogenation of 2-Methylpyridine*.—Typical hydrogenations were as follows :

(a) *Using W2 Raney nickel*. 2-Methylpyridine, b. p. 129—130° (2100 g.), containing suspended W2 Raney nickel (200 g.) (*Org. Synth.*, 21, 15), was hydrogenated in a stainless-steel autoclave at 200°/200 atm. for 24 hours. The liquid product (1886 g.) was fractionated through a Stedman column (equiv. to 50 theoretical plates), giving a main fraction of 2-methylpiperidine (1045 g., 47%), b. p. 117—120°, m. p. —4.5°,  $n_D^{20}$  1.4465.

(b) *Using W6 Raney nickel*. 2-Methylpyridine (1000 g.) containing suspended W6 Raney nickel (100 g.) (Adkins and Billica, *loc. cit.*) was hydrogenated at 150°/200 atm. for 10 hours with approx. theoretical absorption of hydrogen. The liquid product (996 g.) was fractionated as before, giving a main fraction of 2-methylpiperidine (780 g., 73%), b. p. 114—114.5°/700 mm.,  $n_D^{20}$  1.4464.

The purity of these products was apparent from the close correspondence between their physical constants and infra-red absorption spectra with those of pure 2-methylpiperidine, b. p. 116—118°,  $n_D^{20}$  1.4460, obtained by regeneration from the repeatedly crystallised 1-benzoyl derivative (m. p. 48°).

*Pressure Hydrogenolysis of 2-Methylpiperidine*.—2-Methylpiperidine (1000 g.), b. p. 117—120°,  $n_D^{20}$  1.4465, when heated with W2 Raney nickel (100 g.) under hydrogen in a steel autoclave for 6 hours at 250°/200 atm. (total time of heating 12 hours), yielded a mixture of gaseous bases and paraffins (*ca.* 160 g.), and a strongly ammoniacal-smelling liquid (843 g.), which on distillation gave a low-boiling fraction (*A*) (b. p. <140°; 711 g.), and a high-boiling fraction (*B*) (b. p. >140°; 130 g.). These were refractionated.

*Examination of fraction (A)*. Subfraction 1 (31 g.), b. p. 35—90°, on treatment with hydrochloric acid gave a neutral fraction (11 g.) and recovered bases (20 g.), the latter not being further examined. Distillation of the neutral fraction gave peak fractions, (i) b. p. 40—43°,  $n_D^{20}$  1.3698, aniline point 62° (2.3 g.) (Found : C, 83.9; H, 16.2%), and (ii) b. p. 63—65°,  $n_D^{20}$  1.3874, aniline point 51° (1.8 g.) (Found : C, 84.4; H, 15.45%).

The analyses, refractive indices, and aniline points indicated that fraction (i) was a mixture of *n*-pentane 80% (approx.) and cyclopentane, and that fraction (ii) was a mixture of *n*-hexane 60% (approx.) and methylcyclopentane. This was confirmed by their infra-red absorption spectra.

Subfraction 2 (38.5 g.), b. p. 90—92°, was shown by titration with acid to be a water-base azeotrope containing 30—40% of base. By saturation with sodium hydroxide, the supernatant bases were separated and then dried (NaOH). The dry bases (2 g.) in 20% sodium hydroxide solution (10 ml.) were treated with toluene-*p*-sulphonyl chloride (4.5 g.). Separation by the Hinsberg method gave a trace of primary base; the toluene-*p*-sulphonate (3.8 g.), m. p. 54°, of a secondary base crystallised from alcohol, giving no depression in m. p. on admixture with authentic 2-methyl-1-toluene-*p*-sulphonylpiperidine (m. p. 55—56°), and a tertiary base (0.5 g.), which yielded a *picrate*, m. p. 183—184° (Found : C, 45.8; H, 5.2; N, 16.4. C<sub>7</sub>H<sub>15</sub>N, C<sub>6</sub>H<sub>3</sub>O<sub>7</sub>N<sub>3</sub> requires C, 45.6; H, 5.3; N, 16.4%), a *hydrochloride*, m. p. 286—287° (Found : C, 56.6; H, 10.95; Cl, 23.6. C<sub>7</sub>H<sub>15</sub>N.HCl requires C, 56.2; H, 10.8; Cl, 23.7%), and a *methiodide*, m. p. 318° (decomp.) (Found : C, 37.6; H, 7.3; N, 5.7. C<sub>7</sub>H<sub>15</sub>N.CH<sub>3</sub>I requires C, 37.7; H, 7.1; N, 5.5%). Admixture of the above picrate with picrates of 1-ethyl- and 1 : 2-dimethyl-piperidine, and (? *cis*-)1 : 2 : 5-trimethylpyrrolidine (see below) gave depressions of the m. p.

Subfraction 3, b. p. 116—120° (423 g.), was mainly 2-methylpiperidine (infra-red spectrum).

Subfraction 4, b. p. 120—122° (31.5 g.), was not investigated.

*Examination of fraction (B).* Subfraction 5, b. p. <40°/3 mm. (17 g.), was not investigated.

Subfraction 6 (9.5 g.), b. p. 40—60°/3 mm., with toluene-*p*-sulphonyl chloride gave a tertiary base (80%) which yielded a picrate, m. p. 109° (Found: C, 49.6; H, 6.2; N, 14.7. Calc. for  $C_{10}H_{21}N, C_6H_3O_7N_3$ : C, 50.0; H, 6.3; N, 14.7%), giving no depression in m. p. on admixture with 1-*n*-amylpiperidine picrate, m. p. 110°.

Subfraction 7 (7 g.), b. p. 60—70°/3 mm., with toluene-*p*-sulphonyl chloride gave tertiary bases (90%), which on distillation yielded a main fraction, b. p. 185°,  $n_D^{20}$  1.4506 (Found: C, 77.0; H, 13.5; N, 9.2.  $C_{10}H_{21}N$  requires C, 77.3; H, 13.6; N, 9.0%), yielding a *picrate*, m. p. 96—97° (Found: C, 50.4; H, 6.3; N, 14.7.  $C_{10}H_{21}N, C_6H_3O_7N_3$  requires C, 50.0; H, 6.25; N, 14.7%), a *methiodide*, m. p. 193—194° (Found: I, 41.8.  $C_{10}H_{21}N, CH_3I$  requires I, 41.7%), and a very hygroscopic hydrochloride, m. p. 165—167°. Admixture of this picrate with picrates of 1-*n*- or 1-*sec.*-amyl- or 1-*n*- or 1-*sec.*-butyl-2-methylpiperidine led to m. p. depressions.

The infra-red absorption spectrum of the free tertiary base showed a moderately intense band at 6.02  $\mu$ . This was too weak to be due to acyclic  $C=N$  and can be assigned therefore to  $C=C$ .

Subfraction 8 (11 g.), b. p. 80—82°/3 mm., with toluene-*p*-sulphonyl chloride gave tertiary bases (90%), which on distillation yielded main fractions: (i) b. p. 140—150°,  $n_D^{20}$  1.4528, giving a *methiodide*, m. p. 188—189° (Found: C, 46.6; H, 8.0; N, 4.45; I, 40.5.  $C_{11}H_{21}N, CH_3I$  requires C, 46.6; H, 7.8; N, 4.5; I, 41.1%); and (ii) a *base*, b. p. 190°,  $n_D^{20}$  1.4555 (Found: C, 77.7; H, 13.7; N, 9.0.  $C_{10}H_{21}N$  requires C, 77.3; H, 13.7; N, 9.0%), giving a *picrate*, m. p. 76° (Found: C, 50.1; H, 6.5; N, 14.2.  $C_{10}H_{21}N, C_6H_3O_7N_3$  requires C, 50.0; H, 6.3; N, 14.7%).

Subfraction 9 (12 g.), b. p. 115—120°/3 mm., had m. p. 88—89° after recrystallisation from light petroleum (b. p. 40—60°) and repeated sublimation *in vacuo* (Found: C, 64.0, 63.2; H, 9.6, 9.8; N, 12.0, 12.6. Calc. for  $C_6H_{11}ON$ : C, 63.7; H, 9.8; N, 12.4%), m. p. not depressed on admixture with authentic 6-methyl-2-piperidone, m. p. 88°, prepared by Bunzel's method (see below). It formed a *picrate*, m. p. 72—73° (from ether) (Found: C, 41.9; H, 4.1; N, 15.8.  $C_6H_{11}ON, C_6H_3O_7N_3$  requires C, 42.1; H, 4.1; N, 16.4%), a *hydrochloride*, m. p. 150—151° (Found: Cl, 23.6.  $C_6H_{11}ON, HCl$  requires Cl, 23.75%), and a *methiodide*, m. p. 156—157° (decomp.). The infra-red absorption spectrum of the solid, m. p. 88—89°, was identical with that of the synthetic specimen of 6-methyl-2-piperidone. The solid (500 mg.) intimately ground with palladium black (100 mg.) was heated at 260—280° for 3 hours. The solid product was extracted with ether. Two fractional sublimations at 80°/1 mm. gave as main product 6-methyl-2-pyridone, m. p. 159—160° (Found: C, 66.1; H, 6.5; N, 12.8. Calc. for  $C_6H_7ON$ : C, 66.1; H, 6.5; N, 12.8%) [*picrate*, m. p. 146—147° (Found: C, 42.6; H, 3.0; N, 16.6.  $C_6H_7ON, C_6H_3O_7N_3$  requires C, 42.6; H, 3.0; N, 16.6%); dibromo-derivative, m. p. 243—244° (Found: Br, 60.5. Calc. for  $C_6H_5ONBr_2$ ; Br, 59.9%)]. For 6-methyl-2-pyridone Errera (*Ber.*, 1900, 33, 2969) gives m. p. 159°, and for its dibromo-derivative m. p. 238—239°.

A still residue, consisting of a brown tar (50 g.), was not examined.

*Synthesis of 6-Methyl-2-piperidone* (cf. Bunzel, *loc. cit.*).—Potassium permanganate oxidised 1-benzoyl-2-methylpiperidine to 5-benzamidoheptanoic acid, m. p. 151—152° (Found: C, 66.3; H, 7.4; N, 5.9. Calc. for  $C_{13}H_{17}O_3N$ : C, 66.4; H, 7.3; N, 6.0%), which on dry distillation at 268—270°, followed by treatment with aqueous sodium hydroxide and extraction with chloroform, gave 6-methyl-2-piperidone, m. p. 88°, after sublimation at 80°/1 mm. (Found: C 63.4; H, 9.5; N, 12.5. Calc. for  $C_6H_{11}ON$ : C, 63.7; H, 9.8; N, 12.4%).

*Preparation of 6-Methyl-2-piperidone by Hydrogenation of 2-Methylpyridine and Carbon Dioxide.*—Hydrogenation of 2-methylpyridine (200 g.) and carbon dioxide (20 g.) over Raney nickel (20 g.) at 180°/150 atm. for 11 hours and distillation of the products gave crude 6-methyl-2-piperidone (4 g.). Repeated crystallisation from light petroleum (b. p. 40—60°) and sublimation gave a product, m. p. 86—87°. The infra-red absorption spectrum was identical with that of the specimen made by Bunzel's synthesis.

*Preparation of 6-Methyl-2-piperidone by Hydrogenolysis of 1-Formyl-2-methylpiperidine.*—1-Formyl-2-methylpiperidine, b. p. 227—228° (101 g.) [mercurichloride, m. p. 100—101° (Found: N 3.6. Calc. for  $C_7H_{13}ON, HgCl_2$ : N, 3.5%)], was hydrogenolysed over Raney nickel (10 g.) for 7 hours at 250°/160 atm. Fractional distillation gave a crude solid (6 g.), b. p. 90—110°/0.5 mm., which after recrystallisation and sublimation had m. p. 88—89°, alone or on admixture with authentic 6-methyl-2-piperidone, and possessed an infra-red absorption spectrum identical with that of the authentic compound.

*Hydrogenolysis of Piperidine in the Presence of Carbon Dioxide.*—Piperidine (100 g.) containing suspended Raney nickel (10 g.) was placed in a 1-l. steel autoclave, which was then filled with carbon dioxide at 50 atm., followed by hydrogen to a pressure of 160 atm. After 4 hours' heating at 150°/250 atm., the mixture of solid carbonates obtained was dissolved in the minimum quantity of water, filtered, and acidified with concentrated hydrochloric acid. After basification of the mixture with an excess of solid sodium hydroxide ether-extraction gave a yellow oil (110 g.), which on distillation gave mainly unchanged piperidine (62 g.) and 1-formylpiperidine (17 g.), b. p. 215—218° (mercurichloride, m. p. 148—149° alone or on admixture with an authentic sample).

*Preparation of 1-Alkylpiperidines* [with S. E. HUNT].—Various 1-alkylpiperidines were prepared from the free base and the alkyl bromide by Magnusson and Schierz's method (Univ. of Wyoming Publ., 1940, vol. 7, p. 1). 1-*sec.*-Amylpiperidine, b. p. 190°,  $n_D^{20}$  1.4505 [*picrate*, m. p. 93—94° (Found: C, 50.1; H, 6.2; N, 14.4.  $C_{10}H_{21}N, C_6H_3O_7N_3$  requires C, 50.0; H, 6.25; N, 14.7%)], was prepared by Leuckart alkylation of piperidine with methyl *n*-propyl ketone (cf. Smith and Macdonald, *J. Amer. Chem. Soc.*, 1950, **72**, 1037). 1-*cyclo*Pentyl-2-methylpiperidine, b. p. 220—224°,  $n_D^{20}$  1.4834 [*picrate*, m. p. 129—130° (Found: C, 51.5; H, 6.1; N, 13.9.  $C_{11}H_{21}N, C_6H_3O_7N_3$  requires C, 51.5; H, 6.1; N, 14.1%); methiodide, m. p. 193—194°] was prepared by heating *cyclopentanone* and 2-methylpiperidine with Raney nickel and hydrogen (100 atm.) at 140° for 6½ hours. The other compounds prepared were: 1:2-dimethyl-, b. p. 129°,  $n_D^{20}$  1.4412 (*picrate*, m. p. 246°), 2-methyl-1-*n*-propyl-, b. p. 168—170°,  $n_D^{20}$  1.4474 (*picrate*, m. p. 118—119°), 1-*sec.*-butyl-2-methyl-, b. p. 174° (*picrate*, m. p. 139°), 1-*n*-butyl-2-methyl-, b. p. 187°,  $n_D^{20}$  1.4509 (*picrate*, m. p. 114—115°; methiodide, m. p. 218—219°), and 1-*n*-amyl-2-methyl-piperidine, b. p. 204—206°,  $n_D^{20}$  1.4528 (*picrate*, m. p. 94—95°; methiodide, m. p. 197—198°).

*Preparation of (? cis)-1:2:5-Trimethylpyrrolidine.*—2:5-Dimethylpyrrole (*Org. Synth.*, **16**, 25) was hydrogenated over Adams's catalyst in ethanol-acetic acid (1:1). The recovered base on distillation gave 2:5-dimethylpyrrolidine, b. p. 105°, converted into 1:2:5-trimethylpyrrolidine by methyl iodide. The free base yielded a *picrate*, m. p. 209—210° (Found: C, 45.85; H, 5.2; N, 16.6.  $C_7H_{15}N, C_6H_3O_7N_3$  requires C, 45.6; H, 5.3; N, 16.4%).

The work described above formed part of the programme of the Chemical Research Laboratory and is published by permission of the Director. We thank Mr. J. L. Hales for performing the infra-red absorption analyses, and Messrs. E. C. Holt and A. Steven for carrying out much of the distillation work.