11. *Attempts to prepare* 7-*Substituted* bicyclo[1 : 2 : 2]-1-*Azaheptanes.*

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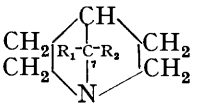
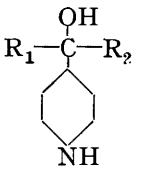
In order to prepare 7-methyl- and 7 : 7-dimethyl-*bicyclo*[1 : 2 : 2]-1-azaheptane the syntheses of methyl- and dimethyl-4-piperidylcarbinols have been investigated, but only the latter compound has been obtained. It was converted into 4-α-bromo*iso*-propylpiperidine, which, however, could not be induced to lose hydrogen bromide in a manner which would form the desired bicyclic base.

Because of their relation to the camphane system, *bicyclo*[1 : 2 : 2]-1-azaheptanes with alkyl groups attached to the 7-carbon atom have considerable interest. Prelog and his co-workers have reported (*Chem. Centr.*, 1939, I, 2603) the failure of their method for the formation of this group of bicyclic bases in the case of (I; $R_1 = R_2 = Me$), although with some difficulty they prepared the monomethyl compound (I; $R_1 = Me$, $R_2 = H$). It was therefore considered desirable to apply the method used for the parent compound (Clemo and Metcalfe, J., 1937, 1523) to this problem. The preparation of the necessary piperidine alcohols (II; $R_1 = R_2 = Me$) and (II; $R_1 = Me$, $R_2 = H$) was attempted by way of the corresponding pyridyl alcohols. *Methyl-4-pyridylcarbinol* was prepared by the reduction of 4-acetylpyridine with aluminium *iso*propoxide or catalytically, and

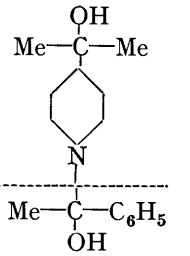
dimethyl-4-pyridylcarbinol by the action of methylmagnesium iodide on ethyl pyridine-4-carboxylate (Sobecki, *Ber.*, 1908, **41**, 4103; Emmert and Asendorf, *ibid.*, 1939, **72**, 1188).



(I.)



(II.)



(III.)

Both compounds were obtained in good yields, but they have resisted all attempts at hydrogenation either catalytically or by the Ladenburg method. The former, when platinum oxide or palladised charcoal in acetic acid, dilute hydrochloric acid, or acetic acid saturated with hydrogen chloride was used, always gave unchanged material, and 4-acetylpyridine yielded only methyl-4-pyridylcarbinol (compare Strong and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 816). Dimethyl-4-pyridylcarbinol was recovered to the extent of 80% from sodium and alcohol reductions, together with a very small amount of a base, isolated only as its picrate. It seemed by analogy with the results of Sobecki (*loc. cit.*) that the latter would be 4-*iso*propylpyridine, and this was confirmed by its preparation from dimethyl-4-pyridylcarbinol by reduction with hydriodic acid and red phosphorus. The properties of this compound agreed with those given by Ladenburg (*Annalen*, 1888, **247**, 1), and the *picrate* was identical with that of the base obtained from the sodium and alcohol reduction. In order to eliminate the possibility of confusion with 4-α-*methylvinylpyridine*, which could be formed by dehydration, this compound was prepared by dehydration of dimethyl-4-pyridylcarbinol with phosphoric oxide, and its *picrate* shown to be quite distinct from the above. Methyl-4-pyridylcarbinol could not be reduced by the Ladenburg method and 4-ethylpyridine was not detected in the gummy product obtained.

Attention was next directed to the preparation of the piperidine alcohols from ethyl piperidine-4-carboxylate by means of the Grignard reaction, but in all cases bases as yet unidentified were isolated (Clemo and Metcalf, *loc. cit.*). Thus *ethyl* 1-*acetylpiperidine*-4-*carboxylate* gave, with methylmagnesium iodide, *dimethyl*-1-*acetyl*-4-*piperidylcarbinol*, which could not be deacetylated satisfactorily. The reaction of methylmagnesium iodide with ethyl 1-benzoylpiperidine-4-carboxylate was very complex, but gave the required compound in 6—7% yield. The gelatinous Grignard addition compound was decomposed in the usual way and small, roughly equivalent amounts of acetophenone and free *dimethyl*-4-*piperidylcarbinol* were at once liberated. These two compounds are probably formed by the decomposition of (III), produced by attack at both the ester and the benzoyl group of the starting material, and this view was strengthened by the isolation of appreciable amounts of piperidine and acetophenone when 1-benzoylpiperidine was subjected to the action of an excess of methylmagnesium iodide under similar conditions. Hydrolysis of the main fraction yielded approximately equivalent amounts of dimethyl-4-piperidylcarbinol and benzoic acid, but a considerable amount of material was left which was unchanged by prolonged boiling with acids or alkalis and its formation accounts for the low yield of the desired product. Varying the amount of the Grignard reagent and the temperature conditions were without significant effect on the proportions of the several substances formed.

By the action of hydrobromic acid on dimethyl-4-piperidylcarbinol, 4-α-*bromoisopropylpiperidine hydrobromide* was readily prepared, but when this compound was treated with alkali under conditions which converted 4-bromomethylpiperidine into the bicyclic base, the only product which could be isolated was dimethyl-4-piperidylcarbinol. Under anhydrous conditions with dry silver oxide or potassium carbonate there was obtained, in addition to small amounts of the same alcohol, an unsaturated secondary *amine*, $C_8H_{15}N$. This was

either an *iso*propyltetrahydropyridine or 4-*iso*propylidenepiperidine, since it was reduced catalytically to 4-*iso*propylpiperidine.

By the action of methylmagnesium iodide on ethyl piperidine-4-carboxylate a *base*, $C_7H_{13}ON$, was obtained in good yield. From the method of preparation this might be expected to be 4-acetylpiperidine. Prelog claims to have prepared this base (*Chem. Centr.*, 1939, I, 116) by the Claisen condensation of the benzoyl derivative of ethyl piperidine-4-carboxylate, but in only 5—10% yield; he does not describe it, and the properties of the derivatives he records do not agree with those found for our compounds. It is true it has not been possible to demonstrate the presence of a carbonyl group in our base, but the nitrogen atom has been methylated to give what appears to be 4-acetyl-1-methylpiperidine.

Experimental.

iso*Nicotinic Acid.*—This compound was prepared by the following modification of the method of Weidel and Herzig (*Monatsh.*, 1880, **1**, 2). 2 : 4-Lutidine (30 g.) in water (3 l.) was stirred at 90° under a condenser, potassium permanganate (20 g.) added, a slow stream of carbon dioxide passed, and stirring continued until the colour was discharged. Fresh permanganate (20 g.) was added, and the process repeated until 250 g. in all had been introduced. The manganese dioxide was filtered off and washed with water, and the combined filtrates evaporated. The residue was made acid to Congo-red (50% hydrochloric acid) and evaporated nearly to dryness, and the paste dried in an open dish, coarsely powdered, and sublimed in superheated steam from a metal-bath at 300°/20—30 cm. The sublimate and yellowish distillate were united, a little concentrated hydrochloric acid added, and the whole evaporated under reduced pressure. The residue was basified (sodium hydroxide solution), and γ-picoline, formed presumably by decarboxylation of 4-methylpyridine-2-carboxylic acid, steam-distilled. The distillate was acidified (hydrochloric acid) and evaporated, the residue basified (sodium hydroxide), and the base taken up in chloroform, dried, and distilled. The fraction, b. p. 141—143°, was dissolved in hot alcohol (20—30 c.c.) and treated with a slight excess of picric acid. The picrate was washed with alcohol and by decomposition gave the base (2·2 g.), b. p. 142°, as a colourless oil. The picrate formed bright yellow clusters of needles, m. p. 166° (Found : C, 44·8; H, 3·5. Calc. for $C_6H_7N,C_6H_3O_7N_3$: C, 44·7; H, 3·2%), and the methiodide separated from dry acetone in colourless plates, m. p. 149° (Found : C, 35·4; H, 4·7. Calc. for $C_7H_{10}NI$: C, 35·7; H, 4·3%).

The alkaline residue from the steam-distillation was acidified (concentrated hydrochloric acid), reduced to 100 c.c., and cooled, and the sodium chloride filtered off and washed with a little 50% hydrochloric acid. The combined filtrates were evaporated and completely dried by the addition and removal in a vacuum of several small amounts of absolute alcohol. Thionyl chloride (80 c.c.) was added and when the reaction subsided the mixture was refluxed (8 hours), and the excess removed. The residue was treated with absolute alcohol (50 c.c.), refluxed for 2—3 hours, and the excess evaporated. Benzene (100 c.c.) was added, followed by sodium carbonate solution until the aqueous layer was alkaline; the benzene layer was removed, dried, and fractionated through a short column in a vacuum. The main fraction, b. p. 110—115°/15 mm., was a bright yellow oil, consisting almost entirely of ethyl pyridine-4-carboxylate. It was dissolved in methyl alcohol (20 c.c.), 50% aqueous potassium hydroxide (1 equiv.) added, and the mixture refluxed for 5 hours, neutralised with the calculated amount of hydrochloric acid, and evaporated to a paste in a vacuum. A little acetone was added, the solid collected and dried, and the *iso*nicotinic acid sublimed under reduced pressure from an oil-bath at 250°. The sublimate, crystallised once from water, gave white needles (9·3 g.), m. p. 311°. For the purposes described below, the uncrystallised sublimate, m. p. 302—303°, was sufficiently pure.

It was found possible to exercise some control over the relative amounts of *iso*nicotinic acid and γ-picoline obtained, by varying the amount of permanganate. Smaller amounts gave more γ-picoline, the highest yield (3·8 g.) being obtained when 130 g. were used. The amount of *iso*nicotinic acid was then much lower (3·2 g.) and appreciable amounts of lutidine escaped oxidation.

Ethyl Pyridine-4-carboxylate.—*iso*Nicotinic acid (12 g.) was refluxed with freshly purified thionyl chloride (50 c.c.) for 4—5 hours, the excess removed by distillation, and absolute alcohol (50 c.c.) cautiously added. After standing for a few minutes and refluxing for 2—3 hours, the mixture was worked up as described for the crude ester above. Ethyl pyridine-4-carboxylate was obtained as a clear liquid of characteristic unpleasant odour (11·5 g.), b. p. 113°/30 mm. The hydrochloride formed white deliquescent needles, m. p. 154° (Pinner, *Ber.*, 1901, **34**, 4234,

gives 167°), which easily sublimed in a vacuum (Found: C, 50·3; H, 5·5. Calc. for $C_8H_9O_2N,HCl$: C, 50·1; H, 5·3%). The *picrate* formed yellow needles, m. p. 142° (Found: C, 44·5; H, 3·1. $C_8H_9O_2N,C_6H_3O_7N_3$ requires C, 44·2; H, 3·2%).

Dimethyl-4-pyridylcarbinol.—A Grignard solution prepared from magnesium (10 g.) and methyl iodide (20 c.c.) in ether (200 c.c.) was evaporated to remove the excess of methyl iodide, the residue taken up in ether (200 c.c.), and the filtered solution cooled to −10°, stirred, and treated with a solution of ethyl pyridine-4-carboxylate (12 g.) in ether (100 c.c.) during 1 hour. After 2 hours' stirring at −10°, the solution was refluxed for 5 hours and cooled, and the addition compound decomposed with ice and acetic acid. The ether was distilled off, the residue basified (sodium carbonate solution), and the oil extracted with chloroform, dried, and fractionated in a vacuum. Dimethyl-4-pyridylcarbinol was obtained as a colourless oil, b. p. 136°/25 mm., solidifying to a colourless crystalline solid (7·5 g.), which gave colourless needles, m. p. 132°, from benzene, freely soluble in alcohol or chloroform but sparingly in water or ether (Found: C, 70·1; H, 8·2. Calc. for $C_8H_{11}ON$: C, 70·0; H, 8·1%). No derivatives of this compound have been described previously. Emmert and Asendorf (*loc. cit.*) give only the m. p. of the compound (135°). The *picrate* separated from benzene as a yellow oil which slowly solidified and crystallised from benzene in slender, light yellow needles, m. p. 95° (Found: C, 46·3; H, 3·9. $C_8H_{11}ON,C_6H_3O_7N_3$ requires C, 45·9; H, 3·9%). The *picrolonate* formed slender yellow needles, decomp. 236°, which contained a molecule of alcohol of crystallisation (Found: C, 53·7; H, 5·5. $C_8H_{11}ON,C_{10}H_8O_5N_4,C_2H_6O$ requires C, 53·7; H, 5·6%). The *platinichloride* separated from dilute hydrochloric acid, on addition of alcohol, in golden-yellow plates, m. p. 194°, very soluble in water or alcohol (Found: C, 28·3; H, 3·4; Pt, 28·6. $2C_8H_{11}ON,H_2PtCl_6$ requires C, 28·1; H, 3·5; Pt, 28·5%).

Attempted Reduction of Dimethyl-4-pyridylcarbinol by Sodium and Alcohol.—A solution of the above compound (5 g.) in dry amyl alcohol or absolute alcohol (500 c.c.) was refluxed whilst sodium (50 g.) was cautiously added during 3 hours. When all the sodium had dissolved, the liquid was diluted with an equal volume of water, acidified (concentrated hydrochloric acid), and evaporated to 100 c.c. The sodium chloride was filtered off and washed with a little 50% hydrochloric acid and the combined filtrates were evaporated, basified with sodium hydroxide solution, and extracted with chloroform. Distillation in a vacuum yielded an oil (0·2 g.), b. p. 65—75°/15 mm., and dimethyl-4-pyridylcarbinol (3·8 g.). The oil had a powerful and distinctive odour and gave a light yellow picrate, m. p. 134°, identical with that of 4-*iso*propylpyridine (*v. infra*) (Found: C, 47·8; H, 4·1%).

4-iso*Propylpyridine.*—Dimethyl-4-pyridylcarbinol (0·7 g.), red phosphorus (1·4 g.), and hydriodic acid (6 c.c., *d* 1·7) were heated in a sealed tube at 140° for 60 hours. The resulting clear liquid was evaporated, the residue basified (sodium carbonate solution), and the liberated oil taken up in ether and distilled. The main fraction (b. p. 70—72°/21 mm.) was converted into the picrolonate and recovered, giving a colourless oil of pleasant odour (0·4 g.), b. p. 173°/760 mm., which was stable to alkaline permanganate (Found: C, 79·0; H, 9·4. Calc. for $C_8H_{11}N$: C, 79·3; H, 9·2%). The *picrate* separated from alcohol in small, light yellow needles, m. p. 135° (Found: C, 48·1; H, 4·3. $C_8H_{11}N,C_6H_3O_7N_3$ requires C, 48·0; H, 4·0%), and the platinichloride from dilute hydrochloric acid in golden-yellow plates, m. p. 202° (Found: C, 29·6; H, 4·1; Pt, 29·9. Calc. for $2C_8H_{11}N,H_2PtCl_6$: C, 29·4; H, 3·7; Pt, 30·0%). The *picrolonate* formed long, deep yellow needles, m. p. 208° (Found: C, 56·2; H, 5·2. $C_8H_{11}N,C_{10}H_8O_5N_4$ requires C, 56·1; H, 5·0%).

α-*Methylvinylpyridine.*—Dimethyl-4-pyridylcarbinol (1·0 g.) and phosphoric oxide (3 g.) were gradually heated to 80—85° in a sealed tube and held at this temperature for ½ hour. A little ice was added, followed by sodium hydroxide solution, and the base was distilled in steam. The distillate (75—100 c.c.) was acidified (concentrated hydrochloric acid) and evaporated to dryness, and the base liberated (sodium hydroxide solution) and extracted with ether. The dried filtered solution was added to a warm solution of picric acid (1·0 g.) in alcohol. The picrate was collected and decomposed (50% hydrochloric acid), giving 4-α-*methylvinylpyridine* as a colourless oil of strong pleasant odour, b. p. 82°/15 mm. (Found: C, 80·3; H, 7·4. C_8H_9N requires C, 80·6; H, 7·6%). It rapidly decolourised bromine water and neutral permanganate, was strongly alkaline to litmus, and was miscible with most organic solvents. The *picrate* separated from alcohol in felted needles containing a molecule of alcohol of crystallisation (Found: C, 49·2; H, 4·9. $C_8H_9N,C_6H_3O_7N_3,C_2H_6O$ requires C, 48·8; H, 4·6%). The *picrolonate* crystallised from alcohol in slender yellow needles, m. p. 231° (discoloured at 225°) (Found: C, 56·3; H, 4·7. $C_8H_9N,C_{10}H_8O_5N_4$ requires C, 56·4; H, 4·5%).

4-*Acetylpyridine.*—The method used was a modification of that given by Pinner (*Ber.*, 1901,

34, 4234). The 4-acetylpyridine was obtained as a colourless oil (2·5 g.) of pleasant odour, b. p. 106°/25 mm. (Found : C, 69·1; H, 6·0. Calc. for C_7H_7ON : C, 69·4; H, 5·9%). The picrate separated from alcohol in bright yellow needles, m. p. 128° (Found : C, 44·6; H, 3·1. Calc. for $C_7H_7ON,C_6H_3O_7N_3$: C, 44·6; H, 2·9%).

Methyl-4-pyridylcarbinol.—(a) 4-Acetylpyridine (1·0 g.) and aluminium *iso*propoxide (4 g.) in dry *iso*propyl alcohol (20 c.c.) were boiled under a short fractionating column until the distillate was free from acetone as tested for with 2 : 4-dinitrophenylhydrazine (2½—3 hours). The excess of the reagent was decomposed (50% hydrochloric acid, 50 c.c.), the solution evaporated to a paste, and the base liberated (sodium carbonate solution), extracted with chloroform, and distilled, giving a colourless oil (0·75 g.), b. p. 138—140°/30 mm., which solidified slowly over phosphoric oxide in a desiccator. The colourless *solid* crystallised from light petroleum (b. p. 40—60°)–benzene in large deliquescent prisms, m. p. 54°, very easily soluble in most organic solvents (Found : C, 68·3; H, 7·1. C_7H_9ON requires C, 68·2; H, 7·4%).

(b) 4-Acetylpyridine (1·0 g.) gave 0·8 g. of the above base when reduced catalytically (Found : C, 68·4; H, 7·3%).

The *picrate* of methyl-4-pyridylcarbinol separated from dry benzene in slender, sulphur-yellow needles which darkened in the light; m. p. 125° (Found : C, 43·9; H, 3·4. $C_7H_9ON,C_6H_3O_7N_3$ requires C, 44·3; H, 3·4%). The *picrolonate* was obtained from alcohol in yellow leaflets, m. p. 232° (Found : C, 52·5; H, 4·1. $C_7H_9ON,C_{10}H_8O_5N_4$ requires C, 52·7; H, 4·4%). The *platinichloride* separated from dilute hydrochloric acid, on addition of a little alcohol, in deep golden-yellow prisms, m. p. 206° (Found for material dried in a vacuum at 120° : C, 25·3; H, 2·9; Pt, 29·8. $2C_7H_9ON,H_2PtCl_6$ requires C, 25·6; H, 3·1; Pt, 29·8%).

Ethyl 1-Acetylpiperidine-4-carboxylate.—Ethyl piperidine-4-carboxylate (5 g.) in dry chloroform (30 c.c.) was cooled in ice, and an ice-cold solution of acetyl chloride (5 c.c.)in chloroform (30 c.c.) cautiously added. The mixture was treated with anhydrous potassium carbonate (10 g.), the whole refluxed for 1 hour, and the liquid filtered and distilled. The main fraction (6 g., b. p. 135—136°/1 mm.) was a colourless oil which did not crystallise (Found : C, 60·0; H, 8·8; N, 7·4. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·6; N, 7·0%).

Reaction of Methylmagnesium Iodide with Ethyl 1-Acetylpiperidine-4-carboxylate.—The above acetyl compound (5 g.) in absolute ether (30 c.c.) was cooled in ice and stirred while a Grignard solution, prepared from magnesium (10 g.) and methyl iodide (28 c.c.) in ether (60 c.c.) and purified as described previously, was slowly dropped in. The grey viscid mass, after standing in the ice overnight, was boiled for a few minutes and then decomposed with ice and acetic acid. The ether was removed, and the residue basified (sodium hydroxide solution) and extracted with chloroform. The oil remaining after removal of the solvent was treated with absolute alcohol (10 c.c.) and kept in a refrigerator for a few days. The colourless crystalline solid which separated was collected and recrystallised from alcohol. This compound (0·5 g.), m. p. 233°, has not been identified; it formed long silky needles which sublimed easily in a vacuum and readily dissolved in water, giving a neutral solution (Found : C, 68·0, 67·8; H, 9·8, 9·85%). The alcoholic mother-liquor from the initial crystallisation of this substance yielded *dimethyl-1-acetyl-4-piperidylcarbinol* as a colourless oil (2·5 g.), b. p. 162—165°/1 mm., which did not crystallise on standing (Found : C, 64·6; H, 10·7; N, 7·7. $C_{10}H_{19}O_2N$ requires C, 64·8; H, 10·4; N, 7·6%). The compound was not attacked by alcoholic potash or concentrated hydrochloric or hydrobromic acid during 2—3 hours' boiling. Further boiling resulted in the formation of a brown gum from which nothing definite could be isolated.

Ethyl 1-Benzoylpiperidine-4-carboxylate.—Ethyl piperidine-4-carboxylate (14 c.c.) in chloroform (40 c.c.) was treated with benzoyl chloride (12·8 c.c.) in chloroform (20 c.c.) with cooling. Anhydrous potassium carbonate (20 g.) was added, the mixture refluxed for 4 hours, and the liquid filtered and fractionated in a vacuum. The fraction, b. p. 190—195°/1 mm., slowly set to a white crystalline solid (18—20 g.), m. p. 60—65°, which was pure enough for subsequent experiments. Crystallisation from benzene–light petroleum gave stout pointed needles, m. p. 77°, very soluble in alcohol but sparingly soluble in ether (Found : C, 69·1; H, 7·4. Calc. for $C_{15}H_{19}O_3N$: C, 68·9; H, 7·3%).

Reaction of Methylmagnesium Iodide with Ethyl 1-Benzoylpiperidine-4-carboxylate.—The treatment of the above benzoyl compound (12 g.) in ether (200 c.c.) and chloroform (50 c.c.) with a purified Grignard solution prepared from magnesium (36 g.) and methyl iodide (80 c.c.) in dry ether (250 c.c.) and the subsequent procedure (3 hours' boiling instead of a few minutes) were the same as those described for the acetyl analogue. The oil finally obtained from the chloroform extract was fractionated in a vacuum. Two main fractions were taken : (A) 0·9—1·0 g., b. p. 80—120°/1 mm.; (B) 5·5—6·0 g., b. p. 175—195°/1 mm. The considerable residue

of organic material crystallised from ethyl acetate in faintly yellow plates, m. p. 205—206° (Found : C, 73·6, 74·1; H, 7·0, 7·5; N, 10·2%). Fraction (A) was dissolved in dilute hydrochloric acid (20 c.c.), the liquid evaporated, and the distillate extracted with ether; distillation of the dried extracts gave acetophenone (0·3 g., b. p. 92—93°/15 mm.), identified as the semicarbazone, m. p. 201°, and the oxime, m. p. 59°, not depressed by authentic specimens. The residue from the evaporation of the acid solution was basified (sodium hydroxide solution) and extracted with chloroform and the oil left after evaporation of the dried extracts was distilled in a vacuum. The product (0·2 g., b. p. 140—143°/25 mm.) solidified on cooling and crystallised in long needles, m. p. 136°, identical with the base prepared by hydrolysing the main fraction (below) (Found : C, 67·2; H, 11·5%). Fraction (B) was dissolved in alcohol (20 c.c.), treated with potassium hydroxide (3·0 g.) in 50% alcohol (20 c.c.), and the mixture refluxed for 6—8 hours. The *dimethyl-4-piperidylcarbinol* was removed in steam, the distillate (400—450 c.c.) acidified (concentrated hydrochloric acid) and evaporated, and the base recovered as a colourless oil, b. p. 140—142°/25 mm., rapidly setting to a crystalline solid (0·6 g.), m. p. 132°. Crystallisation from benzene–light petroleum (b. p. 60—80°) or sublimation from the water-bath gave colourless silky needles, m. p. 136° (Found : C, 67·1; H, 11·6; N, 10·2. $C_8H_{17}ON$ requires C, 67·1; H, 11·9; N, 9·8%). The *picrate* was obtained in dimorphic modifications, one of which, light yellow prisms, m. p. 156° (Found : C, 45·0; H, 5·5. $C_8H_{17}ON,C_6H_3O_7N_3$ requires C, 45·1; H, 5·4%), could be converted into the other, deep golden-yellow needles, m. p. 187° (Found : C, 45·2; H, 5·6%), by solution in alcohol and seeding. The *picrolonate* formed clusters of light yellow needles, m. p. 265° (decomp.), from alcohol (Found : C, 53·1; H, 6·0. $C_8H_{17}ON,C_{10}H_8O_5N_4$ requires C, 53·0; H, 6·2%). Fraction (B) contained, in addition to dimethyl-1-benzoyl-4-piperidylcarbinol, a considerable amount of organic material resistant to hydrolysis. The alkaline residue from the steam-distillation of dimethyl-4-piperidylcarbinol was extracted with chloroform and the oil remaining after removal of the solvent was fractionated through a short column in a vacuum. Two substances were isolated; the first, obtained by many distillations of a fraction, b. p. 175—180°/1 mm., was a colourless viscid oil, b. p. 176°/1 mm. (Found : C, 73·8; H, 8·1; N, 6·7%), and the second, obtained in a similar manner from the fraction, b. p. 195—198°/1 mm., was a faintly yellow liquid which slowly solidified to a colourless crystalline mass, m. p. 25—30° (Found : C, 71·3; H, 8·1; N, 6·3%). These compounds were obtained in approximately equal amounts (2·5 g.).

4-α-*Bromo*iso*propylpiperidine Hydrobromide.*—Dimethyl-4-piperidylcarbinol (1·0 g.) and hydrobromic acid (10 c.c., *d* 1·7) were refluxed for 15 minutes, and the excess of acid at once removed under reduced pressure. The solid residue crystallised from absolute alcohol in colourless plates (1·4 g.), m. p. 192° (Found : C, 33·5; H, 5·9; N, 4·9. $C_8H_{16}NBr,HBr$ requires C, 33·5; H, 6·0; N, 4·9%).

Reaction of 4-α-*Bromo*iso*propylpiperidine Hydrobromide with Silver Oxide.*—The above hydrobromide (1 g.) and dry, freshly prepared silver oxide (2·0 g.) were cautiously mixed in a mortar and sealed up in a number of small thick-walled tubes. Each was gently warmed in the water-bath until a vigorous reaction took place, then heated for ½ hour longer and allowed to cool, and the contents washed out with a little water. The united product was basified (concentrated sodium hydroxide solution) and distilled in steam. The distillate was acidified (concentrated hydrochloric acid) and evaporated to dryness, and the residue basified (sodium hydroxide solution) and extracted with ether. The solvent was removed, light petroleum (b. p. 40—60°, 2 c.c.) added, and the mixture kept at 0° for 12 hours. The small amount of dimethyl-4-piperidylcarbinol was filtered off, and the filtrate distilled, giving a colourless *oil* (0·1 g.), b. p. 58—62°/12 mm. (Found : C, 76·3; H, 11·9. $C_8H_{15}N$ requires C, 76·7; H, 12·1%). The *picrolonate* separated from alcohol in deep yellow prisms, m. p. 221° (Found : C, 55·6; H, 6·2. $C_8H_{15}N,C_{10}H_8O_5N_4$ requires C, 55·5; H, 6·0%).

4-iso*Propylpiperidine.*—The above base (0·1 g.) in glacial acetic acid (5 c.c.) was shaken for 12 hours with platinum oxide (0·01 g.) in hydrogen at 100 lb./sq. in. The liquid was filtered, acidified with a few drops of concentrated hydrochloric acid, and evaporated, and the base recovered as a colourless oil (0·08 g.) of strong unpleasant smell, b. p. 66—70°/15 mm., completely miscible with water, giving a strongly alkaline solution (Found : C, 75·5; H, 12·9. Calc. for $C_8H_{17}N$: C, 75·6; H, 13·4%). The platinichloride separated from dilute hydrochloric acid, on addition of a little alcohol, in orange leaflets, m. p. 182° (Found for material dried at 100°/15 mm. : C, 28·7; H, 5·2; Pt, 29·6. Calc. for $2C_8H_{17}N,H_2PtCl_6$: C, 28·9; H, 5·4; Pt, 29·4%).

Reaction of Ethyl Piperidine-4-carboxylate with Methylmagnesium Iodide.—To a Grignard reagent prepared from magnesium (8 g.) and methyl iodide (25 c.c.), purified in the usual way,

and dissolved in ether (150 c.c.), a solution of ethyl piperidine-4-carboxylate (6 c.c.) in ether (100 c.c.) was slowly added with stirring at − 15°. The mixture was kept at 0° for 12 hours, then cooled strongly and decomposed with ice and acetic acid. The ether was removed on the water-bath, and the residue basified (concentrated sodium hydroxide) and distilled in steam. The steam-distillate (300—350 c.c.) was acidified to Congo-red (concentrated hydrochloric acid) and evaporated under reduced pressure, and the *base* liberated by potassium carbonate solution, extracted with ether, and distilled, giving a colourless oil of pleasant odour (2·5 g.), b. p. 108—110°/25 mm. (Found: C, 66·1, 65·9; H, 11·1, 10·9; N, 11·1. $C_7H_{13}ON$ requires C, 66·1; H, 10·3; N, 11·0%). The *picrate* separated slowly from alcohol in stout yellow needles, m. p. 266° (decomp.) (Found: C, 43·9; H, 4·5. $C_7H_{13}ON,C_6H_3O_7N_3$ requires C, 43·8; H, 4·5%). The *picrolonate* formed small, deep yellow prisms, m. p. 206°, from alcohol (Found: C, 52·3; H, 5·3. $C_7H_{13}ON,C_{10}H_8O_5N_4$ requires C, 52·1; H, 5·4%). The *platinichloride* formed small, deep orange prisms, m. p. 206°, from dilute hydrochloric acid and alcohol (Found: C, 27·0; H, 4·1; Pt, 27·7. $2C_7H_{13}ON,H_2PtCl_6,C_2H_6O$ requires C, 27·0; H, 4·8; Pt, 27·5%). Nothing definite was isolated in attempts to prepare, by the usual methods, the oxime, hydrazone, semicarbazone or phenylhydrazone. The base was recovered unchanged and identified by its picrolonate after treatment with excess of methylmagnesium iodide and after boiling for as long as 84 hours with amalgamated zinc and concentrated hydrochloric acid. The compound also distilled unchanged from zinc dust, gave no acetone on boiling with aluminium *iso*propoxide, and no detectable absorption of hydrogen was noted on shaking with a platinum catalyst in acetic acid. On treatment with phosphorus pentachloride in chloroform a violent reaction took place and the mixture rapidly darkened; nothing definite could be obtained after basification with potassium carbonate and extraction with chloroform. By treating the reaction mixture with 50% hydrochloric acid and granulated tin a small amount of unchanged base was recovered, identified as picrolonate (0·01 g., m. p. 205°, from 0·2 g. of the base). On treatment with methyl iodide a vigorous reaction took place with formation of a gum which crystallised from acetone in colourless prisms, m. p. 170° (after sintering at 152°) (Found: C, 35·7; H, 5·4. $C_7H_{13}ON,CH_3I$ requires C, 35·7; H, 5·9%). This *compound* (0·25 g.) was dissolved in water and treated with freshly prepared silver oxide (2·5 g.); an oil, b. p. 108—109°/25 mm., was obtained by chloroform extraction (Found: C, 67·8; H, 11·1. $C_8H_{15}ON$ requires C, 68·1; H 10·6%). The *picrolonate* of this base formed light yellow leaflets. m. p. 215° (Found: C, 53·1; H, 5·8. $C_8H_{15}ON,C_{10}H_8O_5N_4$ requires C, 53·3; H, 5·7%).

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