312. *Synthetic Analgesics. Part X. Tertiary Carbinols and Derivatives from Mannich Bases.*

By A. L. Morrison and H. Rinderknecht.

By the action of Grignard reagents on Mannich bases derived from acetophenone, *cyclo*hexanone, and 1-tetralone, tertiary carbinols have been made. The acyl derivatives of these carbinols have only slight analgesic activity.

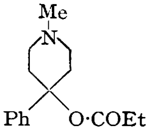
Syntheses of 6-phenyl-3-methyloctahydro-5 : 6-benz-1 : 3-oxazine and 6 : 6-diphenyl-3-methyltetrahydro-1 : 3-oxazine are described.

Some of the compounds have marked spasmolytic action.

The high analgesic potencies of 6-dimethylamino-4 : 4-diphenylheptan-3-one (amidone) (I) and 4-propionoxy-4-phenyl-1-methylpiperidine (II) have now been well established (Report No. PB-981, U.S.A. Office of the Publication Board, Department of Commerce; Foster and Carman, *J. Pharm. Exp. Ther.*, 1947, **91**, 195). The possibility that a compound such as dimethyl-3-propionoxy-3 : 3-diphenylpropylamine (III; R = R′ = Me, R″ = EtCO), in which are combined features of both these potent analgesics, might also possess considerable activity, was considered by us some time ago. The carbinol (III; R = R′ = Me, R″ = H) was readily prepared by the action of phenylmagnesium bromide on the Mannich base made from acetophenone and dimethylamine.

$Ph_2C(COEt){\cdot}CH_2{\cdot}CHMe{\cdot}NMe_2$
(I.)

$Ph_2C(OR''){\cdot}CH_2{\cdot}CH_2{\cdot}NRR'$
(III.)

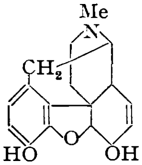


(II.)

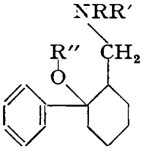
Independently of our work, similar experiments have been reported recently in America (Becker, Ananenko, Glenwood, and Miller, *Fed. Proc.*, 1946, **5**, 163; Ruddy and Buckley, 110th Meeting Amer. Chem. Soc., 14K; Report No. PB-981, U.S.A. Office of the Publication Board, Department of Commerce, p. 38), in Germany (Hoechst Nos. 10,210 and 10,214; I.G. Farbenind., F.P. 890,633/1942), and in England (Winthrop Chemical Co. Inc., B.P. Appl. 2255/47; Adamson, *J.*, 1949, S 144).

We now wish to report the preparation of a number of compounds in this series, and their acyl and other derivatives, details of which will be found in the Experimental section.

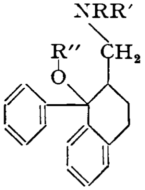
We also considered that acyl derivatives of the carbinols (V and VI; R″ = H), prepared by the action of aryl- and alkyl-magnesium halides on Mannich bases derived from *cyclo*hexanone and 1-tetralone would be of interest as they bear some structural relationship to morphine (IV).



(IV.)



(V.)



(VI.)

Since the completion of this work, Lee, Ziering, Berger, and Heineman (" Jubilee Volume Emil Barell," 1946, p. 264) have reported the preparation of a few representatives of this series.

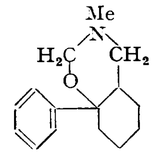
We have found generally that the yields of *tert.*-alcohols formed by the action of Grignard reagents on Mannich bases are not good but can usually be improved if the finely powdered hydrochloride is added in portions to a well-cooled, stirred solution of the Grignard reagent in ether.

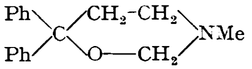
In all the publications cited mention is made, and in some cases details are given, of the dehydration of such tertiary carbinols to the unsaturated compounds, and of the subsequent hydrogenation to give the propane derivatives. We have also dehydrated the tertiary alcohols by heating them for about 48 hours with 98% formic acid and hydrogenated the resultant unsaturated amines.

Finally, in an attempt to simulate the piperidine ring of morphine, 1-phenyl-2-methylaminomethyl*cyclo*hexan-1-ol was treated with formaldehyde to give 6-phenyl-3-methyloctahydro-

5 : 6-benz-1 : 3-oxazine (VII). In the same manner 6 : 6-diphenyl-3-methyltetrahydro-1 : 3-oxazine (VIII) was made from 3-methylamino-1 : 1-diphenylpropan-1-ol.

(VII.)





(VIII.)

None of the compounds reported in this communication possessed analgesic activity greater than that of pethidine. Some, however, exhibited considerable antihistamine and spasmolytic properties and the results of this pharmacological investigation will be reported elsewhere.

EXPERIMENTAL.

3-*Dimethylamino*-1 : 1-*diphenyl*-1-*propanol* (III; R = R′ = Me, R″ = H).—ω-Dimethylaminopropiophenone hydrochloride (19·6 g.) was added in small portions, with cooling and stirring, to an ethereal solution of phenylmagnesium bromide prepared from magnesium (4·9 g.) and bromobenzene (32 g.). The mixture was left for 16 hours at room temperature and then decomposed by stirring with excess of ammonium chloride solution. The product was extracted with benzene and, after removal of the benzene, the solid residue was recrystallised from light petroleum (b. p. 80—100°) to give the pure tertiary alcohol, m. p. 164—165° (11·6 g., 55%) (Found : C, 79·4; H, 8·1; N, 5·6. Calc. for $C_{17}H_{21}ON$: C, 80·0; H, 8·2; N, 5·5%).

When the above base was warmed with acetic anhydride for a short time and then left at room temperature overnight and the excess of acetic anhydride then distilled off, a product was obtained, practically insoluble in water and soluble in ether. It proved to be the *acetate*, m. p. 115—118° when recrystallised from light petroleum (b. p. 80—100°) (Found : C, 70·5; H, 7·6; N, 3·8. $C_{21}H_{27}O_4N$ requires C, 70·6; H, 7·6; N, 3·9%), of the 1-*acetoxy*-base; the latter, crystallised from light petroleum (b. p. 60—80°), had m. p. 111—114° (Found : C, 77·2; H, 7·9; N, 4·6. $C_{19}H_{23}O_2N$ requires C, 76·8; H, 7·7; N, 4·7%).

3-*Dimethylamino*-1-*propionoxy*-1 : 1-*diphenylpropane propionate* (III; R = R′ = Me, R″ = EtCO), prepared similarly, had m. p. 94—96° when recrystallised from light petroleum (b. p. 40—60°) (Found : C, 71·7; H, 8·2; N, 4·1. $C_{23}H_{31}O_4N$ requires C, 71·7; H, 8·0; N, 3·6%).

The base (III; R = R′ = Me, R″ = H) (5 g.) was added to a solution of nicotinyl chloride (5·5 g.) in dry pyridine. After being kept overnight at room temperature, the pyridine was distilled off at 12 mm. The residue was dissolved in benzene and washed with a dilute solution of sodium carbonate and then water. Concentration of the benzene solution left an oily product which became partly crystalline *in vacuo* in presence of concentrated sulphuric acid. Recrystallisation from light petroleum (b. p. 60—80°) gave the pure 1-*nicotinate*, m. p. 92—94° (Found : C, 76·9; H, 6·7; N, 7·15. $C_{23}H_{24}O_2N_2$ requires C, 76·7; H, 6·7; N, 7·8%).

3-*Dimethylamino*-1 : 1-*diphenylprop*-1-*ene*.—Refluxing a solution of (III; R = R′ = Me, R″ = H) in formic acid for 48 hours yielded the unsaturated base with properties described by Adamson (*loc. cit.*). It gave a *picrate*, m. p. 159—160° (Found : C, 59·3; H, 4·8; N, 12·4. $C_{23}H_{22}O_7N_4$ requires C, 59·2; H, 4·7; N, 12·0%). The *picrate* of 3-dimethylamino-1 : 1-diphenylpropane (Found : C, 59·3; H, 4·9; N, 12·3. $C_{23}H_{24}O_7N_4$ requires C, 59·0; H, 5·1; N, 12·0%) also melted at 159° but a mixture of the two picrates melted at 134—140°.

3-*Dimethylamino*-1-*phenyl*-1-o-*tolylpropan*-1-*ol*.—This *base* was prepared in a manner as described for (III; R = R′ = Me, R″ = H), using *o*-tolylmagnesium bromide, and obtained as a solid, m. p. 131—134°, from acetone (Found : C, 80·4; H, 8·8; N, 4·7. $C_{18}H_{23}ON$ requires C, 80·3; H, 8·6; N, 5·2%). Heating it with propionic anhydride gave 3-*dimethylamino*-1-*propionoxy*-1-*phenyl*-1-o-*tolylpropane propionate* m. p. 81—83° [from light petroleum ether (b. p. 40—60°)] (Found : C, 72·8; H, 8·1; N, 3·8. $C_{24}H_{33}O_4N$ requires C, 72·2; H, 8·3; N, 3·5%).

ω-*Benzylmethylaminopropiophenone Hydrochloride*.—Benzylmethylamine hydrochloride (17·5 g.), acetophenone (14 g.), and paraformaldehyde (7 g.) in ethanol (75 ml.) were heated on the steam-bath under reflux for 20 minutes. The clear solution obtained was concentrated to about half its volume and on cooling the *hydrochloride* crystallised, having m. p. 196—198° (9·6 g.) (Found : Cl′, 12·2. $C_{17}H_{20}ONCl$ requires Cl′, 12·3%).

3-*Benzylmethylamino*-1 : 1-*diphenylpropan*-1-*ol* (III; R = Me, R′ = Ph·CH₂, R″ = H).—In the usual manner ω-benzylmethylaminopropiophenone hydrochloride (9·2 g.) was treated with phenylmagnesium bromide, prepared from bromobenzene (11 g.) and magnesium (1·7 g.), to give the tert.-*alcohol*, which distilled at 180—184°/0·2 mm. and had m. p. 100—102° (Found : C, 83·2; H, 7·7; N, 4·9. $C_{23}H_{25}ON$ requires C, 83·4; H, 7·6; N, 4·2%). The *hydrochloride*, crystallised from alcohol–ether, had m. p. 195° (Found : N, 3·9. $C_{23}H_{26}ONCl$ requires N, 3·8%).

3-*Methylamino*-1 : 1-*diphenylpropan*-1-*ol* (III; R = Me, R′ = R″ = H).—The above base (6·9 g.) in alcohol was hydrogenated in the presence of palladium–charcoal in the usual manner, to remove the benzyl group. The product distilled at 140—150°/0·2 mm. and was recrystallised from alcohol to give the pure alcohol, m. p. 145—147° (cf. Adamson, *loc. cit.*) (Found : C, 79·8; H, 7·9; N, 5·9. Calc. for $C_{16}H_{19}ON$: C, 79·7; H, 7·9; N, 5·8%).

6 : 6-*Diphenyl*-3-*methyltetrahydro*-1 : 3-*oxazine* (VIII).—A mixture of 3-methylamino-1 : 1-diphenylpropan-1-ol (1·9 g.), 40% formaldehyde solution (1·2 ml.), and potassium carbonate (1·1 g.) in alcohol (10 ml.) was shaken for 8 hours. Water was then added, the precipitated product extracted with ether, and the ethereal solution well washed with water, dried (Na_2SO_4), and concentrated. The residue

distilled at 133—135°/0·1 mm. to give the *tetrahydro*-1 : 3-*oxazine*, m. p. 83—85° (1·6 g.) (Found : C, 80·9; H, 7·6; N, 5·55; Active H, 0. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5; N, 5·5; Active H, 0%).

3-*Dimethylamino*-1-*phenyl*-1-*benzylpropan*-1-*ol*.—Treatment of ω-dimethylaminopropiophenone hydrochloride (21·3 g.) with benzylmagnesium bromide, prepared from benzyl bromide (44 g.) and magnesium (6 g.) in ether, gave the tert.-*alcohol* in very poor yield. Recrystallised from light petroleum (b. p. 40—60°) it melted at 80—82° (Found : C, 80·6; H, 8·7; N, 4·85. $C_{18}H_{23}ON$ requires C, 80·3; H, 8·6; N, 5·2%).

1-*Dimethylaminomethylpropiophenone Hydrochloride*.—Propiophenone (28 g.), dimethylamine hydrochloride (9·4 g.), and paraformaldehyde (15 g.) in ethanol (100 ml.) were heated under reflux until the aldehyde went into solution. The product left after distilling off the alcohol was recrystallised from 2 : 1 ethanol–acetone, the *hydrochloride*, m. p. 152—154°, being obtained (Found : Cl′, 16·1. $C_{12}H_{18}ONCl$ requires Cl′, 15·4%).

3-*Dimethylamino*-1 : 1-*diphenyl*-2-*methylpropan*-1-*ol*.—The above Mannich base hydrochloride (3 g.) was treated with phenylmagnesium bromide, prepared from bromobenzene (4·6 g.) and magnesium (0·5 g.), to give the tert.-*alcohol* which, recrystallised from acetone, had m. p. 158—161° (Found : C, 79·8; H, 8·1; N, 5·2. $C_{18}H_{23}ON$ requires C, 80·2; H, 8·6; N, 5·2%).

1-*Phenyl*-2-*dimethylaminomethyl*cyclo*hexan*-1-*ol* (V; $R = R' = \text{Me}$, $R'' = \text{H}$).—2-Dimethylamino-*cyclo*hexan-1-one (5 g.) and phenylmagnesium bromide, prepared from bromobenzene (10 g.) and magnesium (1·6 g.), in the usual way gave the tert.-*alcohol*, b. p. 108—111°/0·5 mm. (3·8 g., 50%) (Found : C, 76·5; H, 10·0; N, 5·7. $C_{15}H_{23}ON$ requires C, 77·2; H, 9·9; N, 6·0%). Treatment of the alcohol with acetic anhydride in the usual way gave 1-*acetoxy*-1-*phenyl*-2-*dimethylaminomethyl*cyclo*hexane* (V; $R = R' = \text{Me}$, $R'' = \text{Ac}$), a low-melting solid, b. p. 130—131°/0·8 mm. (Found : C, 74·4; H, 9·25; N, 4·8. $C_{17}H_{25}O_2N$ requires C, 74·2; H, 9·1; N, 5·1%). 1-*Propionoxy*-1-*phenyl*-2-*dimethylaminomethyl*cyclo*hexane* (V; $R = R' = \text{Me}$, $R'' = \text{EtCO}$) was also a low-melting solid, b. p. 123—125°/0·4 mm. (Found : C, 74·35; H, 9·35; N, 4·4. $C_{18}H_{27}O_2N$ requires C, 74·75; H, 9·35; N, 4·9%).

1-*Benzoyloxy*-1-*phenyl*-2-*dimethylaminomethyl*cyclo*hexane* (V; $R = R' = \text{Me}$, $R'' = \text{Bz}$).—Benzoylation of the alcohol (5 g.) was carried out by heating it in acetone (25 ml.) with benzoyl chloride (3·3 g.) under reflux for 1 hour. The acetone was distilled off and water added. The aqueous solution was made alkaline and extracted with ether, and the ethereal solution dried and concentrated. Distillation of the residue gave the *ester* which, recrystallised from alcohol, had m. p. 108—111° (Found : C, 78·1; H, 7·8; N, 4·0. $C_{22}H_{27}O_2N$ requires C, 78·35; H, 8·0; N, 4·15%).

1-*Phenyl*-2-*dimethylaminomethyl*cyclo*hex*-1- *or* -6-*ene*.—The above alcohol (4 g.) was dehydrated by heating it with 98% formic acid (20 ml.) at 140° for 48 hours to give a product, the *picrate* of which had m. p. 140—141° (from alcohol) (Found : C, 56·75; H, 5·4. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4%).

1-*Phenyl*-2-*dimethylaminomethyl*cyclo*hexane*.—Hydrogenation of the above unsaturated base (1 g.) in alcohol (20 ml.) in presence of palladium–charcoal gave the saturated *base*, b. p. 147—149°/13 mm. (Found : C, 82·7; H, 10·5. $C_{15}H_{23}N$ requires C, 82·9; H, 10·6%). It formed a *picrate* m. p. 139—141° (Found : N, 12·6. $C_{21}H_{26}O_7N_4$ requires N, 12·6%). A mixture with the picrate of the starting material melted at 122—128°.

2-*Benzylmethylaminomethyl*cyclo*hexan*-1-*one Hydrochloride*.—Benzylmethylamine hydrochloride (18·2 g.), *cyclo*hexanone (14·7 g.), and paraformaldehyde (9 g.) in ethanol (75 ml.) were heated on the steam-bath under reflux for 30 minutes. The alcohol was then distilled off and the solid residue recrystallised from ethyl acetate to give the pure *hydrochloride*, m. p. 144—146° (16·6 g., 54%) (Found : Cl′, 13·2. $C_{15}H_{22}ONCl$ requires Cl′, 13·3%).

1-*Phenyl*-2-*benzylmethylaminomethyl*cyclo*hexan*-1-*ol* (V; $R = \text{Me}$, $R' = CH_2Ph$, $R'' = \text{H}$).—Reaction of the above Mannich base hydrochloride with 2·2 moles of phenylmagnesium bromide in the usual manner gave a 29% yield of the *alcohol*, which was obtained as a low-melting solid with b. p. 170—173°/0·6 mm. (Found : N, 4·5. $C_{21}H_{27}ON$ requires N, 4·6%).

1-*Phenyl*-2-*methylaminomethyl*cyclo*hexan*-1-*ol* (V; $R = \text{Me}$, $R' = R'' = \text{H}$).—Hydrogenolysis of the benzyl group of the above compound in the usual way gave the *alcohol* as a liquid, b. p. 110—112°/0·4 mm. (Found : C, 76·4; H, 9·4; N, 6·55. $C_{14}H_{21}ON$ requires C, 76·7; H, 9·6; N, 6·4%).

6-*Phenyl*-3-*methyloctahydro*-5 : 6-*benz*-1 : 3-*oxazine* (VII).—The above alcohol (2 g.) was dissolved in ethanol (10 ml.), potassium carbonate (1·26 g.) and 40% formaldehyde solution (1·37 ml.) were added, and the mixture was shaken for 8 hours. Worked up in the normal way, the *oxazine* was obtained as a solid, m. p. 70—72°, b. p. 92—94°/0·3 mm. (Found : C, 77·9; H, 9·1; N, 6·1. $C_{15}H_{21}ON$ requires C, 77·9; H, 9·1; N, 6·1%).

1-*Phenyl*-2-*piperidinomethyl*cyclo*hexan*-1-*ol*.—2-Piperidinomethyl*cyclo*hexan-1-one hydrochloride and phenylmagnesium bromide reacted in the usual manner to give a poor yield of the tert.-*alcohol* which melted at 83—85° when recrystallised from alcohol–water (Found : C, 79·2; H, 9·7; N, 4·8. $C_{18}H_{27}ON$ requires C, 79·1; H, 9·9; N, 5·1%).

6-*Methyl*-2-*dimethylaminomethyl*cyclo*hexan*-1-*one Hydrochloride*.—2-Methyl*cyclo*hexanone (11·2 g.), dimethylamine hydrochloride (9 g.), and paraformaldehyde (6 g.) in ethanol (50 ml.) were heated under reflux for 30 minutes. On concentration of the alcoholic solution the *hydrochloride* crystallised. Recrystallised from alcohol–acetone, it had m. p. 167—169° (Found : Cl′, 16·8. $C_{10}H_{20}ONCl$ requires Cl′, 17·1%).

1-*Phenyl*-6-*methyl*-2-*dimethylaminomethyl*cyclo*hexan*-1-*ol*.—Addition of the above hydrochloride (9 g.) to phenylmagnesium bromide, prepared from bromobenzene (14·8 g.) and magnesium (2·9 g.), gave a 50% yield of the tert.-*alcohol* which was obtained as a low-melting solid, b. p. 106—107°/0·2 mm. (Found : C, 77·7; H, 10·1; N, 5·4. $C_{16}H_{25}ON$ requires C, 77·8; H, 10·1; N, 5·7%).

1-*Phenyl*-2-*dimethylaminomethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol* (VI; $R = R' = \text{Me}$, $R'' = \text{H}$).—2-Dimethylaminomethyl-1-tetralone hydrochloride and phenylmagnesium bromide (2·2 moles) gave a 56% yield of the *tetrahydronaphthol*, a colourless viscous oil, b. p. 170°/0·6 mm. (Found : C, 81·1; H, 8·2; N, 4·5. $C_{19}H_{23}ON$ requires C, 81·1; H, 8·2; N, 5·0%). Acetylation with acetic anhydride gave the 1-*acetate* as a viscous oil, b. p. 170°/0·1 mm. (Found : C, 77·9; H, 7·8; N, 4·3. $C_{21}H_{25}O_2N$ requires C, 78·0; H, 7·7; N, 4·3%).

1-*Phenyl*-2-*dimethylaminomethyl*-3 : 4-*dihydronaphthalene*.—The above tetrahydronaphthol was dehydrated by heating it in formic acid solution for 48 hours. The crude product gave a *picrate* which on recrystallisation from alcohol–acetone melted at 199—200° (Found : C, 61·15; H, 5·0; N, 11·6. $C_{25}H_{24}O_7N_4$ requires C, 61·0; H, 4·9; N, 11·4%).

1-*Phenyl*-2-*dimethylaminomethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*.—Hydrogenation of the crude product obtained in the previous experiment in the presence of palladium–charcoal gave an oil, the *picrate* of which, recrystallised from alcohol, melted at 183—185° (Found : N, 11·5. $C_{25}H_{26}O_7N_4$ requires N, 11·3%).

1-cyclo*Hexyl*-2-*dimethylaminomethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol Hydrochloride*.—Addition of 2-dimethylaminomethyl-1-tetralone hydrochloride to *cyclo*hexylmagnesium bromide in ether gave a small yield of product which yielded a *hydrochloride*, sparingly soluble in water, and on recrystallisation from alcohol melted at 236—237° (Found : C, 70·1; H, 9·25; N, 4·3. $C_{19}H_{30}ONCl$ requires C, 70·6; H, 9·3; N, 4·3%).

1-*Propionoxy*-1-cyclo*hexyl*-2-*dimethylaminomethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene Hydrochloride*.—The above hydrochloride was heated with propionic anhydride at 105° until it had all dissolved; the propionic anhydride was distilled off and the residue recrystallised from acetone–ether. The *hydrochloride* melted at 180° (Found : N, 3·5. $C_{22}H_{34}O_2NCl$ requires N, 3·7%).

2-*Dimethylaminomethyl*-1-*ethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol*.—Addition of 2-dimethylaminomethyl-1-tetralone hydrochloride (12 g.) to ethylmagnesium iodide (17 g. of ethyl iodide, 2·9 g. of magnesium) in ether gave a small yield of product isolated as the *hydrochloride* (4 g.), which, recrystallised from acetone–alcohol, melted at 209—210° (Found : C, 67·0; H, 9·0; N, 4·9. $C_{15}H_{24}ONCl$ requires C, 66·9; H, 8·9; N, 5·2%).

1-*Propionoxy*-2-*dimethylaminomethyl*-1-*ethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*.—Heating the above hydrochloride (0·5 g.) in propionic anhydride (50 ml.) at 90° until all had dissolved, distilling off some of the propionic anhydride, and cooling, yielded the *hydrochloride*, m. p. 183° (Found : C, 66·2; H, 8·6; Cl, 10·7. $C_{18}H_{28}O_2NCl$ requires C, 66·5; H, 8·6; Cl, 10·8%).

1-*Phenyl*-2-*piperidinomethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthol*.—Addition of 2-piperidinomethyl-1-tetralone hydrochloride (8·9 g.) to phenylmagnesium bromide (bromobenzene, 11 g.; magnesium, 1·49 g.) in ether gave the crude *tert*.-alcohol which was isolated as the *hydrochloride*, m. p. 238—239° (decomp.). This was recrystallised from alcohol–ether and from its analysis appears to contain one mole of alcohol of crystallisation (Found : C, 71·3; H, 8·4; N, 3·6. $C_{22}H_{28}ONCl,C_2H_5{\cdot}OH$ requires C, 71·4; H, 8·4; N, 3·5%).

1-*Phenyl*-2-*piperidinomethyl*-3 : 4-*dihydronaphthalene*.—The base (2 g.) liberated from the above hydrochloride was dehydrated in the usual manner to give an oil (1·5 g.) which boiled at 175—180°/0·5 mm. and gave a *hydrochloride*, m. p. 189—190°, containing 1 mole of alcohol of crystallisation (Found : C, 75·0; H, 8·1; N, 4·0. $C_{22}H_{26}NCl,C_2H_5{\cdot}OH$ requires C, 74·7; H, 8·3; N, 3·6%). The *picrate*, crystallised from alcohol, melted at 156—158° (Found : C, 63·3; H, 4·7; N, 10·5. $C_{28}H_{28}O_7N_4$ requires C, 63·2; H, 5·3; N, 10·5%).

1-*Phenyl*-2-*piperidinomethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*.—The base (1·9 g.) liberated from the above hydrochloride was dissolved in glacial acetic acid (20 ml.) and hydrogenated in the presence of platinum oxide (0·1 g.) to give an oil, the *hydrochloride* (1 g.) of which melted at 277—278° after 2 recrystallisations from alcohol–ether (Found : C, 77·0; H, 8·0; N, 4·0. $C_{22}H_{28}NCl$ requires C, 77·3; H, 8·2; N, 4·1%).

RESEARCH DEPARTMENT, ROCHE PRODUCTS LTD.,
WELWYN GARDEN CITY, HERTS.

[*Received, March* 16*th*, 1950.]