123. *Application of Acrylonitrile to the Synthesis of Some Reduced Heterocyclic Compounds.*

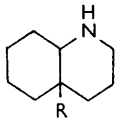
By T. Henshall and E. W. Parnell.

Acrylonitrile has been used in preparations of *cis*- and *trans*-decahydro-4a-methylquinoline (II), octahydro-1-pyrindine (III), and perhydrocyclohepta[*b*]pyridine (VI) (by stereospecific synthesis); it affords also 3-(2-hydroxy-2-methylcyclohexyl)propylamine which has been cyclised to decahydro-8a-methylquinoline (XIII).

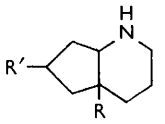
Acrylonitrile appeared to be a convenient reagent for the preparation of a number of reduced heterocyclic systems of known stereochemistry. Previous applications of this substance to the synthesis of reduced heterocycles include the preparation of derivatives of decahydroquinoline [1-3] (I) (in some cases by stereospecific reactions) and of octahydro-1-pyrindines, for example, compounds (IV) [4] and (V).[3] Pure *trans*-octahydro-1-pyrindine and *trans*-perhydrocyclohepta[*b*]pyridine (VI) have been obtained by reduction of the corresponding dihydro-compounds.[5,6]

[1] Terent'ev and Gurvich, *Sbornic Statei obshchei Khim. Akad. Nauk. U.S.S.R.*, 1953, **1**, 404; Boekelheide, *J. Amer. Chem. Soc.*, 1947, **69**, 790; Sugimoto, Kugito, and Fugita, *J. Pharm. Soc. Japan*, 1955, **75**, 117.
[2] Leonard, Miller, and Thomas, *J. Amer. Chem. Soc.*, 1955, **77**, 6595.
[3] Nazarov, Shoekhgeimev, and Rudenko, *Zhur. obshchei Khim.*, 1954, **24**, 3191.
[4] Albertson, *J. Amer. Chem. Soc.*, 1950, **72**, 2594; U.S.P. 2,585,210.
[5] Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, **28**, 1684.
[6] Prelog and Hinden, *Helv. Chim. Acta*, 1944, **27**, 1894.

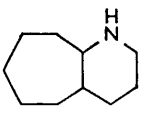
Since the catalytic reduction of $\Delta^{1(8a)}$-octahydroquinoline (VII) with a palladium catalyst gives *cis*-decahydroquinoline [2] (I), it seemed probable that reduction with sodium and ethanol would give the *trans*-isomer and this was realised in practice. These reactions were then applied to the preparation of other reduced heterocyclic ring systems.



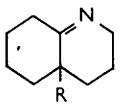
(I: R = H)
(II: R = Me)



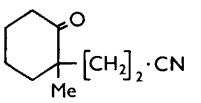
(III: R = R′ = H)
(IV: R = CO_2Et; R′ = H)
(V: R = R′ = Me)



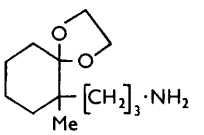
(VI)



(VII: R = H)
(VIII: R = Me)



(IX)



(X)

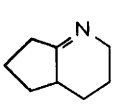
By analogy with Cohen and Witkop's synthesis of $\Delta^{1(8a)}$-octahydroquinoline [7] (VII) 2-2′-cyanoethyl-2-methylcyclohexanone [8] (IX) was converted into the ethylene ketal which was catalytically reduced to the amine (X); this was hydrolysed and cyclised to give $\Delta^{1(8a)}$-octahydro-4a-methylquinoline (VIII) in excellent overall yield. Treatment of this methyl derivative with sodium and ethanol gave pure *trans*-decahydro-4a-methylquinoline (II); catalytic reduction with a palladium–charcoal catalyst also gave predominantly the *trans*-isomer. The octahydro-compound was not reduced by zinc and hydrochloric acid, a method which might have been expected to yield the *cis*-isomer.[9] Catalytic reduction of the octahydro-compound (VIII) over Adams catalyst in acetic acid gave a mixture of bases from which only the picrate of the *trans*-isomer could be isolated. However, reduction in acetic acid containing one or more equivalents of hydrochloric acid gave a product from which a different picrate was obtained and the corresponding amine was assigned the *cis*-configuration.

$\Delta^{1(7a)}$-Hexahydropyrindine (XI) was prepared by methods analogous to those used for $\Delta^{1(8a)}$-octahydro-4a-methylquinoline (VIII). Sodium and ethanol reduced this pyrindine derivative to pure, solid *trans*-octahydropyrindine (III). The boiling point of the base and the melting point of the picrolonate agreed with the reported values but Prelog and Szpilfogel [5] describe their product as a liquid. The hexahydro-compound (XI) was not hydrogenated over palladium–charcoal in ethanol at atmospheric pressure and at temperatures up to 50°, but Adams catalyst was effective under these conditions. The product proved to be predominantly the *trans*-isomer. Reduction in acetic acid over Adams catalyst gave a mixture of isomeric bases from which an *N*-tosyl derivative, m. p. 68—69°, was isolated in 60% yield. This was different from the *trans*-derivative, m. p. 101·5—102·5°, and was therefore assigned the *cis*-configuration.

3,4,4a,5,6,7,8,9-Octahydro-2*H*-cyclohepta[*b*]pyridine (XII) was prepared by methods analogous to those used for the hexahydropyrindine (XI) and its reduction was studied. With sodium and ethanol it gave only the *trans*-perhydro-compound (VI) which formed an alkali-insoluble *N*-tosyl derivative; the boiling point of the base and the melting point of the picrolonate agreed with the literature values.[6] Hydrogenation in acetic acid solution in the presence of Adams catalyst gave a mixture from which a new alkali-insoluble *N*-tosyl derivative, m. p. 56—58°, was isolated; this was assigned the *cis*-configuration.

[7] Cohen and Witkop, *J. Amer. Chem. Soc.*, 1955, **77**, 6595.
[8] Frank and Pierle, *J. Amer. Chem. Soc.*, 1951, **73**, 724.
[9] Weissenborn and Diassi, *J. Amer. Chem. Soc.*, 1956, **78**, 2022.

The chemical and catalytic reductions of such cyclic bases therefore afford stereospecific methods leading to the *cis*- and *trans*-isomers of bicyclic systems containing the piperidine ring. Whereas the chemical reduction is virtually 100% specific for the *trans*-isomer, the specificity of the catalytic reduction depends on the ring system and the conditions; under acid conditions with a platinum catalyst the formation of the *cis*-isomer is favoured.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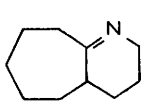
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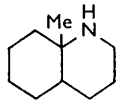
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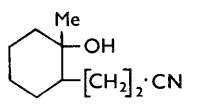
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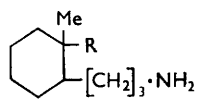
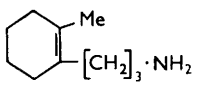

(XV: R = OH)
(XVI: R = Cl)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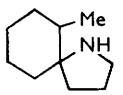
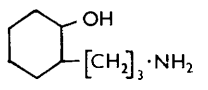

(XVIII)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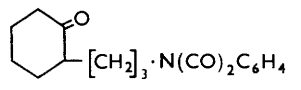
(XX)

We next turned to the synthesis of decahydro-8a-methylquinoline (XIII). 2-2′-Cyanoethylcyclohexanone [10] reacted selectively at the ketonic group with one equivalent of methylmagnesium iodide and the cyclohexanol (XIV) was obtained. This was catalytically reduced to the amine (XV) which was shown to be essentially homogeneous by the formation in good yield of two sharply-melting derivatives. The amino-alcohol (XV) was remarkably stable and distilled unchanged at atmospheric pressure (b. p. 240°), but when it was dissolved in hydrobromic acid only dehydration to the olefinic base (XVII) occurred.

A solution of the amine (XV) in concentrated hydrochloric acid was kept for some days and then carefully basified. A chlorine-containing base was obtained which distilled without decomposition and gave an analysis consistent with the structure (XVI). When this substance was slowly heated a vigorous exothermic reaction occurred at *ca.* 130°; if this was moderated by the use of anisole a good yield of the hydrochloride of the base (XVII) was obtained. Examination of the reaction mother-liquors revealed only a trace of secondary amine.

When the amine (XV) was heated at 300° with anhydrous zinc chloride, the product was a secondary amine whose picrate was obtained pure only after several recrystallisations; the base (XVII) did not form a picrate under the same conditions. The new base is probably a mixture of the *cis*- and *trans*-isomers of the desired decahydro-8a-methylquinoline (XIII) although the spiro-structure (XVIII) cannot be completely excluded and insufficient pure base was obtained for further examination.

It has been shown that addition of a Grignard reagent to acyclic ketones occurs so that the resultant hydroxyl group tends to orientate itself between the least bulky groups on the adjacent carbon atom.[11] This suggested that in the case of a simple cyclic ketone such as 2-2′-cyanoethylcyclohexanone the resultant alcohol (XV) will have the hydroxyl group and the side chain in the *trans*-configuration, and this is in line with the relative stability of the hydroxy-nitrile (XIV) towards dehydrating agents. It seemed possible that the *cis*-isomer of the compound (XV) might show a difference in the ease of cyclisation, but no synthesis of this isomer could be devised. However, syntheses of *cis*- and *trans*-2-3′-aminopropylcyclohexanol (XIX) were attempted in the hope that they might help to resolve this problem.

Reduction of 2-2′-cyanoethylcyclohexanone has been shown [6] to give a low yield of decahydroquinoline (I). This reduction was re-examined and when sodium and ethanol were used *trans*-2-3′-aminopropylcyclohexanol was obtained. This was shown to be

[10] Stork, Terrell, and Szmuskovicz, *J. Amer. Chem. Soc.*, 1954, **76**, 2029.
[11] Cram and Abd Elhafez, *J. Amer. Chem. Soc.*, 1952, **74**, 5828.

stereochemically homogeneous by the preparation of sharply melting derivatives, and from its mode of formation would be expected to have the *trans*-structure. Although a mixture of decahydroquinolines had been obtained by the hydrogenation of 2-2′-cyanoethylcyclohexanone over a nickel catalyst,[3] this reduction was repeated in acetic–hydrochloric acid mixture to see if the *cis*-aminopropyl derivative (XIX) could be obtained: it gave, however, a mixture of *cis*- and *trans*-decahydroquinoline (I). Two modes of formation are possible: either reduction first gives 2-3′-aminopropylcyclohexanone which cyclises to $\Delta^{1(8a)}$-octahydroquinoline (VII) and is then reduced; or the aminopropyl compound (XIX) is formed by reduction and then cyclises to the decahydroquinolines (I). If the first alternative were correct, the product would be expected to be largely the *cis*-isomer, but since it did in fact contain a substantial quantity of the *trans*-isomer the latter route seemed more probable. In order to resolve this point a further attempt was made to prepare the *cis*-isomer (XIX). The ethylene ketal of 2-3′-aminopropylcyclohexanone was treated with phthalic anhydride in acetic acid and the phthalimido-derivative (XX) was obtained by simultaneous hydrolysis of the ketal group. Catalytic reduction of this phthalimide gave a complex mixture; no pure alcohol could be obtained, and this approach was abandoned.

Experimental

trans-*Decahydroquinoline*.—$\Delta^{1(8a)}$-Octahydroquinoline [2] (3·0 g.) in dry ethanol (30 ml.) was treated with sodium (3·0 g.). When the sodium had dissolved the solution was poured into water, and the base was extracted with ether and distilled to give the product (2·6 g.), m. p. 45—47°, b. p. 199—200°/760 mm. The base and the benzoyl derivative, m. p. 52—53°, were identical with authentic material.[12]

1-2′-*Cyanoethyl*-2,2-*ethylenedioxy*-1-*methylcyclohexane*.—2-2′-Cyanoethyl-2-methylcyclohexanone [8] [4-*nitrobenzylidene* derivative, m. p. 107—108° (Found: C, 68·6; H, 6·3; N, 9·1. $C_{17}H_{18}N_2O_3$ requires C, 68·5; H, 6·0; N, 9·3%)], was converted by Cohen and Witkop's method [7] into the ethylene ketal, b. p. 178—180°/14 mm., n_D^{20} 1·4860 (Found: C, 69·9; H, 9·1; N, 6·8. $C_{12}H_{19}NO_2$ requires C, 69·0; H, 9·1; N, 6·7%).

3-(2,2-*Ethylenedioxy*-1-*methylcyclohexyl*)*propylamine*.—The foregoing nitrile (64·5 g.) in ethanol (250 ml.) containing ammonia (41·0 g.) was catalytically reduced at 75°/700 lb. per sq. in. in presence of Raney nickel (*ca.* 6·5 g.) to the amine (47·6 g.), b. p. 152—155°/10 mm., n_D^{20} 1·4920. This did not give a satisfactory analysis; some hydrolysis of the ketal appeared to have occurred and the crude product was used for the next stage.

$\Delta^{1(8a)}$-*Octahydro*-4a-*methylquinoline*.—A mixture of the foregoing amino-ketal (33 g.) and 2N-hydrochloric acid (82·5 ml.) was refluxed for 1 hr. The solution was basified with 50% w/w sodium hydroxide, and the base was extracted with ether. Distillation gave the *octahydroquinoline* (21·5 g.), b. p. 93—94°/10 mm., n_D^{20} 1·4991 (Found: N, 9·4. $C_{10}H_{17}N$ requires N, 9·3%) [*picrate*, m. p. 223—224° (decomp.), bright yellow needles from ethanol (Found: C, 50·7; H, 5·5; N, 14·5. $C_{10}H_{16}N,C_7H_3N_3O_7$ requires C, 50·5; H, 5·2; N, 14·7%)].

trans-*Decahydro*-4a-*methylquinoline*.—The foregoing base (3·0 g.) was reduced in dry ethanol (24 ml.) with sodium (3·0 g.), as described for the parent compound, to give the saturated *base* (2·4 g.), b. p. 222°/760 mm., n_D^{20} 1·4918 (Found: C, 79·1; H, 12·4; N, 8·8. $C_{10}H_{19}N$ requires C, 78·5; H, 12·4; N, 9·1%). The *picrate* (pale yellow needles from ethanol) had m. p. 224—225° (slight decomp.) (Found: C, 50·1; H, 5·8; N, 14·4. $C_{10}H_{19}N,C_6H_3N_3O_7$ requires C, 50·2; H, 5·75; N, 14·65%), depressed by the picrate of the starting material. The *toluene*-p-*sulphonyl derivative*, fine needles from light petroleum (b. p. 60—80°), was insoluble in alkali and had m. p. 118—119° (Found: C, 66·5; H, 8·7; N, 4·3; S, 10·4. $C_{17}H_{25}NO_2S$ requires C, 66·5; H, 8·2; N, 4·6; S, 10·4%). The same base, isolated as the picrate, was obtained by reduction over palladium in ethanol.

cis-*Decahydro*-4a-*methylquinoline*.—The octahydroquinoline (3·3 g.) in acetic acid (16·5 ml.) and concentrated hydrochloric acid (1·0 ml.) was catalytically reduced at *ca.* 20°/1 atm. in the presence of Adams catalyst (0·3 g.). The solution was filtered, the filtrate evaporated to low bulk, and the residue dissolved in water. The base, b. p. 220—222°, n_D^{20} 1·4899, liberated with 50% w/w sodium hydroxide was isolated by extraction with ether. This base gave a mixture

[12] Bamberger and Zugfeld, *Ber.*, 1890, **23**, 1138; Huckel and Stepf, *Annalen*, 1927, **453**, 163.

of picrates with ethereal picric acid; the least soluble picrate, crystallised from ethanol, had m. p. 222—225° and was identical with that of the *trans*-base; the more soluble picrate crystallised from 2N-acetic acid to give the *cis*-picrate, leaflets, m. p. 190—192°, which depressed the m. p. of the *trans*-base picrate (Found: N, 14·5%).

1-2′-*Cyanoethyl*-2,2-*ethylenedioxycyclopentane*.—2-2′-Cyanoethylcyclopentanone [13] was converted into the *ethylene ketal*, b. p. 154—155°/12 mm., n_D^{20} 1·4731 (Found: C, 65·9; H, 8·3; N, 7·7. $C_{10}H_{15}NO_2$ requires C, 66·3; H, 8·3; N, 7·7%), as described above for the cyclohexane derivative.

3-2′,2′-*Ethylenedioxycyclopentylpropylamine*, prepared essentially as described for the cyclohexyl analogue, had b. p. 132—134°/13 mm., n_D^{19} 1·4805 (Found: C, 65·1; H, 10·1; N, 7·7. $C_{10}H_{19}NO_2$ requires C, 64·9; H, 10·2; N, 7·6%).

$\Delta^{1(7a)}$-*Hexahydro*-1-*pyrindine*.—The preceding amino-ketal (10 g.) and 2N-hydrochloric acid (40 ml.) were refluxed for 0·5 hr., and the *product* (5·5 g.) was isolated and distilled; an analytical specimen, dried over solid sodium hydroxide, had b. p. 74—75°/13 mm., n_D^{20} 1·5025 (Found: C, 77·2; H, 10·8; N, 11·3. $C_8H_{13}N$ requires C, 78·1; H, 10·6; N, 11·4%) [*picrate*, m. p. 146—147° (decomp.), deep yellow needles from methanol (Found: C, 47·7; H, 4·6; N, 16·1. $C_8H_{13}N,C_6H_3N_3O_7$ requires C, 47·7; H, 4·5; N, 15·9%)].

trans-*Octahydro*-1-*pyrindine*.—The foregoing base (4·0 g.) in ethanol (32 ml.) was reduced by addition of sodium (4·0 g.), as described for octahydroquinoline, to give the base (3·2 g.), b. p. 63—64°/12 mm. (lit.,[5] 64—66°/13 mm.), n_D^{20} 1·4862, needles, m. p. 29—31·5° (Found: C, 76·5; H, 12·4; N, 11·3. $C_8H_{13}N$ requires C, 76·8; H, 12·0; N, 11·2%) [picrolonate, prepared in ethanol, m. p. 246—248° (decomp.) (from 2-ethoxyethanol) (lit.,[5] 241°) (Found: C, 55·7; H, 5·95; N, 18·2. Calc. for $C_8H_{15}N,C_{10}H_8N_4O_5$: C, 55·5; H, 5·8; N, 18·0%)]. The *toluene*-p-*sulphonyl derivative* was insoluble in alkali and crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 101—102·5° (Found: C, 64·8; H, 7·9; N, 4·75; S, 11·8. $C_{15}H_{21}NO_2S$ requires C, 64·5; H, 7·5; N, 5·0; S, 11·5%).

Catalytic Reduction of $\Delta^{1(7a)}$-*Hexahydropyrindine*.—(*a*) The base (0·5 g.) was reduced at 1 atm. and room temperature in ethanol (5·0 ml.) in the presence of Adams catalyst. The product was converted directly into the picrolonate (1·1 g.), m. p. 232—235° (decomp.). Two recrystallisations from 2-ethoxyethanol raised the m. p. to 240—242° (decomp.), undepressed on admixture with the picrolonate of authentic *trans*-octahydropyrindine.

(*b*) The hexahydropyrindine (6·3 g.) in acetic acid (31·5 ml.) was reduced as described above in the presence of Adams catalyst (0·6 g.). The base was isolated and distilled to give two fractions: cis-*octahydro*-1-*pyrindine* (3·4 g.), b. p. 57—58°/10 mm., n_D^{20} 1·4875 (Found: C, 76·3; H, 12·0; N, 11·1. $C_8H_{15}N$ requires C, 76·8; H, 12·4; N, 11·2%), and a *dimer* (1·85 g.) which after being redistilled had b. p. 151—152°/0·25 mm., n_D^{17} 1·5170 (Found: C, 77·0; H, 12·15; N, 10·75%; *M*, 239. $C_{16}H_{28}N_2$ requires C, 77·5; H, 11·3; N, 11·3%; *M*, 248).

cis-Octahydro-1-pyrindine formed a *toluene*-p-*sulphonyl derivative*, m. p. 58—61°, insoluble in alkali. One crystallisation from methanol gave the pure derivative, m. p. 68—69°, depressed on admixture with the *trans*-derivative (Found: C, 64·8; H, 7·6; N, 4·6; S, 11·8. $C_{15}H_{21}NO_2S$ requires C, 64·8; H, 7·5; N, 5·0; S, 11·5%).

1-2′-*Cyanoethyl*-2,2-*ethylenedioxycycloheptane*.—2-2′-Cyanoethylcycloheptanone [13] was converted into the *ethylene ketal*, b. p. 161—166°/8—9 mm., n_D^{17} 1·4845 (Found: C, 69·6; H, 9·4; N, 6·9. $C_{12}H_{19}NO_2$ requires C, 68·9; H, 9·1; N, 6·7%), as described above.

3-2′,2′-*Ethylenedioxycycloheptylpropylamine*.—The foregoing nitrile (50 g.) was reduced as described for the cyclohexyl analogue, giving the *amine* (40·5 g.), b. p. 153—155°/10 mm., n_D^{22} 1·4931 (Found: C, 67·7; H, 10·9; N, 7·1. $C_{17}H_{23}NO_2$ requires C, 67·6; H, 10·8; N, 6·6%).

3,4,4a,5,6,7,8-*Octahydro*-2H-*cyclohepta*[b]*pyridine* (XII).—The amino-ketal (10 g.) was refluxed in 2N-hydrochloric acid (50 ml.) for 1 hr. The *product* (6·1 g.), isolated in the usual manner, had b. p. 109—111°/10 mm., n_D^{17} 1·5080 (Found: C, 79·1; H, 11·3; N, 9·1. $C_{10}H_{17}N$ requires C, 79·5; H, 11·3; N, 9·3%) [*picrate*, m. p. 160—162° (decomp.), needles from ethanol (Found: C, 50·2; H, 5·3; N, 14·7. $C_{10}H_{17}N,C_6H_3N_3O_7$ requires C, 50·6; H, 5·3; N, 14·7%)].

trans-*Perhydrocyclohepta*[b]*pyridine*.—The unsaturated base (XII) (4·8 g.) in dry ethanol (38 ml.) was reduced by sodium (4·8 g.), as described for octahydroquinoline, giving the perhydro-base (2·66 g.), b. p. 98—99°/10 mm., n_D^{18} 1·4979 (Found: C, 78·5; H, 12·4; N, 9·1. Calc. for $C_{10}H_{19}N$: C, 78·5; H, 12·4; N, 9·1%). The picrolonate formed needles (from

[13] Stork and Landesman, *J. Amer. Chem. Soc.*, 1956, **78**, 5128.

2-ethoxyethanol), m. p. 235—237° (decomp.) (Found: C, 57·5; H, 6·75; N, 16·5. Calc. for $C_{10}H_{19}N,C_{10}H_8N_4O_5$: C, 57·6; H, 6·5; N, 16·8%). The base formed an alkali-insoluble *toluene*-p-*sulphonyl derivative* which crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 82—83° (Found: N, 4·4; S, 10·3. $C_{17}H_{25}NO_2S$ requires N, 4·6; S, 10·4%). Prelog and Hinden [6] give the b. p. of their base as 125—130°/11 mm. and the m. p. of the picrolonate as 225—226°.

cis-*Perhydrocyclohepta*[b]*pyridine*.—The unsaturated base (5·0 g.) was catalytically reduced in acetic acid over Adams catalyst at 1 atm., to give the saturated *base* (4·0 g.), b. p. 97—98°/10 mm., n_D^{18} 1·4991 (Found: C, 78·5; H, 12·6; N, 9·1%). The picrolonate, m. p. 210—220° (decomp.), was not homogeneous and could not be purified by repeated crystallisation. Recrystallisation of the *toluene*-p-*sulphonyl derivative* from methanol at −40° gave needles, m. p. 56—58° (Found: N, 4·7; S, 10·4%), depressed on admixture with the *trans*-derivative.

2-2′-*Cyanoethyl*-1-*methylcyclohexanol*.—The Grignard reagent, prepared from methyl iodide (9·2 ml.) and magnesium turnings (3·54 g.) in ether (50 ml.), was added dropwise to a refluxing solution of 2-2′-cyanoethylcyclohexanone (20 g.) in ether (100 ml.). The mixture was stirred and refluxed for 16 hr., cooled, and treated with saturated aqueous ammonium chloride. The dried ethereal layer afforded the *alcohol* (15·9 g.), b. p. 152—154°/12 mm., n_D^{20} 1·4803. A middle fraction b. p. 152—153°/12 mm., n_D^{20} 1·4799, was analysed (Found: N, 8·6. $C_{10}H_{17}NO$ requires N, 8·4%). The alcohol failed to give a solid derivative with phenyl isocyanate or 3,5-dinitrobenzoyl chloride.

3-(2-*Hydroxy*-2-*methylcyclohexyl*)*propylamine*.—The foregoing nitrile (50 g.) was reduced in ethanol (250 ml.) containing ammonia (27 g.) in the presence of Raney nickel (*ca.* 5 g.) at 79°/700 lb. per sq. in. and gave the *amine* (39·2 g.), b. p. 145—146°/13 mm., n_D^{20} 1·4950 (Found: C, 69·6; H, 12·7; N, 8·3. $C_{12}H_{21}NO$ requires C, 70·0; H, 12·3; N, 8·2%). The *oxalate* crystallised from ethanol–ether as a hemihydrate, m. p. 116—117° (Found: C, 53·1; H, 8·9; N, 5·2; H_2O, 3·6. $C_{10}H_{21}NO,C_2H_2O_4,\frac{1}{2}H_2O$ requires C, 53·4; H, 8·9; N, 5·2; H_2O, 3·4%). The p-*chlorophenylthiourea derivative* crystallised in prisms (from benzene), m. p. 134—135° (Found: C, 60·1; H, 7·2; N, 8·2; Cl, 10·5; S, 9·5. $C_{17}H_{25}ClN_2OS$ requires C, 59·8; H, 7·3; N, 8·2; Cl, 10·4; S, 9·4%). The *toluene*-p-*sulphonyl derivative* formed prisms [from ether–light petroleum (b. p. 60—80°)], m. p. 91·5—93° (Found: C, 62·5; H, 8·2; N, 4·4; S, 9·8. $C_{17}H_{27}NO_3S$ requires C, 62·8; H, 8·3; N, 4·3; S, 9·8%). The base, regenerated from the pure oxalate, had b. p. 144—145°/15 mm., n_D^{20} 1·4950.

Treatment of 3-(2-*Hydroxy*-2-*methylcyclohexyl*)*propylamine with Hydrobromic Acid*.—The amino-alcohol (3·0 g.) was dissolved in 48% aqueous hydrobromic acid (15 ml.) at 10° and kept at room temperature overnight. The crystalline precipitate (4·6 g.) of 3-(2-*methylcyclohex*-1-*enyl*)*propylammonium bromide* recrystallised from ethanol–ether as plates, m. p. 191—193° (decomp.) (Found: C, 51·2; H, 8·5; Br, 33·8; N, 5·6. $C_{10}H_{19}N,HBr$ requires C, 51·3; H, 8·2; Br, 34·2; N, 6·0%). The base (XVII) isolated from this salt had b. p. 116—120°/10 mm., n_D^{20} 1·4881, and was a primary amine (cf. below). The alkali-soluble toluene-p-sulphonyl derivative was a gum but the p-*chlorophenylthiourea derivative* crystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 81—82° (Found: C, 62·8; H, 6·9; Cl, 11·2; N, 8·8. $C_{17}H_{23}ClN_2S$ requires C, 63·2; H, 7·1; Cl, 11·0; N; 8.7%). The base did not give a picrate when treated with etheral picric acid.

3-(2-*Chloro*-2-*methylcyclohexyl*)*propylamine*.—The amino-alcohol (15·9 g.) was added to concentrated hydrochloric acid (48 ml.) at −45°. The stirred mixture was then saturated with hydrogen chloride at 0°. After being kept at room temperature for 7 days, the solution was poured on ice, the solution basified with 50% w/w aqueous sodium hydroxide, and the liberated oil rapidly extracted with ether. The dried ether extract afforded the chloro-amine (11·1 g.), b. p. 76—77°/0·2 mm., n_D^{20} 1·4916 (Found: Cl, 17·3; N, 7·6. Calc. for $C_{10}H_{20}ClN$: Cl, 18·7; N, 7·3%). Attempts to refractionate the product in order to obtain a base with a higher percentage of chlorine failed to give an improved analysis.

Action of Heat on 3-(2-*Chloro*-2-*methylcyclohexyl*)*propylamine*.—The chloro-amine (10·4 g.) was refluxed in dry anisole (52 ml.) for 4 min.; an exothermic reaction occurred and a solid separated. The mixture was cooled and a *hydrochloride* (8·0 g.), m. p. 170—175° (decomp.), was filtered off. It crystallised from ethanol–ether in white leaflets, m. p. 175—177° (decomp.) (Found: C, 63·3; H, 9·5; Cl, 18·9; N, 7·4. $C_{10}H_{19}N,HCl$ requires C, 63·3; H, 10·5; Cl, 18·7; N, 7·3%). The *base* (XVII) regenerated from this hydrochloride had b. p. 118—120°/10 mm., n_D^{20} 1·4901 (Found: C, 77·8; H, 12·1; N, 9·7. $C_{10}H_{19}N$ requires C, 78·4; H, 12·4; N, 9·2%).

It formed a *p*-chlorophenylthiourea derivative, m. p. 83—84°, undepressed by the corresponding derivative prepared after treatment of the amino-alcohol with hydrobromic acid.

Decahydro-8a-methylquinoline.—3-(2-Hydroxy-2-methylcyclohexyl)propylamine (5·0 g.) and anhydrous zinc chloride (4·75 g.) were heated together at 300° for 1 hr. The mixture was cooled, treated with 2N-sodium hydroxide (50 ml.), and extracted with ether. The mixture was filtered, the ether separated, and the aqueous layer extracted with two further portions of ether. The dried (Na_2SO_4) extracts yielded a *base* (1·8 g.), b. p. 90—95°/15 mm. An analytical sample had b. p. 88—90°/15 mm., n_D^{20} 1·4868 (Found: C, 78·7; H, 12·3; N, 9·3. $C_{10}H_{19}N$ requires C, 78·4; H, 12·4; N, 9·2%). The base gave a positive Simon's and Liebermann's nitroso-test but a negative Rimini test, and was therefore a secondary amine. It gave a *picrate* which crystallised from 2N-acetic acid as needles, m. p. 156—157° (Found: C, 50·3; H, 5·9; N, 14·5. $C_{10}H_{19}N,C_6H_3N_3O_7$ requires C, 50·2; H, 5·7; N, 14·6%).

trans-2-3′-*Aminopropylcyclohexanol.*—Sodium (20 g.) was added during 15 min. to a refluxing solution of 2-2′-cyanoethylcyclohexanone (20 g.) in dry ethanol (500 ml.). The mixture was refluxed until all the sodium had dissolved, cooled, carefully acidified with concentrated hydrochloric acid, and evaporated to a small volume. The salts were dissolved in water (200 ml.), and the mixture was extracted with ether. The aqueous layer was basified with 50% w/w aqueous sodium hydroxide to give the *amino-alcohol* (5·0 g.); an analytical specimen had b. p. 148—150°/12 mm., n_D^{20} 1·4960 (Found: C, 69·2; H, 12·6; N, 9·3. $C_9H_{19}NO$ requires C, 68·9; H, 12·1; N, 8·9%). The base formed an alkali-soluble *toluene*-p-*sulphonyl derivative* which crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 86—87° (Found: C, 61·8; H, 8·0; N, 4·4; S, 10·7. $C_{16}H_{25}NO_3S$ requires C, 61·7; H, 8·0; N, 4·5; S, 10·3%). The p-*chlorophenylthiourea derivative* crystallised from ethyl acetate in prisms, m. p. 154—155° (Found: C, 58·9; H, 7·1; Cl, 10·8; N, 8·4; S, 10·1. $C_{16}H_{23}ClN_2OS$ requires C, 59·2; H, 7·1; Cl, 11·0; N, 8·6; S, 9·9%).

Catalytic Reduction of 2-2′-*Cyanoethylcyclohexanone.*—2-2′-Cyanoethylcyclohexanone (20 g.) in acetic acid (40 ml.) was reduced at 70 lb./sq. in. over Adams catalyst (0·8 g.). The catalyst was filtered off, and the filtrate treated with hydrochloric acid (20 ml.) and evaporated under reduced pressure. The residue was fractionally crystallised from ethanol and ethanol–ether to give *trans*- and *cis*-decahydroquinoline hydrochloride, m. p. 276° (decomp.) and m. p. 225—226° (decomp.), respectively [12] identical with authentic material.

3-(2,2-*Ethylenedioxycyclohexyl*)*propylamine.*—1-2′-Cyanoethyl-2,2-ethylenedioxycyclohexane (54 g.) was reduced as described for the methyl analogue. The *amine* (43·5 g.) had b. p. 141—142°/10 mm., n_D^{20} 1·4809 (Found: C, 65·8; H, 11·0; N, 6·9. $C_{11}H_{21}NO_2$ requires C, 66·2; H, 10·5; N, 7·0%). The p-*chlorophenylthiourea derivative*, m. p. 136—137°, crystallised from benzene (Found: Cl, 9·8; N, 7·5. $C_{18}H_{25}ClN_2O_2S$ requires Cl, 9·6; N, 7·5%).

2-(3-*Phthalimidopropyl*)*cyclohexanone.* The foregoing base (1·0 g.), phthalic anhydride (0·8 g.) and acetic acid (10 ml.) were refluxed for 1 hr. and then poured into water (50 ml.). The *product* (isolated by ether) crystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 80—81° (Found: C, 71·6; H, 6·5; N, 5·1. $C_{17}H_{19}NO_3$ requires C, 71·6; H, 6·7; N, 4·9%). It formed a *semicarbazone*, m. p. 172—173° (from methanol) (Found: C, 63·2; H, 6·8; N, 16·1. $C_{18}H_{24}N_4O_3$ requires C, 63·3; H, 6·4; N, 16·3%).

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