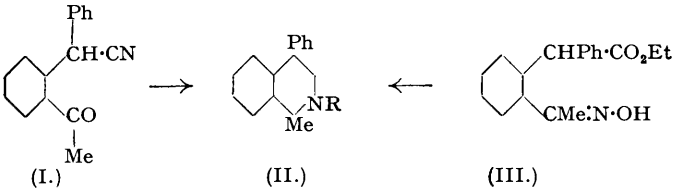
320. *The Synthesis of Piperidine Derivatives. Part V. Decahydroisoquinolines.*

By G. M. Badger, J. W. Cook, and G. M. S. Donald.

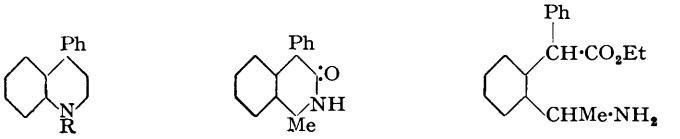
Reductive cyclisation of α-2-acetyl*cyclo*hexylbenzyl cyanide (I) in alcoholic solution by means of hydrogen and a copper chromite catalyst gave two stereoisomeric 2-alkyldecahydro-1-methyl-4-phenyl*iso*quinolines (II), the *N*-alkyl group being provided by the alcohol used as solvent. Hydrogenation of the oxime-ester (III) in methanol also gave some (II; R = Me) together with two stereoisomeric intermediates, decahydro-3-keto-1-methyl-4-phenyl*iso*quinoline (V). The Michael condensation product (XII) of malonamide and 1-phenylacetyl*cyclo*hex-1-ene was converted, through two intermediates, into 1-benzyldecahydro*iso*quinoline (X), which is a structural simplification of Grewe's *N*-methylmorphinan.

In continuation of previous work on the synthesis of piperidine derivatives of possible pharmacological interest as analgesics and spasmolytics, we have now investigated the formation of certain aryldecahydro*iso*quinolines. The methods of reductive cyclisation developed in earlier papers of this series (Barr and Cook, *J.*, 1945, 438; Badger, Cook, and Walker, *J.*, 1948, 2011; 1949, 1141) have again been employed. The synthesis of decahydro-2-methyl-10-phenyl*iso*quinoline has been recorded recently by Boekelheide and Schilling (*J. Amer. Chem. Soc.*, 1950, **72**, 712).

By hydrogenation of the cyanide (I) in alcoholic solution over copper chromite catalyst, we obtained a mixture of two stereoisomeric decahydro*iso*quinolines of general formula (II), in which the *N*-alkyl group is provided by the alcohol used as solvent. In this way, " α "- and " β "-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline (II; R = Me), " α "- and " β "-decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinoline (II; R = Et), and " α "- and " β "-decahydro-1-methyl-4-phenyl-2-*n*-propyl*iso*quinoline (II; R = Pr^n) were isolated as colourless oils, and characterised as the corresponding picrates through which salt the separation was achieved by fractional crystallisation. With the *N*-methyl base, the isomers appeared to be present in approximately



(I.) (II.) (III.)

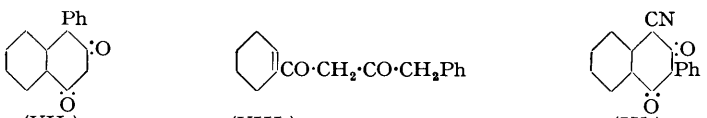


(IV.) (V.) (VI.)

equal quantities; but with the *N*-ethyl, and *N*-*n*-propyl derivatives, the isomer giving the picrate of higher melting point seemed to be present in smaller amount. The formation of these bases in two stereoisomeric forms is of some interest as Badger, Cook, and Walker (*J.*, 1948, 2011) isolated only one isomer of the analogous quinoline derivative (IV) after similar hydrogenation of an oxime-ester. On the other hand Barr and Cook (*loc. cit.*) isolated two 1-ethyl-3 : 4-diphenylpiperidines from the products of the reductive cyclisation of ethyl γ-cyano-βγ-diphenylbutyrate. The two isomers of (II) which have now been isolated are possibly *cis* and *trans* with respect to the phenyl and methyl groups.

We also investigated the possibility of synthesising compounds of type (II) by hydrogenation of suitable oxime-esters (*e.g.*, III; compare Badger, Cook, and Walker, *loc. cit.*). Hydrolysis of the cyanide (I) with alcohol and sulphuric acid gave ethyl α-2-acetyl*cyclo*hexylphenylacetate, characterised by alkaline hydrolysis to the acid. All attempts to obtain a crystalline oxime (III) of the ester were unsuccessful, and the crude product was therefore submitted to hydrogenation. The small yield of basic material was fractionally distilled. The first fraction, a colourless oil, was converted into the picrate, which was found to be that of " β "-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline. In this case, the product appeared to be homogeneous, and unaccompanied by the " α "-isomer. The second fraction of the distillate which was now insoluble in dilute hydrochloric acid, crystallised, and on fractional recrystallisation was separated into two components. In view of the acid-insolubility, and the fact that reductive cyclisations of this nature are known to proceed *via* the piperidones (Koelsch, *J. Amer. Chem. Soc.*, **1933**, **65**, 2093, 2458, 2459, 2460; cf. Barr and Cook, and Badger, Cook, and Walker, *locc. cit.*), these two compounds are regarded as decahydro-3-keto-1-methyl-4-phenyl*iso*quinoline-*A* and -*B* (V). They (V) are presumably formed, during the distillation, by intramolecular cyclisation with loss of the elements of ethanol from the acid-soluble compound (VI). The isomerism is probably of the same nature as that of the compounds of type (II).

It was thought that the keto-ester corresponding to (III) might be more readily available by direct Michael condensation of acetyl*cyclo*hexene and ethyl phenylacetate. In point of fact,



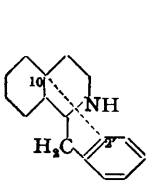
(VII.) (VIII.) (IX.)

however, a Perkin-type, rather than a Michael-type, condensation was found to be favoured. None of the desired keto-ester was isolated, but two isomeric compounds were separated by fractional crystallisation. The composition of these compounds, which both gave dioximes,

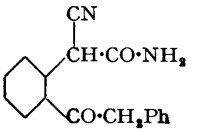
is consistent with the structures (VII) and (VIII), but neither compound gave a colour with ferric chloride.

Similarly, condensation between ethyl cyanoacetate and 1-phenylacetyl*cyclo*hex-1-ene took place by the Perkin rather than by the Michael reaction. In this case only one product was isolated; its composition corresponded with the structure (IX). This compound did not react with carbonyl reagents, but readily formed a *diacetyl* derivative.

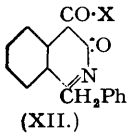
By reactions similar to those described above we have also synthesised a 1-benzyldecahydro-*iso*quinoline (X) which is structurally related to morphinan, the *N*-methyl derivative of which is a potent analgesic (Grewe and Mondon, *Chem. Ber.*, 1948, **81**, 279; Schnider and Grüssner, *Helv. Chim. Acta*, 1949, **32**, 821). In the morphinan structure position 10 of (X) is linked to the 2′-position of the benzene ring, as indicated by the dotted line. Condensation of 1-phenylacetyl*cyclo*hex-1-ene with cyanoacetamide gave α-cyano-α-2-phenylacetyl*cyclo*hexylacetamide



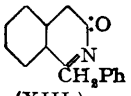
(X.)



(XI.)



(XII.)



(XIII.)

(XI), the amide group of which was hydrolysed by addition of sodium nitrite to a solution of (XI) in hot 50% sulphuric acid. This treatment led also to cyclisation with formation of 1-benzyl-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-octahydro-3-keto*iso*quinoline-4-carboxylic acid (XII; X = OH), which was obtained more conveniently by hydrolysis of its amide (XII; X = NH_2) prepared directly by condensation of phenylacetyl*cyclo*hexene with malonamide in presence of sodium ethoxide.

The action of nitrous acid on (XII; X = NH_2) gave the corresponding acid (XII; X = OH) which was decarboxylated by heat to 1-benzyl-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-octahydro-3-keto*iso*quinoline (XIII). Reduction of this by catalytic hydrogenation over copper chromite was not found possible, but reduction with sodium and dry butanol gave 1-benzyldecahydro*iso*quinoline (X) in satisfactory yield.

Experimental.

α-2-*Acetyl*cyclo*hexylbenzyl Cyanide* (I).—Acetyl chloride and *cyclo*hexene were condensed to give 1-acetyl*cyclo*hex-1-ene by Darzens's method (*Compt. rend.*, 1910, **150**, 709; see also Ruzicka *et al.*, *Helv. Chim. Acta*, 1931, **14**, 1157). The product was characterised as the semicarbazone, m. p. 220° (lit., 220°), and as the *oxime*, the m. p. of which was not in agreement with the published figure. It formed colourless needles, m. p. 61—62°, from aqueous methanol (lit., 90°, 99°), and was unchanged after many recrystallisations (Found: C, 69·3; H, 9·1; N, 9·9. $C_8H_{13}ON$ requires C, 69·1; H, 9·3; N, 10·1%). Acetyl*cyclo*hexene was condensed with benzyl cyanide by the method of Barr and Cook (*loc. cit.*) to give α-2-acetyl*cyclo*hexylbenzyl cyanide, m. p. 119—120°. The *semicarbazone*, prepared in aqueous pyridine, and recrystallised from ethanol, was obtained as small prisms, m. p. 229—230° (decomp.) (Found: C, 68·4; H, 7·4; N, 18·8. $C_{17}H_{22}ON_4$ requires C, 68·5; H, 7·4; N, 18·8%).

*Stereoisomeric Decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinolines* (II; R = Et).—The above acetyl*cyclo*hexylbenzyl cyanide (10·4 g.) in ethanol (500 c.c.) was hydrogenated over copper chromite catalyst (3 g.) at 200°/175 atm. for 2 hours. The basic fraction was isolated as a colourless oil (9·0 g.), b. p. 166°/2·5 mm., and was immediately converted into the picrate, and submitted to fractional crystallisation from ethanol.

*" α "-Decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinoline picrate* formed long yellow needles, m. p. 178—179° (Found: C, 59·3; H, 6·4; N, 11·3. $C_{24}H_{30}O_7N_4$ requires C, 59·3; H, 6·2; N, 11·5%). The free *base* was recovered as a colourless oil, b. p. 155°/2 mm. (Found: C, 84·0; H, 10·3; N, 5·4. $C_{18}H_{27}N$ requires C, 84·0; H, 10·5; N, 5·4%).

The *" β "-picrate* formed small yellow needles, m. p. 209—210° (decomp.) (Found: C, 59·5; H, 6·2; N, 11·7%). It gave the free *base* as a colourless oil, b. p. 136°/1 mm. (Found: C, 84·2; H, 10·3; N, 5·5%).

1-*Methyl-4-phenyl*iso*quinoline*.—A mixture of *" α "*- and *" β "*-decahydro-2-ethyl-1-methyl-4-phenyl*iso*quinoline (1·5 g.) was dehydrogenated by palladium (0·15 g.) at 300—320°, until hydrogen was

no longer evolved (8 hours). Distillation of the product gave a colourless oil (1·25 g.), b. p. 150—154°/1 mm., which was converted into the picrate. Crystallisation from ethanol and from benzene gave 1-methyl-4-phenyl*iso*quinoline picrate as small yellow needles, m. p. 229—230° (decomp.) (Found : C, 59·2; H, 3·6; N, 12·7. Calc. for $C_{22}H_{16}O_7N_4$: C, 58·9; H, 3·6; N, 12·5%). The free base solidified on storage, and after crystallisation from light petroleum, formed elongated colourless prisms, m. p. 78—79° (Found : C, 88·0; H, 6·1; N, 6·4. Calc. for $C_{16}H_{13}N$: C, 87·7; H, 6·0; N, 6·4%). Krabbe (G.P. 652,041; *Chem. Abs.*, 1938, **32**, 1715) gives m. p.s 206° and 79° for the picrate and free base, respectively.

Stereoisomeric Decahydro-1 : 2-*dimethyl*-4-*phenyl*isoquinolines (II; R = Me).—Acetyl*cyclo*hexylbenzyl cyanide (10 g.) in methanol (500 c.c.) was hydrogenated over copper chromite catalyst (3 g.) for 4 hours, at 200°/190 atm. The basic fraction was distilled and gave a colourless oil (7 g.), b. p. 150—155°/2 mm., and a non-volatile residue (2 g.). The oil was converted into the picrate, which was then fractionally crystallised from ethanol. "α"-*Decahydro*-1 : 2-*dimethyl*-4-*phenyl*isoquinoline *picrate* formed small yellow needles, m. p. 176—177° (Found : C, 58·6; H, 6·1; N, 12·1. $C_{23}H_{28}O_7N_4$ requires C, 58·5; H, 5·9; N, 11·9%). The free *base* was obtained as a colourless oil, b. p. 152°/1·5 mm. (Found : C, 84·0; H, 10·3; N, 5·4. $C_{17}H_{25}N$ requires C, 84·2; H, 10·1; N, 5·7%). The "β"-*picrate* formed long yellow needles, m. p. 205—206° (decomp.) (Found : C, 58·7; H, 5·7; N, 12·1%). The free *base* was obtained as a colourless oil, b. p. 141°/1·5 mm. (Found : C, 84·0; H, 10·1; N, 5·8%).

Stereoisomeric Decahydro-1-*methyl*-4-*phenyl*-2-n-*propyl*isoquinolines (II; R = Pr^n).—Acetyl*cyclo*hexylbenzyl cyanide (15 g.) in *n*-propanol (500 c.c.) was hydrogenated over copper chromite (4·5 g.) for 2 hours at 200°/155 atm. The basic fraction was distilled and yielded a colourless oil (15·4 g.), b. p. 173—178°/3 mm. The oil was converted into the picrate, which was then fractionally crystallised from ethanol. "α"-*Decahydro*-1-*methyl*-4-*phenyl*-2-n-*propyl*isoquinoline *picrate* formed yellow needles, m. p. 148—149° (Found : C, 60·0; H, 6·4; N, 11·5. $C_{25}H_{32}O_7N_4$ requires C, 60·0; H, 6·4; N, 11·2%). The *base* was obtained as a colourless oil, b. p. 147—149°/0·8 mm. (Found : C, 83·9; H, 10·3; N, 4·8. $C_{19}H_{29}N$ requires C, 84·1; H, 10·7; N, 5·2%). The "β"-*picrate* formed yellow needles, m. p. 184—185° (decomp.) (Found : C, 60·3; H, 6·2; N, 11·2%). The free *base* was obtained as a colourless oil, b. p. 175° (bath)/0·7 mm. (Found : C, 83·9; H, 10·5; N, 5·0%).

α-2-*Acetyl*cyclo*hexylphenylacetic Acid*.—α-2-Acetyl*cyclo*hexylbenzyl cyanide (4 g.) was hydrolysed by boiling with potassium hydroxide (15 g.) in aqueous ethanol, for 3 hours. The cooled solution was diluted with water (30 c.c.), extracted with ether, acidified with dilute hydrochloric acid, and again extracted with ether. This extract, on evaporation, gave a yellow oil (1·5 g.) which solidified. Crystallisation from light petroleum gave α-2-*acetyl*cyclo*hexylphenylacetic acid* as prisms, m. p. 146—147° (Found : C, 73·7; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). A small quantity (0·4 g.) of ether-insoluble material separated when the alkaline reaction mixture was acidified. It crystallised from light petroleum as plates, m. p. 224—225°, and analysis supports its identification as 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*-1-*methyl*-4-*phenyl*isoquinoline (Found : C, 79·7; H, 8·0; N, 5·9. $C_{16}H_{19}ON$ requires C, 79·7; H, 7·9; N, 5·8%).

As the ester rather than the acid was required for subsequent stages, it was found more satisfactory to carry out the hydrolysis as follows : Acetyl*cyclo*hexylbenzyl cyanide (10 g.) was refluxed for 17 hours with a mixture of 95% ethanol (20 g.) and concentrated sulphuric acid (20 g.). After cooling, the mixture was diluted with water (50 c.c.) and extracted with ether. The extract was washed with dilute aqueous sodium carbonate, dried, and evaporated. The residue, on distillation, gave *ethyl* α-2-*acetyl*cyclo*hexylphenylacetate*, as a colourless oil, b. p. 166—168°/1 mm. (6·0 g.) (Found : C, 75·2; H, 8·3. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·3%). The identity of this ester was confirmed by its hydrolysis with potassium hydroxide in aqueous ethanol to the acid, m. p. 146—147°, not depressed on admixture with a specimen prepared by direct alkaline hydrolysis of the cyanide.

Hydrogenation of the Oxime (III).—It was not found possible to isolate the pure oxime of the above ethyl acetyl*cyclo*hexylphenylacetate, but a crude specimen was successfully hydrogenated. A solution of the ester (5 g.), hydroxylamine hydrochloride (2·5 g.), and sodium acetate (5 g.) in aqueous ethanol was boiled under reflux for 3 hours. The mixture was poured into water, and the product extracted with ether, to give an oil (5 g.) which did not solidify. A portion of this oil (2·5 g.) in methanol (100 c.c.) was hydrogenated at 200°/145 atm. over copper chromite (1 g.) for 2 hours. The basic fraction was distilled and gave two products, (i) a colourless oil (0·2 g.), b. p. 146° (bath)/1 mm., and (ii) a colourless solid (0·3 g.), b. p. 200—220° (bath)/1 mm. The oil was converted into the picrate which, after crystallisation from ethanol, formed yellow needles, m. p. 202—203° (decomp.), not depressed on admixture with authentic "β"-decahydro-1 : 2-dimethyl-4-phenyl*iso*quinoline picrate. The "α"-isomer could not be detected. The solid distillate (ii) was separated by fractional crystallisation from light petroleum into two isomers, both of which were insoluble in dilute hydrochloric acid. *Decahydro*-3-*keto*-1-*methyl*-4-*phenyl*isoquinoline-A (V) formed small colourless needles, m. p. 180—181°, from light petroleum (Found : C, 79·3; H, 8·5; N, 5·9. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·6; N, 5·8%). The B-*isomer* formed small colourless needles, m. p. 168—169°, from light petroleum (Found : C, 79·0; H, 8·7; N, 5·4%).

*Condensation of Acetyl*cyclo*hexene and Ethyl Phenylacetate*.—A solution of sodium ethoxide (from sodium, 6 g., and ethanol, 120 c.c.) was added slowly to a mixture of 1-acetyl*cyclo*hex-1-ene (30 g.) and ethyl phenylacetate (26 g.). After being heated under reflux for 5 hours, the solution was cooled and poured into 10% hydrochloric acid (375 c.c.). The product solidified overnight, and was collected and washed free from traces of oil with light petroleum. The yellow powder (33 g.) was fractionally crystallised from aqueous ethanol, and separated into two isomeric diketones (VII or VIII ?).

Diketone-A formed small colourless needles (from aqueous ethanol), m. p. 197—198° (Found : C, 79·0; H, 7·5. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·4%). Microhydrogenation in acetic acid over Adams's platinum catalyst led to hydrogen absorption equivalent to 6·05 double bonds. The *dioxime*, prepared by heating a pyridine solution with hydroxylamine hydrochloride, formed colourless needles (from

aqueous ethanol), m. p. 124—125° (decomp.) (Found : C, 69·6; H, 7·6; N, 9·9. $C_{16}H_{20}O_2N_2$ requires C, 70·6; H, 7·4; N, 10·3%).

Diketone-B, of which about 10 times as much was present in the crude mixture, formed colourless prisms (from light petroleum, b. p. 80—100°), m. p. 169—170° (Found : C, 79·0; H, 7·4%). Micro-hydrogenation led to absorption of hydrogen equivalent to 5·9 double bonds. The *dioxime* formed colourless needles (from aqueous ethanol), m. p. 218—219° (decomp.) (Found : C, 70·6; H, 7·4; N, 9·9%).

Condensation of Phenylacetylcyclohexene with Ethyl Cyanoacetate.—A solution of sodium ethoxide (from 2·5 g. of sodium and 50 c.c. of ethanol) was added slowly to a mixture of 1-phenylacetyl*cyclo*hex-1-ene (10 g.; Cook and Hewett, *J.*, 1933, 1106) and ethyl cyanoacetate (5·5 g.). After 4½ hours at room temperature the mixture was poured into 10% hydrochloric acid (180 c.c.). The product solidified overnight, and was washed with a little light petroleum to remove traces of oil. The *compound* [?*4-cyanodecahydro*-1 : 3-*diketo*-2-*phenylnaphthalene* (IX)] crystallised from benzene in colourless prisms, m. p. 199—200° (Found : C, 76·2; H, 6·3; N, 5·0; OEt, 0·0. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2; OEt, 0·0%).

Like the diketones-*A* and -*B* this substance did not give an appreciable colour with ferric chloride solution. An oxime, semicarbazone, or dinitrophenylhydrazone could not be obtained. Treatment with acetic anhydride in pyridine, for 3½ hours in the cold, gave a *diacetyl* derivative, which crystallised from light petroleum (b. p. 80—100°) in elongated prisms, m. p. 129—130° (Found : C, 72·1; H, 6·0; N, 4·1. $C_{21}H_{21}O_4N$ requires C, 71·8; H, 6·0; N, 4·0%).

1-*Benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*iso*quinoline* (XIII).—(*a*) 1-Phenylacetyl*cyclo*hex-1-ene (12 g.) was added to a hot solution of malonamide (6·75 g., 10% excess) in dry ethanol (300 c.c.), and then slowly, with stirring, a solution of sodium ethoxide (from 1·7 g. of sodium and 30 c.c. of ethanol). The solution was boiled under reflux for 12 hours, during which some ammonia was evolved, and then evaporated to about 50 c.c. and poured into 10% hydrochloric acid (200 c.c.). After being kept overnight the product was solid and was washed free from oily by-products with a little warm ethanol. Crystallisation from ethanol gave 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*iso*quinoline*-4-*carboxyamide* (XII; X = NH_2) (6·8 g.) as prisms, m. p. 257—258° (decomp.) (Found : C, 71·6; H, 7·0; N, 9·8. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·0; N, 9·9%).

For hydrolysis to the acid, a solution of sodium nitrite (1 g.) in water (10 c.c.) was slowly added, through a capillary tube below the surface of the liquid, to a solution of this amide (2 g.) in 40% sulphuric acid (130 c.c.) at 100°. The solution was then heated for 5 minutes longer, cooled, and diluted with water (200 c.c.). The solid which separated was dissolved in dilute sodium carbonate solution, and the filtered solution acidified. The precipitated solid was crystallised from benzene giving 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*iso*quinoline*-4-*carboxylic acid* (XII; X = OH) (1·8 g.) as colourless plates (or needles), m. p. 206—207° (decomp.) (Found : C, 71·9; H, 6·2; N, 5·0. $C_{17}H_{19}O_3N$ requires C, 71·6; H, 6·7; N, 4·9%).

For decarboxylation, this acid (1·8 g.) was heated at 210°. Carbon dioxide was freely evolved and after ¼ hour the melt resolidified. Crystallisation from ethanol then gave 1-*benzyl*-3 : 4 : 5 : 6 : 7 : 8 : 9 : 10-*octahydro*-3-*keto*iso*quinoline* (XIII) as colourless needles, m. p. 244—245° (decomp.) (1·3 g.) (Found : C, 80·6; H, 7·1; N, 6·1. $C_{16}H_{19}ON$ requires C, 79·7; H, 7·9; N, 5·8%). The analyses are in better agreement with benzyltetrahydro*iso*quinolone ($C_{16}H_{17}ON$) which would require loss of hydrogen during decarboxylation. However, the product was insoluble in aqueous sodium hydroxide.

(*b*) To a hot solution of cyanoacetamide (3·5 g., 10% excess) and phenylacetyl*cyclo*hex-1-ene (7·5 g.) in dry ethanol (75 c.c.) a solution of sodium ethoxide (from 1·1 g. of sodium and 25 c.c. of ethanol) was added slowly, with stirring. The solution was boiled under reflux for 7 hours, during which evolution of ammonia took place, and was then evaporated to about 50 c.c. and poured into 10% hydrochloric acid (100 c.c.). After being kept overnight, the solid product was washed with a little ethanol to remove oily impurity. *α-Cyano-α-2-phenylacetylcyclohexylacetamide* (XI) (2·2 g.) formed colourless needles (from ethanol), m. p. 247—248° (decomp.) (Found : C, 71·9; H, 7·1; N, 10·1. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·0; N, 9·9%). The m. p. was strongly depressed on admixture with the isomeric amide (XII; X = NH_2). This cyanide (0·3 g.) was treated with sodium nitrite as described above in the case of the amide (XII; X = NH_2), except that 50% sulphuric acid (50 c.c.) was used and the reaction carried out at 140°. The acid (0·15 g.) obtained had m. p. 206—207° (decomp.), not depressed by a sample prepared as described under (*a*), and the identification was completed by decarboxylation to the same product (XIII).

1-*Benzyldecahydro*iso*quinoline* (X) (Experiments by G. G. Doig).—The yield of this formed by reduction of (XIII) with sodium and butanol was poor when precautions were not taken to dry the butanol (cf. Koelsch, *J. Amer. Chem. Soc.*, 1943, **65**, 2093). Accordingly, butanol (1 l.) was distilled through a column and the fraction, b. p. 116—117°, was treated with sodium (7 g.), added in small pieces, and then with butyl phthalate (35 g.) (cf. Manske, *J. Amer. Chem. Soc.*, 1931, **53**, 1106). After boiling for an hour, with exclusion of moisture, the solution was distilled through a column and the distillate, protected from moisture, was used for the following reduction : Sodium (1·52 g.) was added to a boiling solution of 1-benzyloctahydro-3-keto*iso*quinoline (XIII) (1 g.) in butanol (20 c.c.). Boiling was continued for ½ hour and the cooled mass was cautiously treated with water (7 c.c.) which dissolved the solid which had separated. The aqueous layer was treated with 2N-hydrochloric acid (20 c.c.), and the butanol was then removed in steam. The residual solution was extracted with ether to remove a trace of coloured material, and then basified and re-extracted with ether. The dried extract, on evaporation, gave crude 1-benzyldecahydro*iso*quinoline (0·7 g.) as a pale yellow oil. It was purified through its oxalate, formed by addition of a solution of oxalic acid (0·02 g.) in dry ether (4 c.c.) to a solution of the base (0·1 g.), also in ether (1 c.c.). The ether was decanted from the precipitated semi-

solid mass, which became completely solid when triturated with ethanol. Crystallisation from dry ethanol gave the *oxalate* of 1-benzyldecahydro*iso*quinoline as colourless microscopic needles, m. p. 230° (decomp.) (Found : C, 74·1 ; H, 8·9 ; N, 5·0. $C_{34}H_{48}O_4N_2$ requires C, 74·3 ; H, 8·8 ; N, 5·1%). 1-*Benzyldecahydroisoquinoline* (X), regenerated from the pure oxalate, was used for the preparation of the following salts. It formed a yellowish liquid, b. p. 135—138°/2 mm. (Found : C, 83·3 ; H, 10·25 ; N, 6·3. $C_{16}H_{23}N$ requires C, 83·8 ; H, 10·1 ; N, 6·1%).

The *hydrogen tartrate*, prepared from the components in dry ether, formed colourless microscopic rosettes, m. p. 176—177° (Found : C, 63·6 ; H, 7·4. $C_{20}H_{29}O_6N$ requires C, 63·8 ; H, 7·7%). The *picrate*, prepared in ethanol, could not be recrystallised on account of dissociation ; it formed yellow prisms, m. p. 137° (Found : N, 12·2. $C_{22}H_{26}O_7N_4$ requires N, 12·45%). The *hydrochloride*, obtained by passing dry hydrogen chloride into a solution of the base in dry ether, was dried in a vacuum-desiccator over potassium hydroxide and recrystallised from ethanol. It formed colourless microscopic prisms, m. p. 156—160° (decomp.), which readily took up moisture (Found : C, 72·3 ; H, 8·5 ; N, 5·5. $C_{16}H_{24}NCl$ requires C, 72·3 ; H, 8·7 ; N, 5·3%).

Our thanks are offered for an I.C.I. Research Fellowship which has enabled one of us (G. M. B.) to take part in this work, and also to the Department of Scientific and Industrial Research for a Maintenance Allowance (to G. M. S. D.). Microanalyses were carried out by Mr. J. M. L. Cameron and Miss R. H. Kennaway.

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