550. *Synthetic and Stereochemical Investigations of Reduced Cyclic Bases. Part VI.* A New Synthesis of* trans-*Octahydroindole and a Re-investigation of its Hofmann Methylation Products.*

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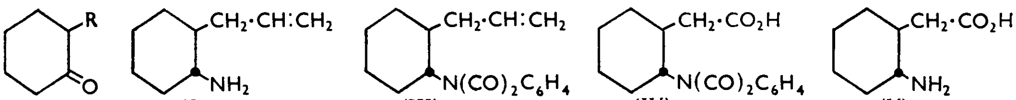
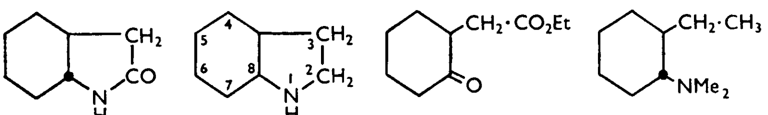
An improved synthesis of *trans*-octahydroindole has been devised starting from 2-allyl*cyclo*hexanone, and with the greater availability of this amine the decomposition of its *N*-methyl methohydroxide has been re-investigated. The newer experiments have apparently given a more readily purified methine and revised melting points of salts of its dihydro-derivative correspond with those of *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine.

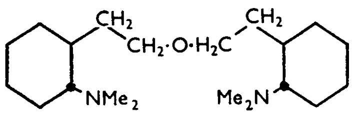
THE synthesis of *cis*- and *trans*-octahydroindole described in Part III [1] requires 2-2′-ethoxyethyl*cyclo*hexanone (I; R = $\cdot CH_2\cdot CH_2\cdot OEt$), the amino-group being introduced at the keto-position either mainly *cis* by the Leuckart reaction, or wholly *trans* by sodium–alcohol reduction of the oxime. The preparation of the ketone (I; R = $\cdot CH_2\cdot CH_2\cdot OEt$) is tedious and the route to *trans*-octahydroindole has been simplified by using the more easily obtainable 2-allyl*cyclo*hexanone [2] (I; R = $\cdot CH_2\cdot CH{:}CH_2$). When the ketoxime was reduced with lithium aluminium hydride a mixture of the isomeric 2-allyl*cyclo*hexylamines was apparently formed, but with sodium–alcohol the sole product was the *trans*-base (II). The derived phthalimide (III) was oxidised with potassium permanganate to 2-phthalimido*cyclo*hexylacetic acid (IV). Removal of the phthaloyl group with hot hydrochloric acid gave the amino-acid (V) as hydrochloride, and distillation of the free amino-acid *in vacuo* or heating its ester caused ring-closure to the amide (VI). Finally, the amide was reduced with lithium aluminium hydride in ether, the product being identical with the known *trans*-octahydroindole (VII).



(I) (II) (III) (IV) (V)



(VI) (VII) (VIII) (IX)



(X)

An alternative synthesis of the amino-acid (V) was explored which began with 1-*cyclo*-hex-1′-enylpyrrolidine from which ethyl 2-oxo*cyclo*hexylacetate (VIII) was formed by treatment with ethyl bromoacetate.[3] However, hydrogenation of the ketoxime in alcoholic ammonia with Raney nickel appeared not to be stereospecific since after hydrolysis with hydrochloric acid the product consisted of the mixed amino-acid salts, and repeated crystallisation was necessary to obtain the pure *trans*-hydrochloride. The method was therefore not pursued.

The larger amounts of *trans*-octahydroindole obtainable by the improved synthesis

* Part V, Booth, King, and Parrick, *J.*, 1958, 2302.
[1] King, Bovey, Mason, and Whitehead, *J.*, 1953, 250.
[2] *Org. Synth.*, Coll. Vol. III, p. 44 (1955).
[3] Stork, Terrell, and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1954, **76**, 2029.

enabled a more precise examination of the decomposition of its *N*-methyl methohydroxide to be made. Former experiments [1] gave a methine which was believed to have a rearranged carbon skeleton since its dihydro-derivative appeared to differ from both products to be expected from normal degradation. The earlier limited specimens of the dihydro-derivative were characterised in the form of the picrate (m. p. 106°), picrolonate (160°), and methiodide [221° (decomp.)]. With the larger quantities now forthcoming, melting points of the derivatives were picrate 123—124°, picrolonate 172—173°, and methiodide 221° (decomp.), indicating higher purity of the degradation product, due probably to improved quality of the octahydroindole.

The melting points of the new specimens of the three derivatives resemble closely (as do other constants, *e.g.*, refractive index and m. p. of the hydriodide) those of *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine [1,4] (IX), so that the product of the Hofmann change is *trans*-*NN*-dimethyl-2-vinyl*cyclo*hexylamine. It is evident, therefore, that scission of the $N-C_{(2)}$ bond has taken place, whereas in the decomposition of *cis*-octahydro-1-methylindole methohydroxide it is the $N-C_{(8)}$ bond which is severed. This contrasting behaviour of the two isomers is not unexpected in view of the conformational features mentioned in Part IV [5] although it is now clear that the consequences for the *trans*-methohydroxide were there incorrectly interpreted.

Ring-scission of the *trans*-isomer differs from that of the *cis*-compound also in the formation from the *trans*-methohydroxide of a by-product $C_{20}H_{40}ON_2$. This has already been recognised as an ether by hydrolysis with hydrobromic acid to a bromo-amine salt, $C_{20}H_{20}NBr,HBr$, and a tentative constitution has been assigned to it.[5] With hydriodic acid the ether gives the presumably analogous iodo-compound which is reduced by zinc and acetic acid to the foregoing *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine, thus disclosing the structure of the ether as (X). The formation of an ether of this type suggests that conditions are unfavourable for proton removal by hydroxyl ion attack at position 3, an essential feature of the Hofmann reaction. Here again conformational factors are probably involved since molecular models reveal that the requirement for easy elimination of the hydrogen at this position is lacking.

EXPERIMENTAL

trans-2-*Allyl*cyclo*hexylamine*.—2-Allyl*cyclo*hexanone [2] (60 g.) was converted by the usual procedure into the oxime (62 g., 93%), m. p. 71—72° (Cope, Hoyle, and Heyl [6] record m. p. 70—70·5°). The oxime (17 g.), in boiling ethanol (200 c.c.), was treated with sodium (50 g.) added in small pieces during 1·5 hr. After the mixture had been refluxed for a further 30 min., excess of sodium was removed by the addition of aqueous ethanol. The cooled solution was acidified with 15% hydrochloric acid, then evaporated to remove ethanol, and non-basic material was removed with ether. The aqueous solution was made alkaline and the liberated base was extracted with ether. trans-2-*Allyl*cyclo*hexylamine* (12·8 g., 83%) was thus isolated as a colourless oil, b. p. 69—70°/9 mm. The base, which was not itself analysed owing to its rapid conversion into carbonate on exposure to air, yielded the following derivatives: *picrate*, crystallising from ethanol in prisms, m. p. 178—179° (Found: C, 49·0; H, 5·8; N, 14·9. $C_{15}H_{20}O_7N_4$ requires C, 48·9; H, 5·5; N, 15·2%); *picrolonate*, needles, m. p. 217—218°, from ethanol (Found: C, 56·8; H, 6·2; N, 17·6. $C_{19}H_{25}O_5N_5$ requires C, 56·6; H, 6·2; N, 17·4%); *acetyl derivative*, crystallising from light petroleum (b. p. 60—80°) in needles, m. p. 107—108° (Found: C, 72·7; H, 10·4; N, 7·7. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·6; N, 7·7%); *benzoyl derivative*, crystallising from ethanol in needles, m. p. 137—138° (Found: C, 79·1; H, 8·8; N, 5·85. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·7; N, 5·8%).

Treatment of the base (2·3 g.) with 40% aqueous formaldehyde (3 c.c.) and 90% formic acid (7 c.c.) for 2 hr. on a steam-bath, followed by ether-extraction of the basified solution, gave *trans*-2-allyl-*NN*-dimethyl*cyclo*hexylamine (2·4 g.). The tertiary base yielded a picrate

[4] King, Barltrop, and Walley, *J.*, 1945, 277.
[5] King and Booth, *J.*, 1954, 3798.
[6] Cope, Hoyle, and Heyl, *J. Amer. Chem. Soc.*, 1941, **63**, 1843.

which crystallised from ethanol in prisms, m. p. 100—101° (Fujise [7] records 101—102°; Bailey, Haworth, and McKenna [8] record 100—101°).

*Reduction of 2-Allyl*cyclo*hexanone Oxime with Lithium Aluminium Hydride.*—The oxime (0·5 g.), in dry ether, was added to a solution of lithium aluminium hydride (0·5 g.) in dry ether. The mixture was refluxed for 2·5 hr. and worked up by ether-extraction of the basified mixture. The resulting oil, which was probably a mixture of *cis*- and *trans*-amines, was converted into the benzoyl derivative, m. p. 109—111°. Five recrystallisations from light petroleum (b. p. 60—80°) gave a poor yield of *trans*-1-allyl-2-benzamido*cyclo*hexane, m. p. and mixed m. p. 137—138°.

N-(trans-*2-Allyl*cyclo*hexyl)phthalamic Acid.*—*trans*-2-Allyl*cyclo*hexylamine (5·8 g.), dry chloroform (50 c.c.), and phthalic anhydride (6·2 g.) were heated under reflux for 1 hr. The cooled mixture was extracted three times with sodium hydrogen carbonate solution and the combined extracts were acidified with dilute hydrochloric acid. The precipitate (7·5 g., 63%) was collected, dried, and crystallised from ethanol. N-(trans-*2-Allyl*cyclo*hexyl)phthalamic acid* was thus obtained in colourless needles, m. p. 161—162° (Found: C, 71·0; H, 7·2; N, 4·8. $C_{17}H_{21}O_3N$ requires C, 71·1; H, 7·4; N, 4·9%).

trans-*1-Allyl-2-phthalimido*cyclo*hexane.*—(i) A solution of the above phthalamic acid (7·5 g.) in acetic anhydride (20 c.c.) was refluxed for 1 hr. and then poured into water. trans-*1-Allyl-2-phthalimido*cyclo*hexane* (4·5 g., 63%) was recovered by filtration. Crystallisation from ethanol gave needles, m. p. 90—91·5° (Found: C, 75·9; H, 7·3; N, 5·35. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). (ii) *trans*-2-Allyl*cyclo*hexylamine (12·8 g.), glacial acetic acid (75 c.c.), and phthalic anhydride (14 g.) were refluxed gently for 5½ hr. The hot mixture was poured into cold water (500 c.c.): an oil was produced which soon solidified. The crude imide was purified by suspending it in dilute sodium carbonate solution and filtering. The residue of *trans*-1-allyl-2-phthalimido*cyclo*hexane (22·4 g., 90%), m. p. 85—87°, crystallised from ethanol in needles, m. p. 90—91·5°.

trans-*2-Phthalimido*cyclo*hexylacetic Acid.*—Potassium permanganate (30 g.) was added during 2 days to a stirred solution of *trans*-1-allyl-2-phthalimido*cyclo*hexane (15·2 g.) in pure dry acetone (600 c.c.). Finally the mixture was filtered and the residue was suspended in dilute sulphuric acid containing crushed ice. Sulphur dioxide was passed through the mixture until no more manganese dioxide remained, after which the solution was filtered. Crystallisation of the residue from aqueous methanol gave trans-*2-phthalimido*cyclo*hexylacetic acid* (12·75 g., 79%), m. p. 172—173·5° (Found: C, 66·8; H, 6·2; N, 4·5. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0; N, 4·9%). The *methyl ester* crystallised from methanol in needles, m. p. 131—132° (Found: C, 67·8; H, 6·3; N, 4·9. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·7%). The *ethyl ester* crystallised from aqueous ethanol in needles, m. p. 67—68° (Found: C, 68·9; H, 6·4; N, 4·6. $C_{18}H_{21}O_4N$ requires C, 68·6; H, 6·7; N, 4·4%).

trans-*2-Acetamido*cyclo*hexylacetic Acid.*—The oxidation of *trans*-1-acetamido-2-allyl*cyclo*hexane (7·2 g.) with potassium permanganate (21 g.) was carried out as described above for the corresponding phthalimido-compound. The resulting *acid* (5·6 g., 71%), m. p. 178—180°, was purified by crystallisation from water, from which it was obtained in needles, m. p. 184—185° (Found: C, 60·7; H, 8·63; N, 7·1. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·6; N, 7·0%).

trans-*2-Amino*cyclo*hexylacetic Acid.*—*trans*-2-Phthalimido*cyclo*hexylacetic acid (15 g.), concentrated hydrochloric acid (200 c.c.) and ethanol (50 c.c.) were heated under reflux for 48 hr. The solution was cooled in the ice-chest, filtered from phthalic acid, and extracted three times with ether. The residual aqueous phase was then evaporated under reduced pressure on a water-bath, giving trans-*2-amino*cyclo*hexylacetic acid hydrochloride* (8·4 g., 83%). Crystallisation from methanol–ether gave needles, m. p. 216—217° (Found: C, 49·8; H, 8·1; N, 7·3; Cl, 18·7. $C_8H_{16}O_2NCl$ requires C, 49·6; H, 8·3; N, 7·2; Cl, 18·3%). The hydrochloride (20 g.) was shaken in the dark with a suspension in water (150 c.c.) of silver carbonate, freshly prepared from silver nitrate (30 g.) and sodium carbonate (10 g.). The mixture was left overnight and then filtered from silver chloride. The filtrate was treated with hydrogen sulphide, filtered from silver sulphide, and evaporated to dryness. Crystallisation of the residue from slightly aqueous methanol gave trans-*2-amino*cyclo*hexylacetic acid monohydrate*, m. p. 221° (decomp.) (11·6 g., 64% from the hydrochloride) (Found: C, 54·8; H, 9·7; N, 8·2. $C_8H_{15}O_2N,H_2O$ requires C, 54·9; H, 9·8; N, 8·0. Found, after drying at 110°: C, 61·3;

[7] Fujise, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1928, **8**, 185.
[8] Bailey, Haworth, and McKenna, *J.*, 1954, 967.

H, 9·9. $C_8H_{15}O_2N$ requires C, 61·1; H, 9·6%). The *picrate*, prepared from the hydrochloride and aqueous sodium picrate, crystallised from water in prisms, m. p. 177—179° (Found: C, 43·8; H, 4·6; N, 14·3. $C_{14}H_{18}O_9N_4$ requires C, 43·5; H, 4·7; N, 14·5%). The *benzoyl derivative* crystallised from methanol in needles or prisms, m. p. 194—195° (Found: C, 68·7; H, 7·3. $C_{15}H_{19}O_3N$ requires C, 69·0; H, 7·3%). The prism form was converted into the needle form, with slight softening, at about 180°.

Methyl trans-2-*Aminocyclohexylacetate*.—The above amino-acid hydrochloride (18·9 g.) was dissolved in dry methanol (250 c.c.) containing hydrochloric acid (about 5% w/v) and heated under reflux for 12 hr. The solution was finally distilled to remove excess of methanol, cooled, and poured into saturated ice-cold potassium carbonate solution (100 c.c.) covered by a layer of ether (100 c.c.). After separation of the ether, the aqueous phase was extracted with further portions of ether (4 × 100 c.c.). Removal of the ether gave *methyl* trans-2-*aminocyclohexylacetate* (12·1 g., 72%), b. p. 135—150° (bath-temp.)/10 mm. (Found: C, 63·4; H, 9·9. $C_9H_{17}O_2N$ requires C, 63·1; H, 10·0%). The amino-ester gave the following derivatives: *hydrochloride*, crystallising from methanol–ether in needles, m. p. 153—154° (Found: C, 52·0; H, 8·6. $C_9H_{18}O_2NCl$ requires C, 52·0 ; H, 8·7%); *picrate*, prepared from the hydrochloride and aqueous sodium picrate, and crystallising from aqueous methanol in needles, m. p. 114—116° (Found: C, 45·3; H, 5·0; N, 14·1. $C_{15}H_{20}O_9N_4$ requires C, 45·0; H, 5·0; N, 14·0%); *benzoyl derivative*, crystallising from methanol in needles, m. p. 138—139° (Found: C, 69·8; H, 7·5; N, 5·1. $C_{16}H_{21}O_3N$ requires C, 69·8; H, 7·7; N, 5·1%); *toluene*-p-*sulphonyl derivative*, crystallising from benzene–light petroleum (b. p. 60—80°) in plates, m. p. 141—142° (Found: C, 59·2; H, 6·9; N, 4·7. $C_{16}H_{23}O_4NS$ requires C, 59·1; H, 7·1; N, 4·3%).

trans-*Octahydro*-2-*oxoindole*.—(i) Methyl *trans*-2-amino*cyclo*hexylacetate (19·9 g.) was heated to 170° for 2 hr. at atmospheric pressure and then distilled under reduced pressure. The distillate of trans-*octahydro*-2-*oxoindole* (11·4 g., 70%), b. p. 167—168°/15 mm., quickly solidified. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave colourless needles, m. p. 82—83·5° (Found: C, 69·2; H, 9·5; N, 10·3. $C_8H_{13}ON$ requires C, 69·0; H, 9·4; N, 10·1%).

(ii) *trans*-2-Amino*cyclo*hexylacetic acid monohydrate (5 g.) was heated to about 250° for 15 min. at atmospheric pressure and then distilled under reduced pressure. The resulting *trans*-octahydro-2-oxoindole (2·8 g., 70%) crystallised from benzene–light petroleum in needles, m. p. 81·5—83°.

trans-*Octahydro*-1-*methylindole Methiodide*.—A solution of *trans*-octahydro-2-oxoindole (11·4 g.) in ether (150 c.c.) was added slowly to a solution of lithium aluminium hydride (5 g.) in ether (150 c.c.). When the initial reaction had subsided, the mixture was heated under reflux for 3 hr., cooled, and treated successively with moist ether and 20% sodium hydroxide solution (100 c.c.). The ethereal layer was then separated, dried (KOH), and evaporated. The residue of *trans*-octahydroindole was characterised by the preparation of the picrate, crystallising from benzene in rhombohedra, m. p. 150—152° (Found: N, 15·4. Calc. for $C_{14}H_{18}O_7N_4$: N, 15·8%), and the picrolonate, prisms (from ethanol), m. p. 236—237° (Found: N, 18·2. Calc. for $C_{18}H_{23}O_5N_5$: N, 18·0%) (King, Bovey, Mason, and Whitehead [1] record m. p. 147° and m. p. 234° for the picrate and picrolonate respectively).

The crude octahydroindole, 90% formic acid (20 c.c.), and 40% aqueous formaldehyde (11 c.c.) were heated under reflux for 7 hr. The mixture was cooled, basified, and extracted with ether. The combined ethereal extracts were dried (KOH) and treated with methyl iodide (10 c.c.). After 24 hr., the white precipitate of *trans*-octahydro-1-methylindole methiodide (18·5 g., 80% from the octahydro-2-oxoindole) recrystallised from acetone as plates, m. p. 236—237° (King *et al.*[1] record 229°) (Found: C, 42·9; H, 7·1; N, 4·9. Calc. for $C_{10}H_{20}NI$: C, 42·7; H, 7·2; N, 5·0%).

1-cyclo*Hex*-1′-*enylpyrrolidine* (cf. Heyl and Herr [9]).—Dry pyrrolidine (14·2 g.), freshly distilled *cyclo*hexanone (4·9 g.), and dry benzene (130 c.c.) were refluxed for 1 hr. in a Dean–Stark separator. Water (1·0 g.) was collected during the first 45 min. The residual solution was heated to remove benzene and then distilled, 1-cyclo*hex*-1′-*enylpyrrolidine* (4·9 g., 65%) being obtained as a pale yellow oil, b. p. 130—133°/24 mm. (Found: C, 79·9; H, 11·2; N, 9·2. $C_{10}H_{17}N$ requires C, 79·4; H, 11·3; N, 9·3%). The *picrate* crystallised from methanol in yellow needles, m. p. 145—156° (Found: C, 50·2; H, 5·4; N, 15·0. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%).

[9] Heyl and Herr, *J. Amer. Chem. Soc.*, 1953, **75**, 1918.

*Ethyl 2-Oxo*cyclo*hexylacetate* (cf. Stork, Terrell, and Szmuszkovicz [3]).—The above *cyclo*hexenylpyrrolidine (3·2 g.) in dry methanol (50 c.c.) was treated with ethyl bromoacetate (4 g.). The mixture, which became warm, was left undisturbed for 1 hr. and then refluxed for 45 min. After the addition of water (10 c.c.), the mixture was heated on the steam-bath for 30 min. and then methanol was removed by distillation The residue was poured into water and the ester was isolated by ether-extraction. Ethyl 2-oxo*cyclo*hexylacetate (1·7 g., 38%) was thus obtained as a colourless oil, b. p. 139°/19 mm. (Chatterjee [10] and Ghosh [11] record 122°/5 mm. and 130°/10 mm. respectively). The semicarbazone had m. p. 199—200° (Chatterjee records 196—197°, Ghosh 196° and Kuehl, Linstead, and Orkin [12] 195—196°). The oxime had m. p. 57—58° (R. L. St. D. Whitehead [13] gives m. p. 61°). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in needles, m. p. 132° (Found: C, 53·1; H, 5·2; N, 15·6. $C_{16}H_{20}O_6N_4$ requires C, 52·7; H, 5·5; N, 15·3%).

*Hydrogenation of Ethyl 2-Hydroxyimino*cyclo*hexylacetate.*—The oxime (4 g.) in ethanolic ammonia (50 c.c.) was hydrogenated for 4 hr. over Raney nickel at 110°/20 atm. (initial). The filtered solution was heated to remove ammonia and ethanol and then refluxed with dilute hydrochloric acid (50 c.c.) for 6 hr. Evaporation of the solution under reduced pressure gave white crystals (3 g.), m. p. 160—170°. This was probably a mixture of *cis*- and *trans*-2-amino*cyclo*hexylacetic acid hydrochlorides. Four successive recrystallisations from ethanol gave *trans*-2-amino*cyclo*hexylacetic acid hydrochloride (0·2 g.), m. p. and mixed m. p. with an authentic specimen (see above), 216—217°.

Exhaustive Methylation of trans-*Octahydroindole* (cf. Part III [1]).—A solution of *trans*-octahydro-1-methylindole methiodide (16·4 g.) in water (50 c.c.) was shaken in the dark with silver oxide, freshly prepared from silver nitrate (16 g.) and sodium hydroxide (4·8 g.). The filtered solution was evaporated under reduced pressure at 45—50° to remove water, and the syrupy quaternary hydroxide which remained was then heated at 125—180°. The residue was purified through the picrate, m. p. 158—160°, and identified as the diamino-ether (2·1 g.) (see below). The distillate was treated with solid potassium hydroxide and worked up by ether-extraction, a basic oil (5·7 g.) being obtained. Distillation of the oil gave 2 fractions:

(i) trans-NN-*dimethyl-2-vinyl*cyclo*hexylamine* (4 g.), b. p. 70—72°/11 mm., n_D^{25} 1·4678 (Found: C, 78·2; H, 12·2; N, 9·2; *C*-Me, 1·4. $C_{10}H_{19}N$ requires C, 78·3; H, 12·5; N, 9·1; *C*-Me, 0%). The base gave a picrate, m. p. 117—119°, a picrolonate, m. p .162—162·5°, and a methiodide, plates (from acetone), m. p. 201° (recorded in Part III,[1] 117—118°, 163°, and 203° respectively). The base (3·5 g.), in methanol (50 c.c.), was neutralised with hydrochloric acid and hydrogenated over 10% palladium-charcoal (1 g.) at room temperature and pressure. Isolation in the usual way gave *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine (3·2 g.), b. p. 191—192°/748 mm., n_D^{19} 1·4571 (recorded in Part I, n_D^{20} 1·4573) (Found: C, 77·3; H, 13·2; N, 9·4; *C*-Me, 4·5. Calc. for $C_{10}H_{21}N$: C, 77·3; H, 13·6; N, 9·0; *C*-Me, 9·7%). The base gave the following derivatives: picrate, plates, m. p. 123—124°, from ethanol (Found: C, 50·0; H, 6·45; N, 14·9. Calc. for $C_{16}H_{24}O_7N_4$: C, 50·0; H, 6·3; N, 14·6%); picrolonate, plates (from ethanol), m. p. 172—173° (Found: C, 57·2; H, 7·1; N, 16·8. Calc. for $C_{20}H_{29}O_5N_5$: C, 57·3; H, 7·0; N, 16·7%); hydriodide, needles (from acetone), m. p. 182—183° (Found: C, 42·8; H, 7·7. Calc. for $C_{10}H_{22}NI$: C, 42·5; H, 7·8%); methiodide, plates (from acetone), m. p. 221° (decomp.) (Found: C, 44·5; H, 8·0 Calc. for $C_{11}H_{24}NI$: C, 44·4; H, 8·1%) (recorded in Part III [1] for authentic samples of picrate, picrolonate, hydriodide, and methiodide: m. p. 126°, 170°, 182°, and 231° respectively).

(ii) Di-[2-(*trans*-2'-dimethylamino*cyclo*hexyl)ethyl] ether (1 g.), b. p. 130°/11 mm. The dipicrate crystallised from ethanol in prisms, m. p. 158—160° (recorded in Part III,[1] 161°) (Found: C, 48·9; H, 5·8. Calc. for $C_{32}H_{46}O_{15}N_8$: C, 49·1; H, 5·9%). In addition to the dipicrolonate and distyphnate described in Part III, the base also gave the following derivatives: *dimethiodide*, crystallising from slightly aqueous acetone in rhombohedral plates, m. p. 210—211° (with resolidification) (Found: C, 43·0; H, 7·6. $C_{22}H_{46}ON_2I_2$ requires C, 43·4; H, 7·6%); *dimethopicrate*, crystallising from methanol in prisms, m. p. 142—144° (Found: C, 50·5; H, 6·2. $C_{34}H_{50}O_{15}N_8$ requires C, 50·4; H, 6·2%). Distillation of the dimethohydroxide from the dimethiodide (3 g.) gave, in addition to the original diamino-ether (0·12 g.), an unsaturated

[10] Chatterjee, *J. Indian Chem. Soc.*, 1935, **12**, 591.
[11] Ghosh, *ibid.*, p. 601.
[12] Kuehl, Linstead, and Orkin, *J.*, 1950, 2213.
[13] R. L. St. D. Whitehead, D. Phil. Thesis, Oxford, 1948.

ether, probably *di-[2-(cyclohex-2'-enyl)ethyl] ether* (0·5 g.), b. p. 180—185° (bath temp.)/15 mm., n_D^{18} 1·4950 (Found: C, 82·6; H, 11·2. $C_{16}H_{26}O$ requires C, 82·0; H, 11·2%).

The diamino-ether (0·08 g.) was heated under reflux with hydriodic acid (10 c.c.) for 20 min. The solution was cooled, diluted with glacial acetic acid (5 c.c.), and treated with zinc dust (0·5 g.), added in portions during 20 min. The mixture was finally refluxed for ½ hr., cooled, and basified with sodium hydroxide solution. Extraction with ether yielded *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine (0·03 g.) (picrate, m. p. and mixed m. p. 123—124°; picrolonate, m. p. and mixed m. p. 171—172°).

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