51. *The Thermal Decomposition of Quaternary Ammonium Hydroxides. Part II.*[1] *Methohydroxides derived from* 1,2,3,4-*Tetrahydroquinolines and* 1,2,3,4,4a,9,9a,10-*Octahydroacridines.*

By D. A. Archer, H. Booth, P. C. Crisp, and J. Parrick.

The thermal decomposition, at 160° under reflux, of the 1-methyl methohydroxide of 1,2,3,4-tetrahydroquinoine gives 95% of 1,2,3,4-tetrahydro-1-methylquinoline and 5% of *o*-allyl-*NN*-dimethylaniline. When the methohydroxide is decomposed at 90°/15 mm. and 160°/15 mm., the unsaturated base, produced in yields of 19% and 49%, respectively, consists largely of *trans*-*NN*-dimethyl-*o*-propenylaniline. Thermal decomposition of the methohydroxides of 1,2,3,4-tetrahydro-1,2-dimethylquinoline and 1,2,3,4-tetrahydro-1,2,2,4-tetramethylquinoline gives principally the expected unsaturated *o*-substituted *NN*-dimethylaniline. Complete resistance to Hofmann elimination is recorded for the methohydroxides of *cis*- and *trans*-1,2,3,4,4a,9,9a,10-octahydro-10-methylacridine, but these findings are intelligible in terms of the preferred conformations of the reactants. Nuclear magnetic resonance spectra are recorded for *cis*- and *trans*-octahydroacridine and derivatives.

In Part I, the thermal decomposition of quaternary anilinium hydroxides was studied with respect to β-elimination (Hofmann fission) and substitution (formation of methanol). The substitution : elimination ratios observed were compared with the ratios for the corresponding methylammonium hydroxides, and indicated that an *N*-phenyl group produced a marked inhibitory effect on β-elimination. However, no example was encountered in which a hydroxide containing β-hydrogen atoms decomposed exclusively by substitution. Now the conformation of the reduced ring in 1,2,3,4-tetrahydroquinoline, or the corresponding 1-methyl methohydroxide (I) is not known. However, if it is supposed, by analogy with tetralin,[2] and the flavanols,[3] that a half-chair conformation is the most stable, then the stereochemical condition for easy elimination, *trans*-coplanarity of the four centres $^{+}\text{N}\cdot\text{C}(\alpha)\cdot\text{C}(\beta)\cdot\text{H}$,[4] is satisfied for the equatorial 3-hydrogen atom, and possibly for both 3-hydrogen atoms if half-chair–half-chair inversion occurs with sufficient speed. These arguments, coupled with the knowledge that decomposition of 1-methyl-1-phenylpiperidinium hydroxide causes appreciable β-elimination,[1] forced us to question the reports [5,6] that the hydroxide (I) decomposes exclusively by extrusion of methanol.

Feer and Koenigs [5] heated a solution of the hydroxide (I) at 150° and atmospheric pressure. Part of the basic product was allowed to distil from the reaction vessel with water, and the remainder was recovered by passing steam into the solution. Knorr [6]

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[1] Part I, preceding paper.

[2] Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21.

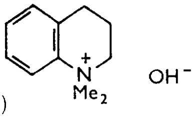
[3] Clark-Lewis and Jackman, *Proc. Chem. Soc.*, 1961, 165.

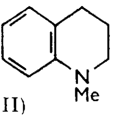
[4] McKenna, *Chem. and Ind.*, 1954, 406.

[5] Feer and Koenigs, *Ber.*, 1885, **18**, 2388.

[6] Knorr, *Ber.*, 1899, **32**, 734.

heated the quaternary iodide with sodium hydroxide solution, but it is not clear from the paper whether or not the solution was finally distilled to dryness.


(I)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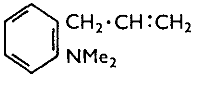
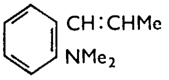

(III)

In our first experiments,[7] a highly concentrated solution of the hydroxide was heated under reflux at 150—160° for 4 hr. The isolated base showed weak maxima in the infrared spectrum at 919 and 990 ($CH=CH_2$), and 956 cm.$^{-1}$ ($Ar{\cdot}NMe_2$; symmetrical C–N stretching of Me_2N [8]), all of which are absent from the spectrum of the base (II). On gas chromatography the base showed two peaks, one (area ~95%) due to (II) and the other (area ~5%) due to *o*-allyl-*NN*-dimethylaniline (III). Whilst the unsaturated base (III) has not been separated from the mixture, its presence was inferred from the infrared figures given above, and irrefutable evidence was obtained in the following experiments. The nuclear magnetic resonance spectrum of the mixture (examined as the pure liquid) showed, in addition to the peaks characteristic of base (II), a doublet at 6·50 τ [benzylic protons of (III)] and a doublet of equal area at 4·94 τ [$=CH_2$ of (III)]. The doublet–quartet–quartet pattern at 3—4 τ characteristic of compound (IV) (see below) was not detectable. Quantitative hydrogenation over palladised charcoal indicated presence of about 8% of the allyl compound; the infrared spectrum of the hydrogenated product retained the band at 956 cm.$^{-1}$ but lacked maxima at 919 and 990 cm.$^{-1}$. Further, the components (II) and (V) of the mixture from the hydrogenation were separated and identified by gas chromatography, and analysis by refractive-index measurements showed that it contained 95·0% of base (II) and 5·0% of base (V).

(IV)


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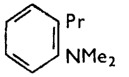

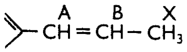
$\overset{A}{CH}=\overset{B}{CH}-\overset{X}{CH_3}$
(VI)

The spectral properties and behaviour on gas chromatography of the authentic unsaturated bases (III) and (IV) and of the authentic saturated base (V) were deduced in the following manner. Thermal decomposition of 2,3-dihydro-1,2-dimethylindole methohydroxide has been reported [9] to give exclusively *NN*-dimethyl-*o*-propenylaniline (IV), but re-examination of the product by nuclear magnetic resonance spectroscopy has shown it to be a mixture of the bases, *trans*-(IV) (~89%) and (III) (~11%). The spectrum shows a well-defined ABX_3 system [cf. (VI)]. The *C*-methyl group (τ 7·97) appears as an almost symmetrical doublet ($J_{BX} \neq 6{\cdot}5$ c./sec.), both components showing further splitting, into doublets, because of the small allylic coupling of the methyl protons with the A proton. The B proton (τ 3·69) appears as two 1 : 3 : 3 : 1 quartets, centred respectively on 3·82 and 3·55 τ (*i.e.*, $J_{AB} \neq 16{\cdot}3$ c./sec., indicative of a *trans*-configuration [10]). The separation of the lines within each quartet was 6·5 c./sec. The A proton (τ 3·02) appears as a doublet (J 16·3 c./sec.), but each component is unsharp, owing to the allylic coupling with the three protons of the methyl group. The presence of the allyl base (III) is proved by the doublet at 6·34 τ (benzylic protons) and a doublet of equal area at 4·72 τ (protons of $=CH_2$). The conclusions based on the nuclear magnetic resonance were reinforced by evidence from infrared spectra and gas chromatography. In the latter case, the mixture showed two peaks, the larger (area ~88%) due to (IV) and the smaller (12%) due to (III). The retention time of the minor component (III) was identical with that of the olefinic base

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[7] For a preliminary account, see Archer and Booth, *Chem. and Ind.*, 1962, 894.

[8] Katritzky and Jones, *J.*, 1959, 3674.

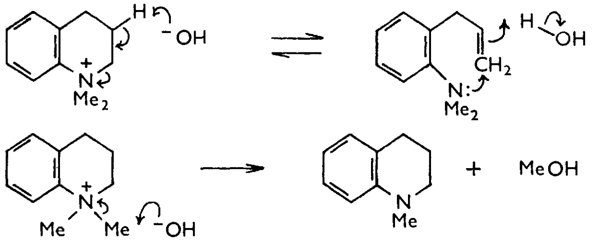
[9] Booth, King, and Parrick, *J.*, 1958, 2302.

[10] Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 85.

from the thermal decomposition of hydroxide (I) at 160° under reflux. The saturated base (V), obtained by hydrogenation of the mixture of (III) and (IV) (cf. ref. 9), gave only one sharp peak on gas chromatography. Conclusive evidence has therefore been gathered that thermal decomposition of the hydroxide (I) at 150—160° under reflux gives the saturated base (II) and an unsaturated base which is exclusively the non-conjugated olefin (III). However, the presence in the unsaturated base of up to 5% of the conjugated olefin (IV) is not excluded by the methods of analysis employed.

When the quaternary hydroxide (I) was decomposed by *distillation* at 90°/15 mm. and 160°/15 mm., the unsaturated, basic fraction now constituted 19% and 48%, respectively, of the total basic material isolated, the remainder in each case being tetrahydro-1-methylquinoline (II). In the preliminary communication,[7] the non-conjugated structure (III) was assigned to the unsaturated base produced in these distillation experiments, but infrared and nuclear magnetic resonance spectra later demonstrated that the unsaturated base was a mixture of (III) and (IV), the latter in greater proportion. For example, the olefinic base from the decomposition at 160°/15 mm. contained 83% of *trans*-(IV) and 17% of (III). The composition of the olefinic base is probably not of great significance, as it is undoubtedly sensitive to the precise ways in which the decomposition and isolation of products are performed. It is, however, of interest that the proportion of β-elimination is higher at 90° under distillation conditions than at 160° under reflux conditions. One explanation involves the assumption that the elimination (1) is reversible, whilst the substitution (2) is irreversible. Alternatively, it is possible that elimination is very strongly favoured when the quaternary hydroxide becomes completely anhydrous, as necessarily happens under distillation conditions (cf. ref. 11).

The Hofmann degradation of some tetrahydro-1-methylquinolines substituted in the reduced heterocyclic ring was next studied. It had been reported[12] that the distillation of 1,2,3,4-tetrahydro-1,2-dimethylquinoline methohydroxide produced methanol and 1,2,3,4-tetrahydro-1,2-dimethylquinoline. We doubted this since elimination of the β-hydrogen atoms of the 2-methyl group should occur about as readily as elimination of the β-hydrogen atoms in *N*-ethyl-*NN*-dimethylanilinium hydroxide.[1] When we repeated the decomposition, β-elimination occurred smoothly to give largely *o*-but-3-enyl-*NN*-dimethylaniline (VII; R = H), characterised by its ready conversion into a dihydro-base and its low reactivity towards methyl iodide. The ultraviolet spectrum of the degradation product showed weak absorption at 305 mμ, indicating the presence of a little 1,2,3,4-tetrahydro-1,2-dimethylquinoline, but the exact proportion was not determined. The position of the double bond was assigned on the basis of the strong absorption at 913 and 999 cm.$^{-1}$ (CH=CH$_2$) by the unsaturated but not by the saturated base. Hofmann fission of 1,2,3,4-tetrahydro-1,2,2,4-tetramethylquinoline methohydroxide also proceeded with ease, to yield largely an unsaturated base formulated as *o*-(1,3-dimethylbut-3-enyl)-*NN*-dimethylaniline (VII; R = Me) on the evidence of spectral properties and conversion into a dihydro-base. As expected, the unsaturated base was contaminated with some 1,2,3,4-tetrahydro-1,2,2,4-tetramethylquinoline, and a sharp separation of the two bases was



······· (1)

······· (2)

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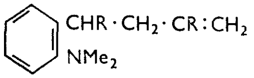
[11] von Braun, Teuffert, and Weissbach, *Annalen*, 1929, **472**, 121.
[12] Möller, *Annalen*, 1887, **242**, 313.

achieved by gas chromatography. The composition of the mixture was estimated from the gas-chromatographic traces as (VII; $R = Me$) 87% and tetrahydrotetramethylquinoline 13%.



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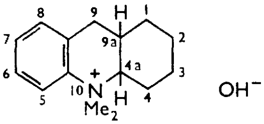
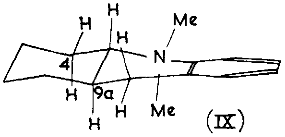


(VIII)

Thermal decomposition of 1,2,3,4,4a,9,9a,10-octahydro-10-methylacridine methohydroxide (VIII; *cis* shown) was investigated since this compound is formally similar to tetrahydro-1,2-dimethylquinoline methohydroxide, although the rigidity of the reduced carbocyclic ring imposes limitations on the directions of the C–H bonds at position 4. The preparation of 1,2,3,4,4a,9,9a,10-octahydroacridine by reduction of 1,2,3,4-tetrahydroacridine with tin and hydrochloric acid gives a mixture of *cis–trans*-octahydroacridine, which Perkin, Sedgwick, and Plant [13,14] separated. The assignment of configuration by Perkin and Sedgwick [15] was later reversed by Cartwright and Plant.[16] The correctness of the latter assignment has now been confirmed by nuclear magnetic resonance studies of the octahydroacridines and their derivatives.[17]

trans-Octahydroacridine was satisfactorily prepared by Perkin and Sedgwick's procedure [13] and was purified through the benzoate and hydrochloride. Attempts to prepare the *trans*-base by hydrogenation of acridine over copper chromite at 190°/180 atm.[18] led only to 9,10-dihydroacridine, probably because the pressure of hydrogen was too low. In the preparation of *cis*-octahydroacridine from 1,2,3,4-tetrahydroacridine, we followed the published method [13,14] but improved the procedure for separating the isomers (cf. p. 337). Both *cis*- and *trans*-octahydroacridine were converted by standard procedures into the 10-methyl methiodides and methohydroxides. The latter were decomposed at about 100° under distillation conditions; in both cases, decomposition occurred solely by extrusion of methanol, since the isolated base consisted entirely of the corresponding octahydro-10-methylacridine. These results are intelligible when reference is made to the probable conformations of the methohydroxides.



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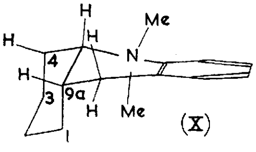
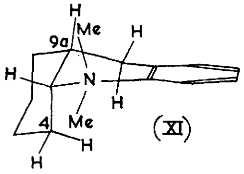


(X)



(XI)

The only possible conformation for the *trans*-methohydroxide is (IX) in which neither of the β-hydrogen atoms, at positions 4 and 9a, satisfies the conformational requirement for easy elimination. For *cis*-octahydroacridine, there are two feasible and possibly interconvertible conformations related to (X) and (XI). The nuclear magnetic resonance spectra indicated that, whilst *cis*-octahydroacridine itself exists preferentially in the conformation related to (X), the derived 10-methyl methiodide (and therefore, presumably, the methohydroxide) is fixed in conformation (XI), in which none of the three β-hydrogen atoms is suitably disposed for easy β-elimination. In the alternative but excluded conformation (X), the requirement for easy elimination is satisfied for the axial 4-hydrogen and the solitary 9a-hydrogen atom. If it is assumed that the *cis*-methohydroxide

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[13] Perkin and Sedgwick, *J.*, 1924, **125**, 2437.
[14] Perkin and Plant, *J.*, 1928, 2583.
[15] Perkin and Sedgwick, *J.*, 1926, 441.
[16] Cartwright and Plant, *J.*, 1931, 1898.
[17] Booth, unpublished work.
[18] Adkins and Coonradt, *J. Amer. Chem. Soc.*, 1941, **63**, 1563.

remains in conformation (XI) at the temperature of thermal decomposition (100°), the failure to undergo β-elimination is readily understood. The preference of the *cis*-methohydroxide for conformation (XI) is not surprising, since the alternative (X) has several repulsive interactions between the axial *N*-methyl group and the axial 1- and 3-hydrogen atoms.

Some nuclear magnetic resonance spectra are recorded in the Table and will be discussed elsewhere.[17] Free bases were generally examined in benzene, as the use of carbon tetrachloride or chloroform may have caused interaction. The position of the N–H resonance in the secondary bases was checked by deuteration.

Chemical shift data (τ values) for 1,2,3,4,4a,9,9a,10-octahydroacridine and its derivatives [for numbering see (VIII)].

Derivative	Solvent	*N*-Me	4a-Proton	9-Protons	Misc.
cis- (unsubst.) ...	1	—	6·84 [a]	Not analysed	*N*-H 7·07
cis-10-D	1	—	6·80 [a]	7·81, 7·77, 7·54, 7·50, 7·33, 7·26, 7·06, 6·99	
cis-10-Ac	2	—	5·23 [b]	7·22, 7·08, 7·03	Ac 7·73
cis-10-Me	3	7·34	*c*	7·93, 7·86, 7·66, 7·59, 7·47, 7·27, 7·20, 7·01	
cis-10-Me, HI	2	6·67	6·21 [d]	6·93	
cis-10-Me, MeI ...	2	6·12, 5·96	5·25 [e]	6·89	
trans-(unsubst.) [f]	1	—	*c*	Not analysed	*N*-H 7·04
trans-10-D [f]	1	—	*c*	7·85, 7·61, 7·51 [g]	
trans-10-Bz	2	—	6·13 [h]	7·54, 7·44, 7·28, 7·07 [i]	
trans-10-Me	1	7·32	*c*	8·01, 7·67, 7·55 [j]	
trans-10-Me, HI ...	2	6·84	*c*	7·3, 7·13, 6·49 [g]	
trans-10-Me, MeI	2	6·49,[k] 6·1[k]	*c*	7·46, 7·1, 6·98 [i]	

Solvents: 1, benzene; 2, chloroform; 3, methylene chloride.

[a] Broad, half-band width 9·2 c./sec. [b] Broad, half-band width 21 c./sec. [c] Not seen. [d] Centre of poorly resolved doublet, $J \neq 11$ c./sec. [e] Centre of doublet, $J \neq 10$ c./sec. [f] Poor curve, owing to insufficient material. [g] Prominent peaks in multiplet which includes 4a-proton. [h] Centre of triplet, $J \neq 8$ c./sec. [i] Prominent peaks in multiplet which includes 9a-proton. [j] Prominent peaks in multiplet which includes 4a- and 9a-protons. [k] Includes 4a-proton.

EXPERIMENTAL

The general remarks of Part I apply here. Nuclear magnetic resonance spectra were obtained on an A.E.I. spectrometer R.S.II, operating at 60 Mc. Tetramethylsilane was employed as internal reference. Deuteration of secondary amines was carried out as described by Fales and Robertson.[19]

Hofmann Degradation of 2,3-*Dihydro*-1,2-*dimethylindole* (cf. ref. 9).—The isolated base *had* n_D^{19} 1·5556, $\nu_{max.}$ (in CCl_4) 918, 942, 957, 972, 987, 1640, 1652, and 1666 cm.$^{-1}$ (ε 26, 89, 82, 39, 88, 14, 12, and 11, respectively). Examination by gas chromatography showed peaks due to *o*-allyl-*NN*-dimethylaniline (12%, by area measurements) at 7 min. 10 sec., and to *trans*-*NN*-dimethyl-*o*-propenylaniline (88%) at 9 min. 12 sec. The hydrogenated degradation product (see below) showed no peak at 9 min. 0 sec., thus proving the absence in the degradation product of 2,3-dihydro-1,2-dimethylindole (retention time, 9 min. 0 sec.).

The nuclear magnetic resonance spectrum of the degradation product in carbon tetrachloride showed: (i) doublet at 7·97 τ, splitting 6·52 c./sec. (protons of methyl attached to double-bond), each component slightly split (1 c./sec.), owing to allylic coupling; (ii) singlet at 7·16 τ (*N*-methyl); (iii) doublet at 6·34 τ, splitting 6·4 c./sec. (benzylic protons of allyl base); (iv) doublet, equal in area to the previous doublet, at 4·72 τ ($=CH_2$ of allyl base); (V) two 1 : 3 : 3 : 1 quartets, centred respectively on 3·82 and 3·55 τ. The separation between the quartets was 16·2 c./sec., and the splittings within each quartet were 6·52 c./sec. (olefinic proton, remote from aromatic ring, of propenyl base); (vi) doublet, superimposed on resonance due to aromatic protons, at 3·02 τ, splitting 16·3 c./sec. (olefinic proton, adjacent to aromatic ring, of propenyl base). From the areas of (i) and (ii) the mixture was calculated to contain 11% of *o*-allyl-*NN*-dimethylaniline and 89% of *trans*-*NN*-dimethyl-*o*-propenylaniline.

Hydrogenation of the above mixture (cf. ref. 9) gave *NN*-dimethyl-*o*-propylaniline, n_D^{16} 1·5137, $\nu_{max.}$ (in CCl_4) 902, 911, 952, and 1600 cm.$^{-1}$ (ε 9·3, 9·3, 120, and 41, respectively). Gas chromatography showed 1 peak only, of retention time 6 min. 36 sec.

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[19] Fales and Robertson, *Tetrahedron Letters*, 1962, 111.

1,2,3,4-*Tetrahydro*-1-*methylquinoline*.—1,2,3,4-Tetrahydroquinoline was prepared by hydrogenating quinoline in ethanol over Raney nickel at 100—110°/120 atm. during 5 hr. The product, purified through the 1-benzoyl derivative, had b. p. 123°/14 mm., n_D^{23} 1·5948, $\nu_{max.}$ (in CCl_4) 3500 cm.$^{-1}$. The tertiary base was prepared from the pure tetrahydroquinoline by treatment with methyl iodide (1·1 mol.) in boiling acetone containing anhydrous sodium carbonate. The usual method of working-up gave pure 1,2,3,4-tetrahydro-1-methylquinoline, b. p. 121°/13 mm., n_D^{21} 1·5800 (recent values,[20-22] n_D^{20} 1·5800, n_D^{25} 1·5800, n_D^{23} 1·5795), $\nu_{max.}$ (in CCl_4) 930, 1607, and 1680 (ε 22, 160, and 9·6, respectively). There was no absorption at 3500 cm.$^{-1}$. Gas chromatography showed 1 peak, of retention time 12 min. 48 sec. The methiodide had m. p. 172° (lit.,[6,20] 172—174° and 174°).

Hofmann Degradation of 1,2,3,4-*Tetrahydro*-1-*methylquinoline under Reflux*.—The syrupy quaternary hydroxide, prepared in the usual way (silver oxide) from 1,2,3,4-tetrahydro-1-methylquinoline methiodide (8 g.) was heated under reflux at 160° for 4 hr. The solution was diluted with water (5 ml.) and extracted several times with ether. The aqueous residue was unchanged methohydroxide [derived picrate, m. p. 124° (lit.,[23] 124°)]. The combined ethereal extracts were dried (KOH) and heated to remove ether. Total distillation of the residue in a bulb-tube gave a liquid, n_D^{20} 1·5778, $\nu_{max.}$ (in CCl_4) 919, 930, 956, 1607, 1641, and 1673 cm.$^{-1}$ (ε 15, 24, 13, 160, 13, and 8·1, respectively). Gas chromatography showed peaks due to 1,2,3,4-tetrahydro-1-methylquinoline (95%, by area) at 12 min. 48 sec. and *o*-allyl-*NN*-dimethylaniline (5%) at 7 min. 10 sec.

The nuclear magnetic resonance spectrum of the liquid showed the peaks due to 1,2,3,4-tetrahydro-1-methylquinoline and also: (i) doublet at 6·50 τ (splitting 6·6 c./sec.), due to benzylic protons; (ii) doublet, equal in area to (i), at 4·94 τ (splitting 15·5 c./sec.), due to terminal olefinic protons. Measurements of areas gave the composition of the mixture as 92% of 1,2,3,4-tetrahydro-1-methylquinoline, 8% of *o*-allyl-*NN*-dimethylaniline.

Hydrogenation of the above mixture, in methanol over 10% palladised charcoal, at room temperature and pressure, caused the uptake of 0·08 mol. of hydrogen. The product of hydrogenation, when isolated in the usual way and totally distilled (bulb-tube), had n_D^{20} 1·5766, corresponding on a calibration curve to a mixture of 95% of 1,2,3,4-tetrahydro-1-methylquinoline and 5·0% of *NN*-dimethyl-*o*-propylaniline. Gas-chromatography showed peaks at 12 min. 48 sec. and (smaller) 6 min. 36 sec. The mixture had $\nu_{max.}$ (in CCl_4) 930, 953, 1608, and 1677 cm.$^{-1}$ (ε 21, 11, 130, and 9·9, respectively). An artificial mixture of 91% of 1,2,3,4-tetrahydro-1-methylquinoline and 9% of *NN*-dimethyl-*o*-propylaniline had $\nu_{max.}$ (in CCl_4) 930, 952, 1607, and 1680 cm.$^{-1}$ (ε 22, 15, 150, and 10, respectively).

When the methohydroxide was decomposed at 180° and 200° under reflux, for 4 hr., total distillation of the hydrogenated degradation products gave liquids of n_D^{20} 1·5766 and 1·5758, respectively.

Hofmann Degradation of 1,2,3,4-*Tetrahydro*-1-*methylquinoline under Distillation Conditions*.—(*a*) The methohydroxide was decomposed at 12 mm. by raising the temperature from 50° to 90°. Complete decomposition occurred, as no unchanged methohydroxide could be detected. The basic product was isolated by ether-extraction of the distillate and entire apparatus. Total distillation of the dried ethereal extracts gave ether and a liquid of n_D^{23} 1·5750. Hydrogenation of the liquid over palladised charcoal gave, after the usual working-up, a liquid of n_D^{23} 1·5660, corresponding to a mixture of 81% of 1,2,3,4-tetrahydro-1-methylquinoline and 19% of *NN*-dimethyl-*o*-propylaniline. (*b*) The dry methohydroxide was heated rapidly to 160°/15 mm. and maintained at this temperature; decomposition occurred extremely rapidly. The basic product, after total distillation, had n_D^{21} 1·5645, $\nu_{max.}$ (in CCl_4) 914, 927, 938, 952, 967, 982, 1607, 1642, 1672, and 1690 (ε 15, 20, 32, 34, 15, 27, 110, 12, 9·8, and 9·8, respectively), and was a mixture of 51% of 1,2,3,4-tetrahydro-1-methylquinoline, 41% of *trans*-*NN*-dimethyl-*o*-propenylaniline and 8% of *o*-allyl-*NN*-dimethylaniline. The nuclear magnetic resonance spectrum of the mixture was determined as neat liquid and as solution in carbon tetrachloride. The spectrum in the latter case showed: (i) doublet at 8·05 τ, splitting 6·4 c./sec. (protons of methyl attached to double bond), superimposed on multiplet at 7·98 τ (CH_2, position 3 of 1,2,3,4-tetrahydro-1-methylquinoline); (ii) singlet at 7·22 τ (*N*-methyl of *N*-Me_2); (iii) singlet

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[20] Kost and Yudin, *Zhur. obshchei Khim.*, 1956, **26**, 1720.

[21] Gray and Heitmeier, *J. Amer. Chem. Soc.*, 1958, **80**, 6274.

[22] Huisgen and Konig, *Chem. Ber.*, 1959, **92**, 203.

[23] Decker, *Ber.*, 1903, **36**, 2568.

at 7·02 τ (*N*-methyl of 1,2,3,4-tetrahydro-1-methylquinoline); (iv) triplet, partly obscured by peaks (ii) and (iii) (CH_2, position 4 of tetrahydromethylquinoline); (v) triplet at 6·75 τ (CH_2, position 2 of tetrahydromethylquinoline). The spectrum in the low-field region was better resolved in the determination on the neat liquid. This spectrum showed (vi) doublet at 6·53 τ, splitting 6·4 c./sec. (benzylic protons of allyl base); (vii) doublet at 5·02 τ, splitting 16·4 c./sec. (=CH_2 of allyl base); (viii) two 1 : 3 : 3 : 1 quartets, centred respectively on 4·22 and 3·96 τ: the separation between the quartets was 15·6 c./sec. and the splittings within the quartets were each 6·45 c./sec. (olefinic proton, remote from aromatic ring, of propenyl base); (ix) multiplet, due to aromatic protons and olefinic proton, adjacent to aromatic ring, of propenyl base. It was calculated from the areas under the peaks that the olefinic portion contained 83% of *trans*-*NN*-dimethyl-*o*-propenylaniline and 17% of *o*-allyl-*NN*-dimethylaniline.

Hydrogenation of the mixture from the degradation over palladised charcoal gave, after the usual working-up, a liquid of n_D^{24} 1·5440, corresponding to 51% of 1,2,3,4-tetrahydro-1-methylquinoline and 49% of *NN*-dimethyl-*o*-propylaniline.

Hofmann Degradation of 1,2,3,4-*Tetrahydro*-1,2-*dimethylquinoline*.—1,2,3,4-Tetrahydro-2-methylquinoline was prepared by reduction of 2-methylquinoline with sodium and boiling ethanol.[24] The product was purified through the benzoyl derivative, m. p. 119° (Walter [25] records 118°), $\lambda_{max.}$ 265 mμ (ε 8210 in EtOH) and finally obtained with b. p. 114°/10 mm., $\lambda_{max.}$ 206, 250, and 301 mμ (ε 28,950, 9060, and 2310, respectively, in EtOH). A mixture of the pure base (10·2 g.) and methyl iodide (9·9 g.) was heated under reflux for 2 hr., cooled, and basified with aqueous sodium hydroxide. Extraction with ether yielded 1,2,3,4-tetrahydro-1,2-dimethylquinoline (5·73 g., 51%), b. p. 115—116°/10 mm., n_D^{22} 1·5700 (Freund and Richard [26] give b. p. 253°/756 mm., n_D^{19} 1·5678), $\lambda_{max.}$ 208, 256, and 306 mμ (ε 24,250, 12,200, and 2800, respectively, in EtOH). The picrate had m. p. 117—119° (lit.,[26] 150°) (Found: C, 52·3; H, 4·75. Calc. for $C_{17}H_{18}N_4O_7$: C, 52·3; H, 4·65%). The methiodide had m. p. 204° (Möller [12] gives m. p. 205°), $\lambda_{max.}$ 262 and 269 mμ (ε 470 and 390, respectively, in EtOH).

The methohydroxide from the above methiodide (21 g.) was decomposed at 80—100°, yielding o-*but*-3-*enyl*-NN-*dimethylaniline* (5·74 g., 47%), b. p. 54—56°/0·55 mm., n_D^{19} 1·5332 (Found: C, 82·0; H, 9·6; N, 8·0. $C_{12}H_{17}N$ requires C, 82·2; H, 9·8; N, 8·0%), $\lambda_{max.}$ 208, 253, and 305 mμ (infl.) (ε 18,410, 6440, and 790, respectively, in EtOH), $\nu_{max.}$ (liquid film) 913, 999, 1638, 2768, and 2812 cm.$^{-1}$. The *picrate*, crystallised from ethanol, had m. p. 148—149° (Found: C, 53·2; H, 5·1; N, 13·5. $C_{18}H_{20}N_4O_7$ requires C, 53·5; H, 5·0; N, 13·9%). The *methiodide*, colourless needles from ethanol, had m. p. 193—194° (Found: C 48·8; H, 6·1; N, 4·3. $C_{13}H_{20}IN$ requires C, 49·1; H, 6·4; N, 4·4%).

o-*Butyl*-NN-*dimethylaniline*.—The above base (1·67 g.) was hydrogenated in the form of its hydrochloride in methanol (50 ml.) over 5% palladised charcoal (0·2 g.) at room temperature and pressure (1·06 mol. absorbed). The filtered solution was evaporated to remove methanol, basified, and extracted with ether. o-*Butyl*-NN-*dimethylaniline* thus obtained (1·0 g., 59%) had b. p. 108—118°(bath-temp.)/8 mm. (Found: C, 80·9; H, 10·2; N, 7·8. $C_{12}H_{19}N$ requires C, 81·2; H, 10·8; N, 7·9%), $\lambda_{max.}$ 208 and 251 mμ (ε 24,000 and 5980, respectively, in EtOH), $\nu_{max.}$ (liquid film) 1377, 2768, and 2812 cm.$^{-1}$ but no max. at 913, 999, or 1638 cm.$^{-1}$. The *picrate*, yellow plates from ethanol, had m. p. 165° (Found: C, 53·0; H, 5·5; N, 13·5. $C_{18}H_{22}N_4O_7$ requires C, 53·2; H, 5·5; N, 13·8%).

1,2,3,4-*Tetrahydro*-1,2,2,4-*tetramethylquinoline*.—A mixture of 1,2,3,4-tetrahydro-2,2,4-trimethylquinoline (m. p. 41°; from Monsanto) (17·5 g.), methyl iodide (15·5 g.), sodium carbonate (10 g.), and acetone (100 ml.) was heated under reflux for 48 hr. The solution was distilled to remove acetone and extracted several times with ether. Evaporation of the dried (KOH) extracts gave 1,2,3,4-*tetrahydro*-1,2,2,4-*tetramethylquinoline* (16 g., 85%), b. p. 140°/12 mm., n_D^{24} 1·5545 (Found: C, 82·4; H, 10·1; N, 7·2. $C_{13}H_{19}N$ requires C, 82·5; H, 10·05; N, 7·0%), $\lambda_{max.}$ 209, 256, and 305 mμ (ε 23,700, 11,950, and 2615, respectively, in EtOH), $\lambda_{max.}$ 210 (infl.), 256, 261, and 270 mμ (ε 9240, 374, 453, and 294, respectively, in ethanolic 0·1N-hydrochloric acid). The *picrate*, sublimed, had m. p. 174° (Found: C, 54·2; H, 5·2; N, 13·2. $C_{19}H_{22}N_4O_7$ requires C, 54·5; H, 5·3; N, 13·4%). The *methiodide* had m. p. 184° (Found: C, 50·8; H, 6·6; N, 4·2. $C_{14}H_{22}IN$ requires C, 50·7; H, 6·9; N, 4·2%), $\lambda_{max.}$ 256, 262, and 269 mμ (ε 346, 438, and 368, respectively, in EtOH).

[24] Oldham and Johns, *J. Amer. Chem. Soc.*, 1939, **61**, 3289.
[25] Walter, *Ber.*, 1892, **25**, 1263.
[26] Freund and Richard, *Ber.*, 1909, **42**, 1110.

Hofmann Degradation of 1,2,3,4-*Tetrahydro*-1,2,2,4-*tetramethylquinoline*.—The methohydroxide, prepared in the usual way from the above methiodide, was heated under reflux at 160° for 3 hr. The product (~80%) was isolated by ether-extraction and total distillation at 120—140°/13 mm. In the distillate gas chromatography disclosed 1,2,3,4-tetrahydro-1,2,2,4-tetramethylquinoline (13 mol. %) and *o*-1,3-dimethylbut-3-enyl-*NN*-dimethylaniline (87 mol. %) (see below).

Fractionation of the distillate gave o-1,3-*dimethylbut*-3-*enyl*-NN-*dimethylaniline*, b. p. 120°/13 mm., n_D^{24} 1·5139 (Found: C, 83·0; H, 10·5; N, 7·2. $C_{14}H_{21}N$ requires C, 82·75; H, 10·35; N, 6·9%), $\lambda_{max.}$ 247 mμ (ε 3445 in EtOH), $\nu_{max.}$ (in CCl_4) 895, 1652, 2784, and 2824 cm.$^{-1}$. The *picrate* had m. p. 122—123° (Found: C, 55·4; H, 5·3; N, 12·8. $C_{20}H_{24}N_4O_7$ requires C, 55·5; H, 5·3; N, 13·0%).

o-(1,3-*Dimethylbutyl*)-NN-*dimethylaniline*.—The above unsaturated base (3·9 g.), dissolved in methanol containing enough concentrated hydrochloric acid to give an acid solution, was hydrogenated over 10% palladised charcoal (0·4 g.) at room temperature and pressure (1·0 mol. absorbed in 24 hr.). The usual method of working-up gave o-1,3-*dimethylbutyl*-NN-*dimethylaniline* (3·8 g.), b. p. 120°/14 mm. (Found: C, 82·1; H, 10·9; N, 7·2. $C_{14}H_{23}N$ requires C, 82·0; H, 11·1; N, 6·8%), $\lambda_{max.}$ 208 and 251 mμ (ε 14,800 and 4300, respectively, in MeOH), no max. at 1652 and 895 cm.$^{-1}$ (in CCl_4). The *picrate* had m. p. 93—95° (Found: C, 55·4; H, 5·9; N, 12·9. $C_{20}H_{26}N_4O_7$ requires C, 55·4; H, 5·8; N, 12·9%).

cis-1,2,3,4,4a,9,9a,10-*Octahydroacridine* (cf. Perkin, Sedgwick, and Plant [13,14]).—A mixture of 1,2,3,4-tetrahydroacridine [13] (30 g.), ethanol (120 ml.), and granulated tin (120 g.) was heated on a water-bath for 6 hr. The hot mixture was filtered through glass wool and heated to remove ethanol and then basified with 40% aqueous sodium hydroxide (500 ml.). After the mixture had been filtered through glass wool (filtrate *A*), the solid residue was pressed until dry and triturated with ether (3 × 150 ml.). The solid remaining was then ground with 40% aqueous sodium hydroxide (50 ml.), and the mixture was filtered and combined with filtrate *A*. The solid was again triturated with ether (2 × 100 ml.), after which little remained undissolved. The combined alkaline filtrates were extracted with ether (2 × 200 ml.), and all the ethereal extracts were combined and washed with water. Distillation of the dried (KOH) ethereal extracts gave crude octahydroacridine (25·3 g.), b. p. 138—148°/2—3 mm. A mixture of the crude base (23 g.), and acetic anhydride (50 ml.) was heated under reflux for 1 hr., then poured into water (500 ml.). After 24 hr. the solution was filtered and the yellow solid was triturated with ether (3 × 10 ml.) (ethereal solution *B*). The white solid remaining (m. p. 130—135°), when recrystallised from aqueous ethanol, gave *cis*-10-acetyl-1,2,3,4,4a,9,9a,10-octahydroacridine as colourless prisms (14 g.), m. p. 137—138° (lit.,[13] 136°) (Found: C, 78·2; H, 8·4. Calc. for $C_{15}H_{19}NO$: C, 78·5; H, 8·4%). Hydrolysis of the acetyl derivative (13·5 g.) with aqueous-methanolic potassium hydroxide, followed by the usual method of working-up, gave *cis*-1,2,3,4,4a,9,9a,10-octahydroacridine (8·5 g.) as prisms, m. p. 71—72° (lit.,[13] 72°) (Found: C, 83·6; H, 8·9. Calc. for $C_{13}H_{17}N$: C, 83·4; H, 9·1%).

The ethereal solution *B* was evaporated to dryness and the solid residue (5 g.) was heated for 2 days under reflux with aqueous-methanolic potassium hydroxide. Methanol was removed by distillation and the base was extracted with ether. When the ether solution was shaken with dilute hydrochloric acid, an insoluble hydrochloride was precipitated and was removed; treatment with aqueous alkali gave the crude *trans*-base, m. p. 79—81°. Benzoylation (Schotten–Baumann) gave a solid, m. p. 176—181°, from which *trans*-10-benzoyl-1,2,3,4,4a,9,9a,10-octahydroacridine (1·4 g.), m. p. and mixed m. p. with authentic specimen (see below) 185—187°, was obtained after several crystallisations from ethanol.

cis-1,2,3,4,4a,9,9a,10-*Octahydro*-10-*methylacridine*.—Dimethyl sulphate (5 g.) was added during 1 hr. to a stirred mixture of *cis*-octahydroacridine (2 g.; m. p. 71—72°), acetone (10 ml.). and 40% aqueous sodium hydroxide (10 ml.), the temperature being maintained at 50°. Subsequently, stirring was continued for a further 1 hr. and then acetone was distilled off on a water-bath. The base recovered by ether-extraction of the residue was heated under reflux with acetic anhydride for 1 hr. The mixture was poured into water (20 ml.), and the solution was washed several times with ether, basified, and extracted with ether. Evaporation of the dried (K_2CO_3) ethereal extracts yielded cis-1,2,3,4,4a,9,9a,10-*octahydro*-10-*methylacridine* (0·9 g.), b. p. 120—125° (bath-temp.)/0·1 mm., n_D^{17} 1·5847 (Found: C, 83·4; H, 9·6. $C_{14}H_{19}N$ requires C, 83·5; H, 9·5%). The *picrate* crystallised from methanol in prisms, m. p. 172—174° (decomp.) (Found: C, 56·1; H, 5·3. $C_{20}H_{22}N_4O_7$ requires C, 55·8; H, 5·2%). The *hydriodide*, prepared by addition of a solution of sodium iodide (0·15 g.) in dilute acetic acid (1 ml.) to the tertiary base (0·2 g.) in glacial acetic acid (0·5 ml.), crystallised from acetone–ethyl acetate in prisms, m. p. 169—170° (Perkin and Sedgwick [13] record m. p. 217° for the " methiodide " of the secondary base) (Found: C, 51·4; H, 6·3. $C_{14}H_{20}IN$ requires C, 51·1; H, 6·1%).

cis-1,2,3,4,4a,9,9a,10-*Octahydro*-10-*methylacridine Methiodide*.—(i) Direct interaction of the above base (0·2 g.) and methyl iodide (4 ml.) in boiling ether for 18 hr. gave the salt in poor yield (0·06 g.; m. p. 169—170°). The pure *methiodide* crystallised from acetone–ethyl acetate in prisms, m. p. 170—171° (Found: C, 52·7; H, 6·3. $C_{15}H_{22}IN$ requires C, 52·5; H, 6·5%). A mixed m. p. determination with the tertiary base hydriodide gave m. p. 145—158°.

(ii) *cis*-1,2,3,4,4a,9,9a,10-Octahydroacridine (4 g.), potassium hydroxide (1·2 g.), water (5 ml.), and methyl iodide (20 g.) were heated on a steam-bath for 6 hr. The solution was cooled to 0° for 2 hr. and the precipitated methiodide was removed. Chloroform-extraction of the filtrate yielded a further quantity of the salt (total 7·0 g., 95%). Crystallisation from ethanol–ether gave prisms, m. p. and mixed m. p. 170—171°.

Hofmann Degradation of cis-1,2,3,4,4a,9,9a,10-*Octahydro*-10-*methylacridine*.—The methohydroxide from the foregoing methiodide (5·8 g.) was decomposed at 100—105°/10 mm. Ether-extraction of the product gave *cis*-1,2,3,4,4a,9,9a,10-octahydro-10-methylacridine (2·5 g., 74%), b. p. 105—110° (bath-temp.)/0·1 mm., n_D^{17} 1·5849. The picrate (96% yield) had m. p. and mixed m. p. 172—174° (decomp.).

trans-1,2,3,4,4a,9,9a,10-*Octahydroacridine* (cf. Perkin and Sedgwick [13]).—5% Sodium amalgam (150 g.) was added to a stirred solution of 1,2,3,4,9,10-hexahydro-9-oxoacridine [27] (6 g.) in boiling ethanol (300 ml.) during 4 hr. Stirring and heating were continued for a further 6 hr., after which the solution was decanted from the mercury and evaporated to dryness. Ether-extraction of the residue, followed by distillation, gave an oil (5·8 g.), b. p. 107—115°/0·03 mm. Benzoylation (Schotten–Baumann) gave a white solid, three crystallisations of which yielded *trans*-10-benzoyl-1,2,3,4,4a,9,9a,10-octahydroacridine (2·9 g.), m. p. 186—187° (lit.,[16,18] 185° and 186—187°) (Found: C, 82·4; H, 7·2. Calc. for $C_{20}H_{21}NO$: C, 82·4; H, 7·3%). The base recovered by hydrolysis (ethanolic potassium hydroxide) of this derivative was dissolved in dry ether, and dry hydrogen chloride was passed through the solution. Recrystallisation of the precipitated solid (1·75 g.) from ethanol–ether gave trans-1,2,3,4,4a,9,9a,10-*octahydroacridine hydrochloride* as prisms, m. p. 257—259° (Found: C, 70·2; H, 8·2. $C_{13}H_{18}ClN$ requires C, 69·8; H, 8·1%). Decomposition of the hydrochloride with dilute aqueous ammonia afforded pure *trans*-1,2,3,4,4a,9,9a,10-octahydroacridine, crystallising from light petroleum (b. p. 40—60°) in needles (1·35 g.), m. p. 82—83° (lit.,[13] 82°) (Found: C, 83·2; H, 9·0%).

trans-1,2,3,4,4a,9,9a,10-*Octahydro*-10-*methylacridine*.—The method used to prepare the *cis*-10-methyl base was applied to the foregoing base. The product was trans-1,2,3,4,4a,9,9a,10-*octahydro*-10-*methylacridine*, m. p. 64—65° (Perkin and Sedgwick [13] record the base as an oil, b. p. 140°) (Found: C, 83·6; H, 9·3%). The *picrate* crystallised from ethanol as yellow prisms, m. p. 136—138° (lit.,[13] 160°) (Found: C, 55·9; H, 5·2%). The *hydriodide* crystallised from ethanol–ether in colourless needles, m. p. 197—198° (lit.,[13] 212° for the " methiodide " of the secondary base) (Found: C, 50·8; 4·60%). The *methiodide*, prepared in moderate yield from the tertiary base and methyl iodide, crystallised from ethanol–ether in colourless prisms, m. p. 185—186° (Found: C, 52·7; H, 6·5%).

Hofmann Degradation of trans-1,2,3,4,4a,9,9a,10-*Octahydro*-10-*methylacridine*.—*trans*-Octahydroacridine (2 g.; m. p. 82—83°), 1·5% aqueous sodium hydroxide (24 ml.), and methyl iodide (4 ml.) were heated under reflux for 3 hr. Extraction with chloroform and precipitation with ether from the chloroform solution gave the 10-methyl methiodide (3·5 g., 95%), m. p. 185—186°, identical with the salt from the foregoing preparation. The methohydroxide from the above methiodide (2·6 g.) was decomposed at 90—100°/10 mm. Ether-extraction, followed by distillation of the dried ($MgSO_4$) extracts, gave *trans*-1,2,3,4,4a,9,9a,10-octahydro-10-methylacridine (1·3 g., 82%), b. p. 105—110° (bath-temp.)/0·1 mm., m. p. 63—65°, mixed m. p. 64—65°.

We are indebted to Monsanto Chemicals Limited for 1,2,3,4-tetrahydro-2,2,4-trimethylquinoline.

THE UNIVERSITY, NOTTINGHAM. [*Received, August* 10*th*, 1962.]

[27] Reed, *J.*, 1944, 425.