Conformational Equilibria in *cis*-*C*-Methyldecahydroquinolines: Studies at Low Temperature using ^{13}C and ^{1}H Magnetic Resonance Spectroscopy

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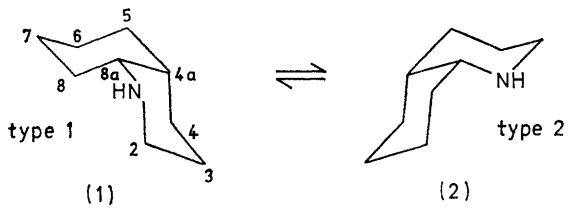
A number of *cis*- and *trans*-methyldecahydroquinolines, substituted at C-2, -3, -4, -4a, and -8a, have been synthesised and their preferred conformations established by variable temperature ^{13}C and ^{1}H n.m.r. spectroscopy. The conformational preference, for the equatorial orientation, of a methyl at C-4 of *cis*-decahydroquinoline, is similar to that of a methyl in cyclohexane, whereas that of a methyl at C-2 or -8a is considerably greater.

PREVIOUS work,[1,2] using ^{13}C n.m.r. spectroscopy, has shown that the conformational equilibrium (1) ⇌ (2) in *cis*-decahydroquinoline favours type 2 conformation

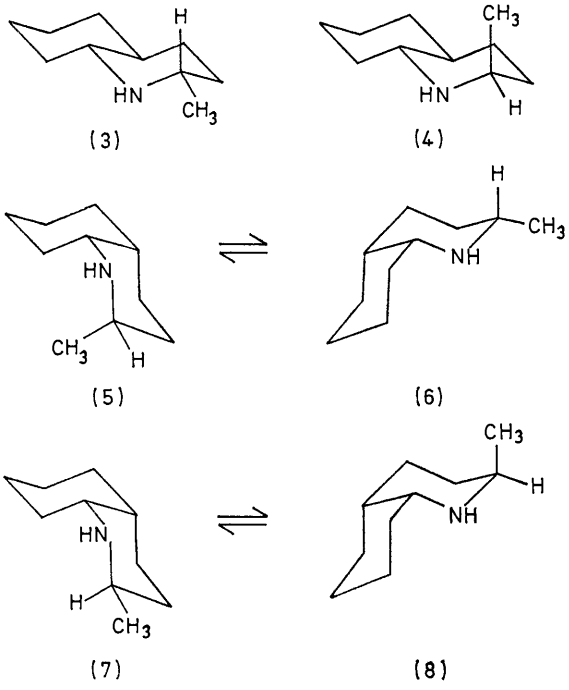


(2), the proportions of (1) and (2) at 199 K being 6.5 and 93.5% respectively. The effect of *N*-alkylation on the equilibrium (1) ⇌ (2) has already been reported.[2] In present work we have determined the effect on (1) ⇌ (2) caused by the presence of a methyl group at positions 2, 3, 4, 4a, and 8a.

The conformational preference ($-\Delta G^0$, or A value) of a methyl group in cyclohexane is generally taken as 1.7 kcal mol^{-1},[3,4] and this is sufficiently large to ensure that a methyl-substituted *cis*-decalin exists almost exclusively in a conformation with methyl equatorial.[5] However, the bias already present in (1) ⇌ (2), together with the probable occurrence of attractive and repulsive interactions arising from the heteroatom and its lone pair, should cause *cis*-*C*-methyldecahydroquinolines to give interesting results. Indeed, the

[1] H. Booth and D. V. Griffiths, *J.C.S. Perkin II*, 1973, 842.
[2] H. Booth and D. V. Griffiths, *J.C.S. Perkin II*, 1975, 111.
[3] F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, 1971, **98**, 258.
[4] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Interscience, New York, 1965.
[5] D. K. Dalling, D. M. Grant, and E. G. Paul, *J. Amer. Chem. Soc.*, 1973, **95**, 3718.

primary aim of these investigations is to extend our knowledge of the nature and strength of the fundamental



forces which control the conformations of flexible molecules in solution.

The four isomers of 2-methyldecahydroquinoline were obtained by hydrogenation of 2-methylquinoline (quinaldine) and separation of the isomeric bases by preparative g.l.c. (*cf.* refs. 6 and 7). Previous work on these compounds involved synthesis [8] and analysis of all four isomers involved hydrogenation of quinaldine hydrochloride over Raney nickel in water at 160 atm. and 150°. Separation of the crude product by preparative g.l.c. was very tedious, particularly for the least abundant isomers (4) and (7) ⇌ (8), but was rewarded with samples of high purity.

N.m.r. spectral data for the four isomers are included in Tables 1 (^{1}H) and Tables 2 and 3 (^{13}C). The ^{1}H spectrum of *trans*(2H,4aH),*trans*(4aH,8aH)-2-methyldecahydroquinoline (3) showed two low-field signals, that at τ 7.34 ($\nu_{\frac{1}{2}}$ 24 Hz) being assigned to 2-H because the methyl doublet at τ 8.94 collapsed to a singlet on irradiation of this signal. The signal at τ 7.88 was assigned to the ring junction proton 8a-H, and the chemical shift indicated a *trans*-ring fusion.[6] In addition, the measured separation of the outer lines of the 2-H signal was 32 Hz. The spin system involved is complex, but may be roughly considered as $ABXK_3$, where A and B are the geminal protons at C-3, X is 2-H, and K_3 are the methyl protons. Since both vicinal couplings, J_{AX} and J_{BX}, will be positive, and since the relationship between X and K_3 is first order, the separation of the outer lines for H_X is approximately $[J_{AX} + J_{BX} + 3J_{XK}]$. Now J_{XK} is known to be 6.05 Hz from the splitting of the methyl doublet. Hence $J_{AX} + J_{BX}$ is 13.85 Hz, a value which is only consistent with 2-H being axial in character. The stereochemistry of (3) was confirmed by the carbon-13 shifts (Table 2), which showed excellent agreement with shifts calculated from the parent, *trans*-decahydroquinoline,[1] and parameters for equatorial methyl.[1] As usual, off-resonance experiments disclosed the number of hydrogens carried by each carbon responsible for the signals in the noise-decoupled spectrum.

TABLE 1

Chemical shifts (τ) for protons in *C*-methyldecahydroquinolines ($CDCl_3$; 100 and 220 MHz)

Position of Me	Stereochemistry	Formula	Chemical shifts 2eq-H	2ax-H	8a-H	Me
2	*trans*(2H,4aH),*trans*(4aH,8aH)	(3)		7.34	7.88	8.94
2	*cis*(2H,4aH),*trans*(4aH,8aH)	(4)	6.71		7.60	8.80
2	*cis*(2H,4aH),*cis*(4aH,8aH)	(6)		7.37	7.12	8.93
2	*trans*(2H,4aH),*cis*(4aH,8aH)	(7)		←——7.11——→		9.00
4	*trans*(4H,4aH),*trans*(4aH,8aH)	(9)		7.31	7.90	9.12
4	*cis*(4H,4aH),*trans*(4aH,8aH)	(10)	7.23	7.10	7.56	9.07
4	*cis*(4H,4aH),*cis*(4aH,8aH)	(12)	6.94	7.36	7.25	9.14
4	*trans*(4H,4aH),*cis*(4aH,8aH)	(13) ⇌ (14)	←——6.90—7.25——→			9.04
3	*cis*(3H,4aH),*trans*(4aH,8aH)	(15)	7.06	7.82		9.22
3	*trans*(3H,4aH),*cis*(4aH,8aH)	(17)	7.00	7.78	7.24	9.26
3	*cis*(3H,4aH),*cis*(4aH,8aH)	(18) *	7,47	8.04	7.23	9.16
4a	*trans*	(20)	6.96	7.38	7.82	9.08
4a	*cis*	(21) ⇌ (22)	7.00	7.44	7.61	9.08
8a	*cis*	(23) ⇌ (24)	←——7.28——→			8.96

* τ 7.52 (CH_2CH_3) and 8.86 (CH_2CH_3).

the ^{1}H n.m.r. spectra at 40 MHz and room temperature.[9] In our first experiments, hydrogenation of quinaldine in cyclohexane over Raney nickel at 110 atm. and 170° gave a mixture containing *ca.* 75% of isomer (3). However, the most convenient method for the isolation of *cis*(2H,4aH),*trans*(4aH,8aH)-2-Methyldecahydroquinoline (4), the least abundant isomer present in the hydrogenation product, gave low-field signals at τ 6.71 and 7.60 in the ^{1}H n.m.r. spectrum. The high-field

[6] H. Booth and A. H. Bostock, *J.C.S. Perkin II*, 1972, 616.
[7] F. W. Vierhapper and E. L. Eliel, *J. Amer. Chem. Soc.*, 1974, **96**, 2256.
[8] G. Buchmann and R. Schmuck, *Wiss. Z. tech. Hochschule Chem. Leuna-Merseburg*, 1961, **4**, 127.
[9] V. I. Artuhin, D. V. Sokolov, L. K. Orazbaeva, and G. S. Litvinenko, *Izvest. Akad. Nauk. S.S.S.R. Ser. khim.*, 1967, **17**(5), 57.

region (τ 8—9.2) was an uninterpretable broad envelope, apart from the methyl doublet at τ 8.80. The signal at τ 7.60 was a poorly resolved triplet, with $\nu_{\frac{1}{2}}$ 25 Hz, as expected from a *trans*-fused system; its chemical shift, the 2-H signal at τ 6.71 was only 27.9 Hz. Since $J_{Me.CH}$ was found to be 6.75 Hz, the sum of the vicinal couplings ($J_{2,3eq} + J_{2,3ax}$) was only 7.65 Hz, a value requiring 2-H to be equatorial. In a double resonance

TABLE 2

^{13}C Chemical shifts for *C*-methyldecahydroquinolines (*trans*-fusion) in $CDCl_3$ (p.p.m. downfield from Me_4Si) (calculated shifts in parentheses)

Formula	(3) [a]	(4)	(9)	(10)	(15)	(20)
Methyl position	2	2	4	4	3	4a
C Atom						
2	53.0 (53.3)	47.6 (45.1)	47.3 (47.6)	41.1 (41.2)	54.8 (54.7)	48.2 (47.6)
3	35.7 (35.7)	31.2 (31.0)	36.8 (36.8)	34.7 (33.0)	32.7 (32.9)	23.0 (22.6)
4	33.2 (33.6)	26.7 (26.7)	37.0 (39.6)	31.1 (34.3)	41.3 (41.8)	40.5 (40.7)
5	32.9 (33.2)	32.5 (32.9)	29.4 (30.3)	29.8 (30.9)	32.5 (32.9)	39.9 (40.7)
6	27.0 (26.9)	26.3 (26.5)	27.1 (26.5)	26.6 (26.5)	26.1 (26.5)	21.5 (21.5)
7	26.1 (26.2)	25.6 (25.9)	26.1 (25.9)	25.6 (25.9)	25.6 (25.9)	26.0 (25.9)
8	34.4 (34.4)	34.2 (34.1)	34.3 (34.1)	34.7 (34.1)	33.6 (34.1)	28.9 (29.1)
8a	62.7 (63.2)	54.0 (56.3)	62.1 (62.5)	54.0 (56.1)	61.5 (62.5)	64.3 (64.8)
4a	43.2 (43.7)	43.8 (43.5)	50.0 (52.7)	46.4 (48.9)	43.0 (43.5)	33.9 (34.4)
CH_3	23.3 (23.5) [b]	18.5 (18.7)	19.7 (20.4)	13.1 (11.8)	19.6 (19.9) [c]	15.6 (15.8) [d]

[a] Solvent C_6D_6. [b] In *cis*-2,6-dimethylpiperidine. [c] In 3-methylpiperidine. [d] In *trans*-9-methyldecalin.

TABLE 3

^{13}C Chemical shifts for *C*-methyldecahydroquinolines (*cis*-fusion) in $CDCl_3$ (p.p.m. downfield from Me_4Si) (calculated shifts in parentheses)

Formula	(6) [a]	(7)	(12)	(13) ⇌ (14)	(13)	(14)	(17)	(18) [e]	(21) ⇌ (22)	(21)	(22)	(23) ⇌ (24)	(23)	(24)
T/K	293	293	293	324	210	210	293	293	317	220	220	321	213	213
C Atom														
2	53.6 (53.3)	45.3 (44.7)	47.4 (47.9)	40.7	40.6 (39.3)	42.3 (41.5)	55.5 (55.0)	54.0 (53.4)	46.6	*c* (39.3)	47.4 (47.9)	41.3	40.5 (41.1)	40.9 (42.9)
3	30.0 (29.0)	35.5 (37.2)	29.3 (30.4)	32.7	36.2 (38.6)	27.6 (26.6)	26.7 (26.5)	31.4 (33.6)	23.2	*c* (24.1)	22.6 (23.0)	24.9	27.5 (29.4)	20.6 (21.2)
4	31.4 (31.1)	25.2 (24.3)	35.0 (37.4)	28.5	26.1 (30.6)	32.6 (32.1)	40.1 (39.6)	33.3 (32.3)	38.4	27.4 (28.8)	39.4 (39.8)	26.3	25.6 (25.7)	25.8 (25.7)
5	25.6 (25.0)	31.8 (31.6)	19.3 (18.0)	27.4	27.4 (29.0)	27.2 (25.0)	26.6 (25.0)	31.9 (31.6)	31.4	40.4 (40.7)	29.1 (29.9)	28.4	28.9 (26.6)	26.3 (26.8)
6	27.4 (26.3)	21.5 (21.2)	26.3 (26.3)	22.5	20.1 (21.2)	26.7 (26.3)	26.2 (26.3)	21.2 (21.2)	22.0	21.3 (23.0)	21.6 (21.3)	23.3	20.0 (21.2)	26.5 (26.3)
7	20.8 (20.4)	26.5 (26.6)	20.9 (20.4)	24.3	26.7 (26.6)	20.1 (20.4)	20.7 (20.4)	25.8 (26.6)	21.2	25.9 (26.6)	20.0 (20.4)	22.9	23.4 (21.6)	21.6 (22.2)
8	33.8 (32.8)	27.7 (27.0)	32.8 (32.8)	28.5	26.7 (27.0)	32.6 (32.8)	32.6 (32.8)	16.7 (19.7)	28.5	28.4 (28.8)	28.2 (27.8)	35.3	29.3 (31.9)	41.1 (41.9)
8a	55.6 (54.9)	55.3 (54.0)	56.3 (54.9)	52.8	54.8 (54.0)	49.6 (48.5)	54.7 (54.9)	58.0 (61.0)	60.3	58.8 (58.9)	59.8 (59.8)	51.5	51.8 (50.0)	50.5 (45.9)
4a	35.7 (35.2)	36.0 (35.6)	41.1 (44.4)	42.5	43.4 (44.8)	41.4 (40.6)	36.1 (35.2)	35.4 (34.5)	32.4	32.5 (31.6)	32.0 (31.2)	40.6	40.9 (40.5)	38.3 (40.1)
CH_3	23.3 (23.5)	23.6 (23.5)	19.3 (19.8)	19.3	18.8 (20.4)	20.8 (*b*)	19.7 (20.0)	19.8 (20.0)	26.6	*c* (*b*)	26.3 (28.2) [d]	27.5	28.1 (*b*)	26.0 (*b*)

[a] Solvent C_6D_6. [b] Model compound not available. [c] Not seen. [d] In *cis*-9-methyldecalin. [e] CH_2 and CH_3 of Et at 47.3 and 12.9 p.p.m., respectively.

0.31 p.p.m. downfield from that in *trans*-decahydroquinoline itself, implies that the methyl substituent was axial.[10,11] Moreover, the separation of outer lines in experiment set up to measure nuclear Overhauser effects, the signal due to the methyl protons was saturated whilst the integral of 8a-H was recorded. The enhancement of the integral, over the integral recorded in a normal experiment, amounted to 14.8%, the average of several experiments. Thus, although only

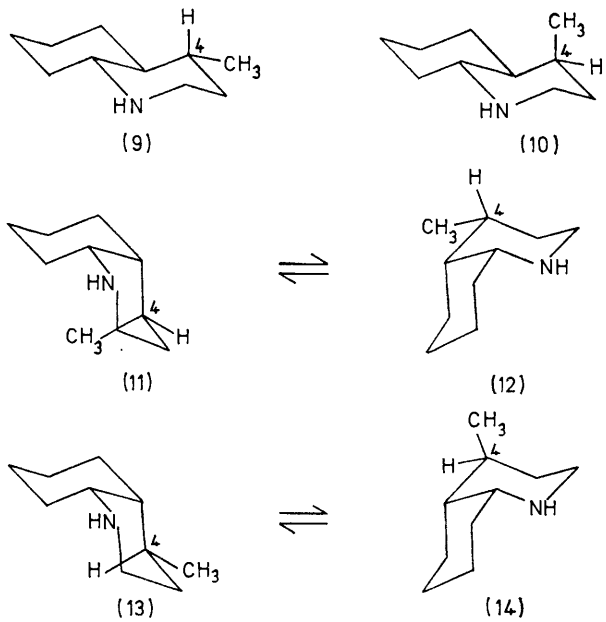
[10] H. Booth, *Tetrahedron*, 1966, **22**, 615.
[11] D. Danneels and M. Anteunis, *Org. Magnetic Resonance*, 1974, **6**, 617.

two of the fifteen carbon-attached ring protons of (4) could be assigned in the ^{1}H spectrum, the stereochemistry of the molecule was established with complete confidence. The carbon-13 spectrum of (4) was interpreted in the usual manner; however, there is unavoidable ambiguity with respect to the assignments of C-4, -6, and -7, the lines for which all appear in the range 25.7—26.7 p.p.m. (Table 2). The shift of the methyl carbon, at 18.5 p.p.m., is characteristic of an axial environment.[1]

The major component of the hydrogenation of quinaldine hydrochloride was *cis*(2H,4aH),*cis*(4aH,8aH)-2-methyldecahydroquinoline (5) ⇌ (6). In *cis*-decahydroquinoline (1) ⇌ (2), (2) is preferred to the extent of 1.06 kcal mol^{-1} at 199 K, and this bias is expected to be accentuated in (5) ⇌ (6), where the exaggerated stability of (6), relative to (5), is due to the severe repulsive interactions experienced by the ' inside,' axial methyl in (5). It was not surprising, therefore, that experiments at low temperature failed to reveal the carbon-13 signals due to conformation (5), although calculations allowed us to predict exactly where such signals should appear. The ^{1}H spectrum of (6) (Table 1) showed only two low-field signals, at τ 7.12 and 7.37, in addition to a broad envelope at high field and a methyl doublet at τ 8.93. The signal at τ 7.12 had $\nu_{\frac{1}{2}}$ of only 6.7 Hz, a clear indication of the type 2 conformation (6), in which 8a-H is subject to relatively small couplings with 4a-, 8eq-, and 8ax-H. Further, the well resolved, symmetrical multiplet at τ 7.37, assigned to 2-H, had a separation of 33 Hz between the outer lines. Since the coupling J_{MeOH} was 6.05 Hz, the sum of the vicinal couplings ($J_{2,3eq} + J_{2,3ax}$) was 14.75 Hz, a value requiring 2-H to be axial. Thus the predominance of conformation (6) was established from the ^{1}H spectrum alone. At the same time, the observed ^{13}C shifts (Table 3) are in excellent agreement with those calculated on the basis of conformation (6).

trans(2H,4aH),*cis*(4aH,8aH)-2-Methyldecahydroquinoline (7) ⇌ (8) was the second least abundant isomer isolated, and that with the longest retention time by g.l.c. The ^{1}H spectrum consisted of a methyl doublet at τ 9.0, a broad envelope between τ 7.8 and 9.2, and a two proton multiplet at τ 7.11, due to overlap of signals due to 2- and 8a-H (Table 1). Irradiation of the multiplet caused the methyl doublet to collapse to a singlet. However, no stereochemical information could be deduced from the ^{1}H spectrum. The observed ^{13}C shifts (Table 3) show good agreement with the shifts calculated for conformation (7). In addition, the spectrum showed no broadening of lines at temperatures down to 228 K, thus excluding an appreciable proportion of (8). The ring inversion process in *cis*-decahydroquinoline is readily detected in ^{13}C spectra at 270—300 K owing to the relatively high activation energy (*ca.* 15 kcal mol^{-1}) and the large chemical shift differences (125—300 Hz at 25 MHz) between some of the structurally identical carbons in the extreme conformations; consequently, the presence of $\geqslant$3% of conformation (8) would have caused selective line-broadening in the ^{13}C spectrum of (7) ⇌ (8) at 228 K. The bias towards (7) is considerably more pronounced than expected from the preference for (2) in (1) ⇌ (2) (1.1 kcal mol^{-1}) in opposition to the conformational free energy of the methyl substituent, which is 1.7 at room temperature and 1.6 kcal mol^{-1} at 163 K,[3] in cyclohexane. Since (7) is preferred by at least 1.6 kcal mol^{-1} [corresponding to 97% (7) at 228 K], the conformational free energy of the methyl at C-2 in *cis*-decahydroquinoline is, at the very least, 2.7 kcal mol^{-1}, with the usual assumption of additivity. This conclusion is also threatened by our ignorance of the effect, if any, of the methyl substituent on the position of equilibrium with respect to nitrogen inversion. In spite of these limitations, the result is significant, and is probably a consequence of the fact that the C–N bond is rather shorter (at 1.47 Å) than the C–C bond (1.54 Å). The consequent ring puckering in the vicinity of the nitrogen causes 2,6-axial bonds to be forced slightly inwards, thus increasing syn-axial repulsions, particularly between substituents at C-2 and -6. Thus (8) is appreciably destabilised.

The hydrogenation of 4-methylquinoline in cyclohexane over Raney nickel at 170° and 110 atm. gave a mixture of perhydro-bases containing *ca.* 90% of *trans*(4H,4aH),*trans*(4aH,8aH)-4-methyldecahydroquinoline (9). Methods which would give appreciable



yields of all isomers were therefore investigated. The hydrogenation of 4-methylquinoline hydrochloride in water over Raney nickel unexpectedly came to an end at the tetrahydro-stage, the product being 4-methyl-5,6,7,8-tetrahydroquinoline. Attempted reduction of the latter in concentrated hydrochloric acid, in an all-glass apparatus, with platinum black or platinum oxide as catalyst, proved unsuccessful; no hydrogen uptake

whatever was realised (*cf.* ref. 7). However, complete reduction of the tetrahydro-base occurred using sodium in boiling n-butanol. The product was separated by preparative g.l.c. into (9) (65%), *cis*(4H,4aH),*trans*-(4aH,8aH)-4-methyldecahydroquinoline (10) (14%) and a third constituent not investigated. The two perhydro-4-methylquinolines possessing a *cis*-ring fusion were obtained in the following way. Controlled hydrogenation of 4-methylquinoline in cyclohexane produced a mixture containing perhydro-4-methylquinoline (5.5%), 4-methyl-1,2,3,4- (58.5%), and 4-methyl-5,6,7,8-tetrahydroquinoline (36%). The mixed hydrochlorides derived from this product were hydrogenated in water over Raney nickel, yielding perhydro-bases rich in compounds with a *cis*-ring fusion. Pure samples of *cis*(4H,4aH),*cis*(4aH,8aH)-4-methyldecahydroquinoline (11) ⇌ (12) and *trans*(4H,4aH),*cis*(4aH,8aH)-4-methyldecahydroquinoline (13) ⇌ (14) were then obtained by distillation followed by careful preparative g.l.c.

The 100 MHz ^{1}H spectrum of (9) showed only two signals at low field, but at 220 MHz four one-proton multiplets were clearly seen at τ 6.98, 7.31, 7.90, and 8.08. The only interpretable part of the complex high-field region was the methyl doublet (J 6 Hz) at τ 9.12. The signal at τ 6.98 was assigned to 2eq-H in view of its doublet character (J *ca.* 12 Hz), with at least three small additional couplings clearly resolved. The signal at τ 7.31, assigned to 2ax-H, was a triplet of doublets (J *ca.* 12 and 2.7 Hz), whilst the angular proton 8a-H was a triplet (J *ca.* 11 Hz) at τ 7.90, each part showing further splitting. The fine structure of the signal due to 8a-H indicates a *trans*-ring fusion. In addition, the shifts of 8a- and 2ax-H are close to the corresponding shifts in *trans*-decahydroquinoline;[6] the lack of deshielding from the 4-methyl group (*cf.* ref. 10) established the equatorial character of the substituent. Further, the doublet (J *ca.* 10 Hz) at τ 8.08, absent in this region of the spectrum of *trans*-decahydroquinoline, is clearly due to 5eq-H, abnormally deshielded by a *peri*-interaction (Me–H), which is expected to be similar to a syn-axial interaction (Me–H). The strong evidence from the ^{1}H spectrum (Table 1) for (9) is again substantiated by the observed ^{13}C shifts (Table 2), which show good agreement with the calculated shifts. As in earlier work,[2] the shifts calculated for C-5 and Me included a mutual shielding effect of 2.6 p.p.m.

In the 220 MHz ^{1}H spectrum of *cis*(4H,4aH),*trans*-(4aH,8aH)-4-methyldecahydroquinoline (10), the angular proton 8a-H appears as a triplet of doublets (J *ca.* 13 and 4 Hz), establishing the *trans*-nature of the ring fusion. The chemical shifts of 8a-H (τ 7.56), deshielded by 0.35 p.p.m. compared with its shift in (9), and in *trans*-decahydroquinoline itself, together with a similar, comparative deshielding of 0.25 p.p.m. for 2a-H, proved conclusively that the 4-methyl substituent is axial. The deshielding suffered by 2ax-H in (10) causes this signal to appear at lower field than that due to 2eq-H (Table 1), an interesting but understandable reversal of the normal situation. The ^{13}C shifts of (10), both observed and calculated, appear in Table 2. The shifts of the methyl carbon and C-5 were adjusted after reference to the published ^{13}C shifts[12] for methylcyclohexane (CH_3eq, 23.1, CH_3ax 18.9 p.p.m.) and for 'frozen' *cis*-1,2-dimethylcyclohexane[13] (CH_3eq 21.06, CH_3ax 11.83 p.p.m.). The discrepancies between the calculated and observed shifts for both C-5 and the methyl are a reflection of the unsatisfactory nature of the model compounds, in this instance.

The most abundant isomer from the hydrogenation of the mixed tetrahydro-bases in aqueous solution was *cis*(4H,4aH),*cis*(4aH,8aH)-4-methyldecahydroquinoline (11) ⇌ (12). The 220 MHz ^{1}H spectrum showed at τ 7.25 a narrow signal ($\nu_{\frac{1}{2}}$ 6.3 Hz) characteristic of the angular proton 8a-H in the type 2 conformation (12). The signals at τ 6.94 and 7.36 were assigned to 2eq- and 2ax-H respectively, in view of their multiplicities. The chemical shifts of 8a- and 2ax-H are little different from their counterparts in *cis*-decahydroquinoline, which exists largely in the type 2 conformation (2). The absence of deshielding effects on 8a- and 2ax-H indicates that the 4-methyl substituent must be equatorial. Thus the ^{1}H spectrum identifies the isolated base as (11) ⇌ (12) and conclusively establishes the preponderance of the type 2 conformation (12), a situation which is hardly surprising in view of the severe repulsions experienced by the 'inside' axial methyl in conformation (11). These conclusions were corroborated by the carbon-13 shifts (Table 3), which showed good agreement between those observed, and those calculated for conformation (12).

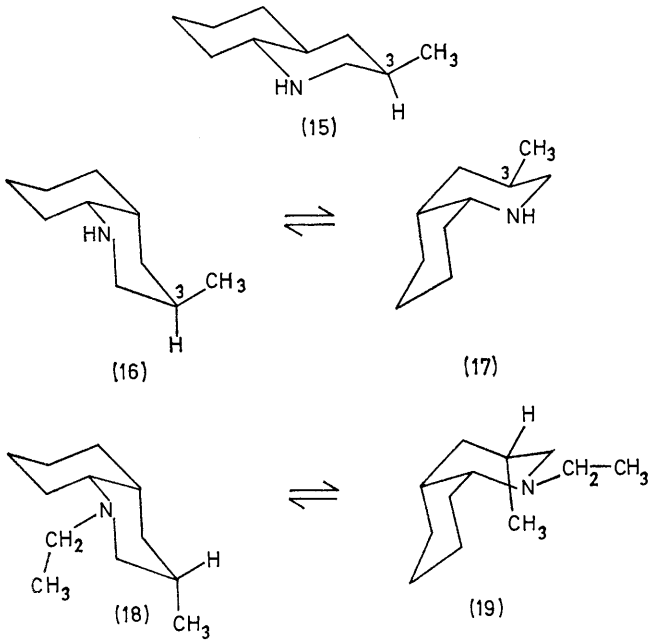
The minor component from the hydrogenation of the mixed tetrahydro-bases was *trans*(4H,4aH),*cis*-(4aH,8aH)-4-methyldecahydroquinoline (13) ⇌ (14). The room temperature ^{1}H spectrum (100 MHz) gave broad signals, characteristic of a conformational exchange occurring relatively slowly at that temperature Both increase and decrease in temperature led to a sharpening of signals, but at reduced temperatures the overlapping of resonances frustrated an identification of the conformations involved. However, the two methyl doublets, at τ 8.93 and 9.12, observed in the ^{1}H spectrum at 208 K, had approximately equal areas. In this case the simplicity of the noise-decoupled ^{13}C spectrum proved invaluable. The spectrum at 324 K showed nine signals, those for C-5 and -6 being coincident. Selective broadening was evident even at this temperature, the signals for C-3, -5, -6, and -7 being particularly broad, corresponding to chemical shift differences in the two conformations of *ca.* 12, 4, 5, and 6 p.p.m. (Table 3). The ^{13}C spectrum at 210 K showed 15 lines, rather than the maximum of 20, due to accidental overlap of some signals. The ratio of (13) to (14), estimated from the areas of the well separated signals for C-8a using a planimeter, was 1.08, equivalent to a free

[12] D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, 1972, **94**, 5318.

[13] H-J. Schneider, R. Price, and T. Keller, *Angew. Chem. Internat. Edn.*, 1971, **10**, 730.

energy difference, at 210 K of 0.03 kcal mol^{-1}. The *peri*-interaction (Me–H) in (13) between CH_3 and 5eq-H is expected to amount to *ca.* 0.85 kcal mol^{-1}, as it involves the same stereochemistry as that of a syn-axial Me–H interaction. Consequently, this conformational preference of a methyl substituent at position 4 of a *cis*-decahydroquinoline can be roughly estimated as (1.1 + 0.85 + 0.03) = 1.98 kcal mol^{-1}, a value similar to the 1.70 kcal mol^{-1} generally taken as the *A* value of methyl in a cyclohexane ring.

The hydrogenation of 3-methylquinoline in cyclohexane over Raney nickel gave a large preponderance of *cis*(3H,4aH),*trans*(4aH,8aH)-3-methyldecahydroquinoline (15), a solid easily purified by sublimation. The ^{1}H spectrum established the transoid nature of the ring fusion, since the low-field region of the spectrum showed only two one-proton signals well separated from



the envelope at high field.[6] The doublet at τ 7.06 (separation 11 Hz) was assigned to 2eq-H; the triplet at τ 7.82 (separations *ca.* 11.5 Hz) was coupled to the doublet, and was therefore assigned to 2ax-H. The equatorial orientation of the methyl was evident from the good agreement of observed and calculated carbon-13 chemical shifts (Table 2). The methyl shift (19.6 p.p.m.) agrees with that of the methyl in 3-methylpiperidine (19.96 p.p.m.[1]), and since the shifts of C-2, -3, -4, and -4a are closely dependent on the orientation of the methyl substituent,[1] the stereochemistry indicated in (15) can be assigned to the solid base with confidence.

When the hydrogenation of 3-methylquinoline was carried out in cyclohexane containing a small quantity of ethanol (due to inadequate washing of the catalyst with cyclohexane), the reaction took a different course, producing a mixture of *trans*(3H,4aH),*cis*(4aH,8aH)-3-methyl- (16) ⇌ (17) and *cis*(3H,4aH),*cis*(4aH,8aH)-1-ethyl-3-methyl-decahydroquinoline (18) ⇌ (19). A pure sample of each component was readily isolated by preparative g.l.c. The minor component (16) ⇌ (17) existed largely in a single conformation, since a one-proton signal at τ 7.24 in the ^{1}H spectrum had a half-intensity width ($\nu_{\frac{1}{2}}$) of only 8 Hz, thus identifying it unambiguously as the 8a-H signal in the type 2 conformation (17). The signal for 2eq-H appeared at τ 7.0 as a doublet (separation *ca.* 11 Hz) and that for 2ax-H at τ 7.78 as a triplet (separation *ca.* 11 Hz). The ^{13}C shifts of (16) ⇌ (17) (Table 3) confirmed the predominance of a type 2 conformation and established the equatorial nature of the methyl, as in (17). The excellent agreement between observed shifts, and those calculated for (17), together with the absence of broadening at room temperature, eliminates from consideration a proportion of (16) $\geqslant$3%. The ^{13}C shifts calculated for C-2 and -4 in conformation (16) are 44.7 and 29.6 p.p.m. respectively, values which are no less than 10 p.p.m. different from the corresponding shifts in (17). The strong preference for the type 2 conformation (17) finds a ready explanation in the bias already found in the parent *cis*-decahydroquinoline (6.5% type 1, 93.5% type 2) together with the marked preference of methyl for an equatorial orientation.

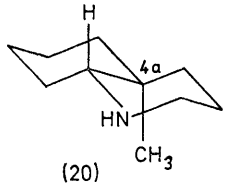
The ^{1}H shifts in the spectrum of the 1-ethyl base (18) ⇌ (19) are given in Table 1. The signal at τ 7.23, assigned to 8a-H, was a quintet (separations *ca.* 5 Hz). The separation between outer lines (20.5 Hz) was sufficiently great to ensure that a vicinal axial–axial coupling must be involved. Therefore the type 1 conformation is strongly favoured over the type 2 conformation.[6] That the actual stereochemistry was represented by (18), with methyl equatorial, was clear from the observed ^{13}C shifts, which showed reasonable agreement with those calculated for conformation (18). The calculation employed shift parameters for replacement of (N)H by (N)Et (*cf.* ref. 14) and for replacement of hydrogen at position 3 by a methyl substituent.[1] It was assumed that *N*-ethyl was largely equatorial, and that, consequently, the carbons C-8 and CH_2 of Et were mutually shielded by 6.2 p.p.m., *i.e.* by a similar effect to the well known γ_a effect (*cf.* ref. 1) involving a ring carbon situated γ to an axial methyl within the same ring. The observed ^{13}C shifts for (18) ⇌ (19) exclude the presence of $\geqslant$3% of (19), bearing in mind the ^{13}C shifts expected for (19), and the absence of selective line broadening in the room temperature spectrum. Finally, the conformational preference of the methyl group, taken in conjunction with the known position of equilibrium [2] in *cis*-1-ethyldecahydroquinoline (86% type 1, 14% type 2) are adequate to explain the bias observed in the equilibrium (18) ⇌ (19). Unfortunately, the molecule identical in configuration to (18) ⇌ (19), but lacking the *N*-ethyl group, was not detected in the mixture of compounds obtained in the hydrogenation.

4a-Methyl-*trans*-decahydroquinoline (20) and the *cis*-isomer (21) ⇌ (22) were synthesised by a published

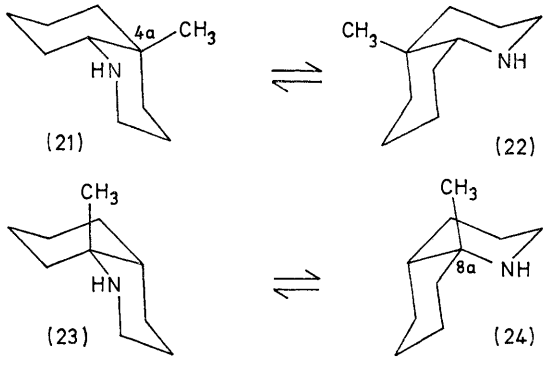
[14] G. Ellis and R. G. Jones, *J.C.S. Perkin II*, 1972, 437.

procedure,[15] and separated by preparative g.l.c. Proton chemical shifts are recorded in Table 1; for the *trans*-base, the multiplicities for 2eq-H (doublet, separation *ca.* 11 Hz), and 2ax-H (triplet of doublets, separations *ca.* 12 and *ca.* 3.5 Hz) were unexceptional The signal assigned to 8a-H was a ' deceptively simple ' [16] triplet, due to 8eq- and 8ax-H having identical, or nearly identical, chemical shifts, itself a result of the normal deshielding of 8ax-H by the axial methyl group.[10,11] The separation of outer triplet lines was 15.0 Hz, the sum of the coupling constants $J_{8a,8ax}$ and $J_{8a,8eq}$. The apparent coupling of 7.50 Hz is, of course, the mean coupling constant, and this analysis is entirely consistent with the stereochemistry represented by (20). As anticipated, the ^{13}C spectrum of (20) was independent of temperature change, and the observed shifts are in good agreement with calculated shifts (Table 2). In this case the shift parameters due to the ring-junction methyl were derived by comparison of the ^{13}C shifts in *trans*-decalin and in *trans*-9-methyldecalin (Table 4).[5]

The ^1H spectrum of *cis*-4a-methyldecahydroquinoline (21) $\rightleftharpoons$ (22) was interpreted in terms of a preponderance of type 2 conformation (22). Thus the signal for 8a-H was a narrow triplet, with separations of *ca.* 3 Hz,



(20)

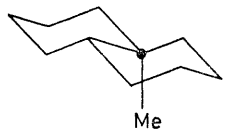
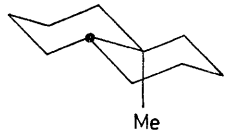
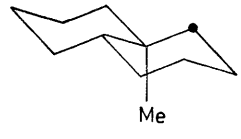
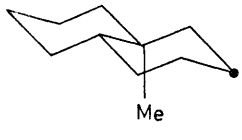


(21) (22) (23) (24)

whilst the shifts of 2eq-H (doublet, separation *ca.* 12 Hz) and 2ax-H (triplet of doublets, separations *ca.* 11 and 3.5 Hz) were close to those in decahydroquinoline (Table 1). However, the presence of a small proportion of (21) could not be excluded, and this possibility was confirmed by the room temperature ^{13}C spectrum which showed that several of the ten expected lines were considerably broadened compared with the remainder. In the sharply resolved ^{13}C spectrum obtained at low temperature (220 K), the ten lines of the predominant isomer were easily identified, along with seven lines (two as shoulders) assigned to the minor isomer. A comparison of the integrals for signals due to C-8a led to an estimation of $6 \pm 2\%$ for the proportion of the minor conformation. The three lines of the minor isomer not observed were almost certainly masked by the strong lines due to the major isomer. Assignment of ^{13}C signals involved several techniques, including (*a*) a

TABLE 4

Effects on ^{13}C shifts in *trans*-decalin caused by replacement of ring junction hydrogens by methyl substituent (p.p.m., positive ≡ increasing downfield shift)

Structure	Description of effect	Effect (p.p.m.)
 Me	α_a	−9·1
 Me	$j\beta_a$	+2·3
 Me	β_a	+7·8
 Me	γ_a	−5·0

determination of off-resonance spectra at 293 and 317 K; (*b*) a study of the progress of line-broadening with decrease in temperature, and (*c*) a comparison of observed shifts with calculated shifts (Table 3). The dominant conformation was clearly (22), as the room temperature ^1H spectrum had suggested. The free energy difference $\Delta G_{(21)\rightarrow(22)}$ was −1.2 kcal mol^{-1} at 220 K, a value which is little different from that in *cis*-decahydroquinoline. From this comparison, it can be argued that an axial methyl substituent at the 3-position of a piperidine is energetically equivalent to an axial methyl in cyclohexane, provided the methyl causes little or no distortion at the ring junction.

The ^{13}C shift parameters for the ring junction methyl in (21) $\rightleftharpoons$ (22) were obtained from the published shifts [5] for *cis*-decalin and *cis*-9-methyldecalin at reduced temperatures. These parameters are listed in Table 5.

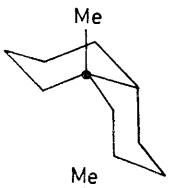
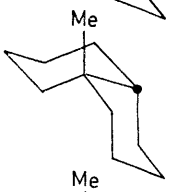
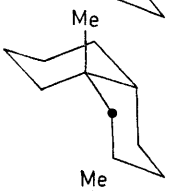
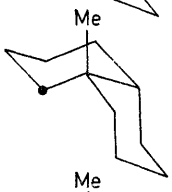
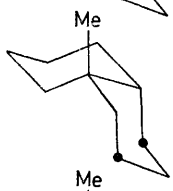
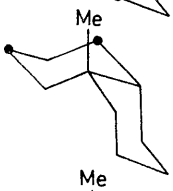
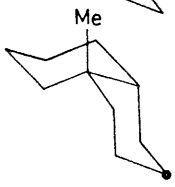
cis-8a-Methyldecahydroquinoline (23) $\rightleftharpoons$ (24) was synthesised by the addition of methyl-lithium to 2,3,4,4a,5,6,7,8-octahydroquinoline. The corresponding *trans*-isomer was not detected in the product, and

[15] T. Henshall and E. W. Parnell, *J. Chem. Soc.*, 1962, 661.
[16] R. J. Abraham and H. J. Bernstein, *Canad. J. Chem.*, 1961, **39**, 216.

the stereospecificity of the nucleophilic addition is probably due to steric factors. Addition of Me^- to the preferred conformation (25) of the octahydroquinoline is

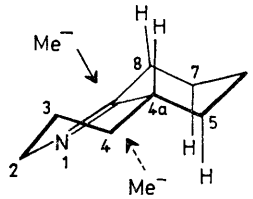
TABLE 5

Effects on ^{13}C shifts in *cis*-decalin caused by replacement of ring junction hydrogen by methyl substituent (p.p.m., positive ≡ increasing downfield shift)

Structure	Description of effect	Effect (p.p.m.)
	α_{ea}	−4·0
	$j\beta_{ea}$	+4·9
	β_e	+9·1
	β_a	+4·9
	γ_e	+1·8
	γ_a	−5·0
	δ_e	0

less hindered from the upper side (hindrance by 4a- and 8ax-H) than from the lower side (hindrance by 5ax- and 7ax-H).

The ^1H n.m.r. spectrum of (23) ⇌ (24) was not informative (Table 1). Apart from the methyl singlet at τ 8.96 and a fairly narrow ring-proton envelope at τ 8.2—9.1, the only characteristic feature was a moderately broad two-proton signal at τ 7.3 due to 2eq- and 2ax-H. The ^{13}C spectrum at 321 K showed ten lines (Table 3), the line at 35.3 p.p.m. being very broad, and those at 24.9 and 23.3 p.p.m. being moderately broad, compared with other signals. At 213 K, the spectrum showed 19 sharp lines, two of the expected



(25)

20 lines being coincident. The 18 lines representing single carbon atoms clearly comprised nine due to a major and nine due to a minor conformation; the remaining strong line at 40.9 p.p.m. thus consisted of a signal due to a carbon in the major conformation superimposed on one due to a carbon in the minor conformation. ^{13}C Shifts for each conformation (Table 3) were calculated from the observed ^{13}C shifts in the conformations of *cis*-decahydroquinoline, together with the parameters of Table 5. The large difference in chemical shift between C-8 in (23) and C-8 in (25) is especially important; the very broad signal at 35.3 p.p.m. in the spectrum at 321 K can at once be assigned to C-8 in the rapidly exchanging situation (23) ⇌ (24). Now in the spectrum recorded at 213 K, there is a convenient absence of signals in the region between 29 and 38 p.p.m. Consequently, the two signals due to C-8 in the low temperature spectrum must lie, one in the region <29 p.p.m. and the other in the region >38 p.p.m. Now in this spectrum there are seven major and six minor signals at <29 p.p.m., and three major and four minor signals at >38 p.p.m. Consequently, the signals for C-8 consist of a major signal <29 p.p.m. and a minor signal >38 p.p.m. Reference to the calculated shifts (Table 3) shows that the major conformation is (23) and the minor conformation is (24). Although this interpretation is based entirely on the analysis of one signal, with close reference to calculated shifts, its correctness was confirmed by the good agreement between observed and calculated shifts for the remaining carbon atoms. The proportions of (23) and (24) were estimated to be 66 and 34% respectively, equivalent to a free energy difference at 213 K of 0.3 kcal mol^{-1}. This result is significant, since it establishes the preference of a methyl group for the axial orientation in a cyclohexane, rather than the axial orientation at the 2 (or 6) position in a piperidine. Additionally, the result confirms the previous finding [from the position of equilibrium in (7) ⇌ (8)] of a relatively high conformational free energy of a methyl group in the 2 (or 6) position of a piperidine.

The findings reported here for *cis*-*C*-methyldecahydroquinolines and summarised in Table 6 suggested further

work aimed at establishing the position of equilibrium in *C*-alkylpiperidines, and this work is in progress.

The error limits of Table 6 were obtained in the following way. The possible error in temperature

TABLE 6

Position of conformational equilibrium in *C*-methyldecahydroquinolines (*cis*-fusion) and associated free energies $-\Delta G^0$ for type 1 ⟶ type 2 [a]

Structure	Position of Me	T/K	% Type 1	% Type 2	$-\Delta G^0$/ kcal mol^{-1}
(1) ⇌ (2) [b]		199	6.5	93.5	1.1
(5) ⇌ (6)	2	228	<3	>97	>1.6
(7) ⇌ (8)	2	228	>97	<3	<−1.6
(11) ⇌ (12)	4	294	<3	>97	>2.0
(13) ⇌ (14)	4	210	52	48	−0.03
(16) ⇌ (17)	3	294	<3	>97	>2.0
(21) ⇌ (22)	4a	220	6	94	1.2
(23) ⇌ (24)	8a	213	66	34	−0.3

[a] ΔG^0 Values are accurate to ±0.06 kcal mol^{-1}. [b] Ref. 1.

determination is estimated to be ±4 K. Possible errors in area determination, by integration or planimeter, lead to errors in the equilibrium constant K which vary from ±2% (in favourable cases of K *ca.* 1) to ±10% (in the unfavourable cases of K *ca.* 20). After combining the possible errors, it is concluded that ΔG^0 values are accurate to *ca.* ±0.06 kcal mol^{-1} or better.

EXPERIMENTAL

General details with respect to the measurement of ^{1}H and ^{13}C n.m.r. spectra, and for analysis by g.l.c. have been given previously.[2] The JEOL variable temperature accessory was calibrated against a chromel–alumel thermocouple immersed in $CHCl_3$ or pentane in a stationary sample tube in the n.m.r. probe. Preparative g.l.c. used 35 ft × ¼ in and 100 ft × ⅜ in column, both packed with 20% Carbowax 20M on alkali-treated Chromosorb W.

trans(2H,4aH),trans(4aH,8aH)-2-*Methyldecahydroquinoline*.—2-Methylquinoline (50 g) in cyclohexane (75 ml) was reduced with hydrogen at 110 atm. and 170° in the presence of Raney nickel (12 g; T-1 grade [17]). After 3 days the mixture was filtered and distilled. The crude base, b.p. 95—97° at 1 mmHg, showed five peaks when examined by analytical g.l.c. (9 ft × ¼ in column, 20% Carbowax 20M on Chromosorb W), although one component constituted *ca.* 75% of the total. The mixture was treated with a slight excess of 3,5-dinitrobenzoic acid in warm ethyl acetate, and the salt which was collected on cooling was recrystallised several times from ethyl acetate to constant m.p. (202—203°). The pure base was recovered from the salt by treatment with an excess of sodium hydroxide solution, extraction into ether, and evaporation of the dried extracts. The product, *trans*(2H,4aH),*trans*-(4aH,8aH)-2-methyldecahydroquinoline (3) was a liquid, b.p. 202.5° at 760 mmHg (Found: M^+, 153.151. $C_{10}H_{19}N$ requires M, 153.151). The derived picrate had m.p. 155—156° (lit.,[9] 149—150°) (Found: C, 50.4; H, 6.0; N, 14.5. Calc. for $C_{16}H_{22}N_4O_7$: C, 50.3; H, 5.8; N, 14.7%). The N-*carboxyanilide*, from the base and phenyl isocyanate in ether, had m.p. 126—126.5° (from $CHCl_3$) (Found: N, 10.2. $C_{17}H_{22}N_2O$ requires N, 10.3%).

Hydrogenation of 2-Methylquinoline Hydrochloride.—2-Methylquinoline hydrochloride (15 g) in water (200 ml) was hydrogenated at 160 atm. pressure of hydrogen and 150° over Raney nickel (2 g; T-1 grade). After two weeks the mixture was filtered, basified with aqueous sodium hydroxide (30%), and extracted several times with ether. The crude bases were isolated by evaporation of the combined ethereal extracts after drying ($CaSO_4$). Analytical g.l.c. showed the presence of five components, A—E (this being the order of elution), the order of abundance being A > B > E > C > D. Preparative g.l.c., in some cases involving retention times in excess of 12 h, gave pure samples of each component. Component C was shown to be *trans*-decahydroquinoline by comparison with an authentic sample.[6] Component B was *trans*(2H,4aH),*trans*(4aH,8aH)-2-methyldecahydroquinoline (see above). Component D was *cis*-(2H,4aH),*trans*(4aH,8aH)-2-methyldecahydroquinoline (4), a liquid (Found: M^+, 153.151). Component A was *cis*(2H,4aH),*cis*(4aH,8aH)-2-methyldecahydroquinoline (5) ⇌ (6), a liquid, b.p. 211° at 760 mmHg (Found: M^+, 153.152). The picrate, from ethanol, had m.p. 170—171° (lit.,[9] 166—167°) (Found: C, 50.0; H, 5.8; N, 14.4%). Component E was *trans*(2H,4aH),*cis*(4aH,8aH)-2-methyldecahydroquinoline (7) ⇌ (8), a liquid, b.p. 219° at 760 mmHg (Found: M^+, 153.152). The picrate, from ethanol, had m.p. 198—199° (lit.,[9] 192—193°) (Found: C, 50.4; H, 5.8; N, 14.5%).

trans(4H,4aH),trans(4aH,8aH)-4-*Methyldecahydroquinoline*.—4-Methylquinoline (50 g) in cyclohexane (75 ml) was hydrogenated at 170° and 110 atm. over Raney nickel (12 g; T-1 grade). After 3 days the mixture was filtered and distilled, the crude bases having b.p. 91—94° at 1 mmHg. The mixture, analysed by g.l.c., showed one isomer present to the extent of 90%. Purification *via* the salt with 3,5-dinitrobenzoic acid, crystallised to constant m.p., gave pure trans(4H,4aH),trans(4aH,8aH)-4-*methyldecahydroquinoline* (9), b.p. 222° at 760 mmHg. The *picrate* (from ethanol) had m.p. 153—155° (Found: C, 50.5; H, 6.0; N, 14.4. $C_{16}H_{22}N_4O_7$ requires C, 50.3; H, 5.8; N, 14.7%). The *3,5-dinitrobenzoic acid salt* had m.p. 183—185° (Found: C, 55.7; H, 6.2; N, 11.2. $C_{17}H_{23}N_3O_6$ requires C, 55.9; H, 6.4; N, 11.5%).

4-Methyl-5,6,7,8-tetrahydroquinoline.— 4-Methylquinoline hydrochloride (from 25 g base) in water (100 ml) was hydrogenated at 200° and 200 atm. over Raney nickel (20 g; T-1 grade). After 3 weeks, the usual work-up gave *4-methyl-5,6,7,8-tetrahydroquinoline* (20 g), τ ($CDCl_3$) 1.67 (d, J 5 Hz, 2-H), 3.11 (d, J 5 Hz, 3-H), 7.07 (2 H, m, 8-H), 7.37 (2 H, m, 5-H), 8.16 (4 H, m, 6-, 7-H), and 7.82 (3 H, Me). The *picrate*, from ethanol–acetone, had m.p. 181.5—182.5° (Found: C, 51.0; H, 4.4; N, 15.1. $C_{16}H_{16}N_4O_7$ requires C, 51.1; H, 4.3; N, 14.9%).

Reduction of 4-Methyl-5,6,7,8-tetrahydroquinoline.—The foregoing product (5.5 g) in boiling butan-1-ol (250 ml) was treated with sodium (20 g) added in small pieces during 1 h. The mixture was heated under reflux for 12 h and then treated with ether saturated with water to decompose excess of sodium. The solution was acidified with concentrated hydrochloric acid, evaporated to a small volume, and shaken with ether to remove neutral material. The aqueous phase was basified with aqueous sodium hydroxide

[17] A. Dominguez, I. C. Lopez, and R. Franco, *J. Org. Chem.*, 1961, **26**, 1625.

(30%) and then worked-up by extraction into ether. The crude, undistilled product showed the presence of three components, in addition to traces of starting material. Careful preparative g.l.c., using the 100 ft × $\frac{3}{8}$ in column at 180°, gave pure samples of the two bases (A and B) with the shortest retention times. Component A (R_t 2.16 h, 65% abundance) was *trans*(4H,4aH),*trans*(4aH,8aH)-4-methyldecahydroquinoline (9), identical to material prepared above. Component B (R_t 2.6 h, 14% abundance) was cis(4H,4aH),trans(4aH,8aH)-4-*methyldecahydroquinoline* (10), m.p. 66—67°, b.p. 228° at 760 mmHg (Found: M^+, 153.151).

cis(4H,4aH),cis(4aH,8aH)-4-*Methyldecahydroquinoline and* trans(4H,4aH),cis(4aH,8aH)-4-*Methyldecahydroquinoline.*—4-Methylquinoline (30 g) in cyclohexane (250 ml) was hydrogenated at 100° and 25 atm. over Raney nickel (12 g; T-1 grade). When 2 mol. equiv. hydrogen had been taken up the hydrogenation was stopped and the mixture was worked-up in the usual way. The crude product was analysed by g.l.c. on a 9 ft × $\frac{1}{2}$ in column packed with Carbowax 20M on alkali-washed Chromosorb W, and shown to consist of 4-methyldecahydroquinoline (5.5%; retention time 5.7 min), 4-methyl-1,2,3,4-tetrahydroquinoline (58.5%; R_t 22.4 min) and 4-methyl-5,6,7,8-tetrahydroquinoline (36%; R_t 38.8 min).

The mixed bases were treated with an excess of hydrochloric acid (20%) and the solution evaporated to dryness. The mixed hydrochlorides (10 g) in water (50 ml) were hydrogenated at 200° and 200 atm. over Raney nickel (10 g). After 3 weeks, the normal work-up gave a mixture of bases, shown by g.l.c. to consist of unreduced 4-methyl-5,6,7,8-tetrahydroquinoline (28%), and two fully reduced bases C (61%) and D (11%). Fractional distillation up a spinning band column, at 35 mmHg, gave a fraction, b.p. 118—121°, containing C and D in equal proportions, tetrahydro-base being absent. Careful preparative g.l.c. (conditions as in previous experiment) separated this fraction into pure samples of C and D.

Component C was cis(4H,4aH),cis(4aH,8aH)-4-*methyldecahydroquinoline* (11) ⇌ (12), b.p. 231° at 760 mmHg (R_t 2.25 h). The derived *picrate* (from ethanol) had m.p. 119—120° (Found: C, 50.3; H, 5.9; N, 14.6. $C_{16}H_{22}N_4O_7$ requires C, 50.3; H, 5.8; N, 14.7%). Component D was trans(4H,4aH),cis(4aH,8aH)-4-*methyldecahydroquinoline* (13) ⇌ (14), b.p. 227° at 760 mmHg (R_t 2.61 h). The *picrate* had m.p. 134.5—135.5° (from ethanol) (Found: C, 50.0; H, 5.9; N, 14.4. $C_{16}H_{22}N_4O_7$ requires C, 50.3; H, 5.8; N, 14.7%).

cis(3H,4aH),trans(4aH,8aH)-3-*Methyldecahydroquinoline.*—3-Methylquinoline [18] (8.0 g) was hydrogenated in cyclohexane (200 ml) at 180° and 100 atm. over Raney nickel (1 teaspoonful). After 10 days, the mixture was filtered and evaporated to dryness. The crystalline solid remaining (7.7 g, 90%) was purified by sublimation to give needles of cis(3H,4aH),trans(4aH,8aH)-3-*methyldecahydroquinoline* (15), m.p. 79—80°. The *picrate* (from ethanol) had m.p. 175—176° (Found: C, 50.2; H, 6.0; N, 14.2. $C_{16}H_{22}N_4O_7$ requires C, 50.3; H, 5.8; N, 14.7%).

Hydrogenation of 3-*Methylquinoline in Cyclohexane containing a Trace of Ethanol.*—The above experiment was repeated using cyclohexane containing some ethanol. The resulting oil (6.8 g) contained two components, and was separated by preparative g.l.c. using the 35 ft × $\frac{1}{4}$ in column at 145°. trans(3H,4aH),cis(4aH,8aH)-3-*Methyldecahydroquinoline* (17) was a liquid, and the derived *picrate*, from ethanol, had m.p. 154—155° (Found: C, 50.1; H, 5.8; N, 15.1%). cis(3H,4aH),cis(4aH,8aH)-1-*Ethyl*-3-*methyldecahydroquinoline* (18) was a liquid, of which the *picrate* had m.p. 94—95° (from ethanol) (Found: C, 52.9; H, 6.5; N, 13.7. $C_{18}H_{26}N_4O_7$ requires C, 52.7; H, 6.3; N, 13.7%).

cis- *and* trans-4a-*Methyldecahydroquinoline.*—The literature method [15] gave a mixture of isomers, separated by preparative g.l.c. (35 ft × $\frac{1}{4}$ in column; 145°) into pure components. The *cis*-base gave a picrate, m.p. 191—193° (lit.,[15] 190—192°) and the *trans*-base a picrate, m.p. 222—223° (lit.,[15] 222—225°).

8a-*Methyl*-cis-*decahydroquinoline.*— 2,3,4,4a,5,6,7,8-Octahydroquinoline [19] (4.1 g), in dry ether (12 ml) was added to a solution of methyl-lithium from lithium (4.0 g) in dry ether (40 ml). The mixture was stirred at room temperature for 2 h, then decomposed with water (20 ml). The ether layer was separated, washed with water, dried ($MgSO_4$), and evaporated. The resulting pale green oil (3.2 g) consisted of 50% starting material and 50% product. Preparative g.l.c. gave 8a-*methyl*-cis-*decahydroquinoline* (23) ⇌ (24) as an oil; the *picrate* (from ethanol) had m.p. 202—203° (Found: C, 50.1; H, 5.9; N, 14.8. $C_{16}H_{22}N_4O_7$ requires C, 50.3; H, 5.8; N, 14.7%).

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