Conformational Equilibria in *N*-Alkyl-*cis*-decahydroquinolines

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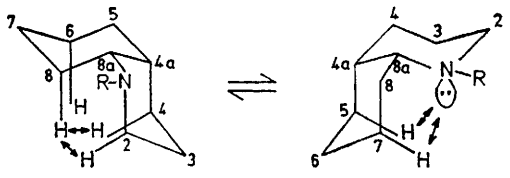
Analyses of low temperature ^{1}H, ^{13}C, and ^{19}F n.m.r. spectra show that replacement of the nitrogen-attached hydrogen in *cis*-decahydroquinoline by the alkyl groups methyl, ethyl, and βββ-trifluoroethyl leads to a shift in the conformational equilibrium from a preference for type 2 conformation to preference for type 1. The activation energy E_a for the interconversion 1 ⟶ 2 of 1-(βββ-trifluoroethyl)-*cis*-decahydroquinoline was determined as 68 kJ mol^{-1} by a full line-shape analysis of the ^{19}F spectra recorded between 245 and 312 K.

In previous papers,[1,2] the conformational equilibrium (1) ⇌ (2) in *cis*-decahydroquinoline and its 1-acyl derivatives was investigated by analysis of the ^{1}H n.m.r. spectra recorded at room temperature. *cis*-Decahydroquinoline itself has a strong preference for type 2 conformation, whereas the acyl derivatives prefer type 1. The result for *cis*-decahydroquinoline was confirmed by the low temperature ^{13}C spectrum,[3] which also gave the proportions of (1; R = H) and (2; R = H) at 199 K as 6·5 and 93·5% respectively. Our present knowledge of the quantitative aspects of interactions (both attractive and repulsive) between nuclei and electrons does not allow us to make an accurate analysis of the equilibrium (1 ⇌ 2; R = H). However, the strong preference for (2; R = H) is probably

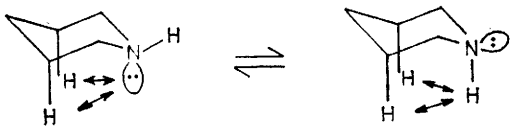
[1] H. Booth and A. H. Bostock, *Chem. Comm.*, 1967, 179.
[2] H. Booth and A. H. Bostock, *J.C.S. Perkin II*, 1972, 616.
[3] H. Booth and D. V. Griffiths, *J.C.S. Perkin II*, 1973, 842.

due in large measure to the possibility in (2; R = H) of NH being equatorial, leading to the existence of two 1,4 hydrogen–lone pair interactions. It is suggested that these are appreciably smaller than the corresponding



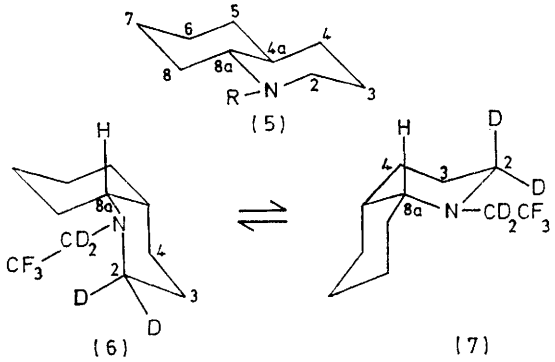
(1) (2)

1,4 hydrogen–hydrogen interactions in conformation (1; R = H). The 1,4 interactions characteristic of *cis*-fused twin-chair systems are to be contrasted with the typical 1,3 interactions of monocyclic systems. The 1,3 hydrogen–lone pair interactions in the N–H equatorial conformation (3) of piperidine are presumably similar to the 1,3 hydrogen–hydrogen interactions in (4) since the available evidence [4] suggests that (3) and (4) differ in free energy by less than 1·7 kJ mol^{-1}.


(3) (4)

We have now investigated the effects on the position of equilibrium in (1 ⇌ 2; R = H) caused by a replacement of the nitrogen-attached hydrogen by alkyl groups of increasing size. The compounds examined in detail were 1-methyl-, 1-ethyl-, and 1-(βββ-trifluoroethyl)-*cis*-decahydroquinoline. In addition, the earlier interpretation [1,2] of the ^{1}H spectrum of *cis*-decahydroquinoline was confirmed by analysis of the ^{1}H spectrum of 2,2-dideuterio-*cis*-decahydroquinoline, synthesised from 3,4-dihydroquinolin-2(1*H*)-one by successive reductions with lithium aluminium deuteride, and hydrogen over platinum black catalyst. The 100 MHz spectrum of the product showed at low field only a single signal, τ 7·16 (1H, s, $W_{1/2}$ 10 Hz, 8a-H). All the 1-alkyl derivatives showed profound changes in their ^{1}H and ^{13}C spectra at reduced temperatures, and the aim was to identify the conformations involved and to determine their proportions as accurately as possible at the slow exchange limit. At the same time, it was important to make certain that the process being slowed was indeed one of ring inversion (1) ⇌ (2), and not, for example, one of nitrogen inversion. Two lines of investigation suggested that ring inversion processes were under study. First, the corresponding *trans*-amines (5), which possess a rigid twin-chair conformation,[5] gave spectra which were unaltered by variation in temperature. Secondly, a full line-shape analysis (described later) was carried out on the ^{19}F spectrum of (1 ⇌ 2; R = CH_2CF_3) and gave for E_a [(1) ⟶ (2)] 68·1 kJ mol^{-1}, a value close to published values [6] for derivatives of *cis*-decalin, where ring inversion is the sole possibility.

The ^{1}H spectrum of 1-methyl-*trans*-decahydroquinoline (5; R = Me) at 220 MHz ($CDCl_3$) showed an unresolved envelope at high field, containing 12 protons, but five low-field signals could be assigned (see Table 1)


(5) (6) (7)

on the basis of their multiplicities, which are dominated by the relatively large geminal and vicinal axial–axial couplings of *ca.* 12 Hz, and on the expectation that 8*eq*-H would be deshielded by the largely equatorial *N*-methyl group (1,3-*syn* axial effect, *cf.* ref. 7). The spectrum was unchanged when the sample was cooled to 224 K. Carbon-13 shifts for (5; R = Me) are given in Table 2. Assignments were made from off-resonance experiments, and by comparison of observed shifts with

TABLE 1

Chemical shifts (τ values) of protons in 1-substituted *trans*-decahydroquinolines (5) (220 MHz; $CDCl_3$)

1-Substituent	2*eq*-H	2*ax*-H	8*eq*-H	8*a*-H	NMe	NCH_2	CMe
Me	7·13	7·94	7·92	8·59	7·76		
CH_2Me	7·11	7·80	7·92			7·20 *	9·03
						7·29 *	
CH_2CF_3	6·97	7·46				6·80 †	
						7·00 †	

* Non-equivalent methylene protons (J_{gem} — 14, J_{vic} 7 Hz).
† Non-equivalent methylene protons (J_{gem} — 15·5, J_{HF} 10·5 Hz).

those calculated from the shifts in *trans*-decahydroquinoline, together with the NMe parameters derived from earlier work with piperidines.[3] The δ(N) effect, mistakenly listed in ref. 3 as −0·84 p.p.m., is −0·68 p.p.m. In the calculation, it was assumed that the NMe substituent was largely equatorial (*cf.* ref. 8), and therefore the shifts of C-8 and NMe were adjusted for a mutual effect (−2·6 p.p.m.), itself derived from the methyl shifts in methylcyclohexane (22·2 p.p.m.) and *trans*-1,2-dimethylcyclohexane (19·6 p.p.m.).[9]

The ^{1}H spectrum of 1-methyl-*cis*-decahydroquinoline

[4] R. A. Y. Jones, A. R. Katritzky, A. C. Richards, R. J. Wyatt, R. J. Bishop, and L. E. Sutton, *J. Chem. Soc.* (*B*), 1970, 127.
[5] H. Booth and D. V. Griffiths, *J.C.S. Perkin II*, 1972, 2361.
[6] J. T. Gerig and J. D. Roberts, *J. Amer. Chem. Soc.*, 1966, **88**, 2791.
[7] H. Booth, *Tetrahedron*, 1966, **22**, 615.
[8] E. L. Eliel and F. W. Vierhapper, *J. Amer. Chem. Soc.*, 1974, **96**, 2257.
[9] D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, 1967, **89**, 6612.

(1 ⇌ 2; R = Me) at 220 MHz ($CDCl_3$; 323 K) gave a complex envelope of overlapping resonances between τ 7·8 and 8·8, a sharp singlet at 7·8 (NMe), and a multiplet at 7·32 (H). No stereochemical conclusions could be drawn from this spectrum. When the sample was cooled, a broadening of signals occurred, in agreement with a slowing of the ring inversion (1 ⇌ 2). Further cooling led to a sharpening of signals, and at 243 K *two* NMe resonances, at τ 7·62 and 7·82, were observed, the ratio being *ca.* 2 : 1. Considerable overlapping of these signals with those of other protons prevented an accurate estimation of proportions and, moreover, the complexity of the spectrum ruled out an identification of 2 : 1 for major to minor conformation allowed us to use chemical shifts to correlate a pair of signals at 223 K with the averaged signal at 337 K. Next, carbon-13 shifts calculated for carbons in both conformations were used to confirm the correctness of the pairing of major and minor signals in the low temperature spectrum, and to make assignments to every signal (Table 2).

The determination of the relative proportions of (1; R = Me) and (2; R = Me) from the spectrum at 223 K presented difficulties, since the integrals in a noise-decoupled, multi-pulse carbon-13 experiment may be subject to distortions arising from two sources. First, nuclear Overhauser enhancements (NOE) arising

TABLE 2

^{13}C Chemical shifts for 1-alkyldecahydroquinolines in $CDCl_3$ (p.p.m. downfield from Me_4Si) (calculated shifts in parentheses)

Ring fusion	*trans*	*trans*	*trans*	*cis*	*cis*	*cis*	*cis*	*cis*	*cis*	*cis*	*cis*	*cis*
Formula	(5)	(5)	(5)	(1) ⇌ (2)	(1) (Minor)	(2) (Major)	(1)⇌(2)	(1) (Major)	(2) (Minor)	(1⇌2)	(1) (Major)	(2) (Minor)
Alkyl	Me	CH_2Me	CH_2CF_3	Me	Me	Me	CD_2Me	CD_2Me	CD_2Me	CH_2CF_3	CH_2CF_3	CH_2CF_3
T/K	293	293	293	337	223	223	328	218 [a]	218 [a]	287	208	208
C Atom												
2	58·0 (56·6)	52·6	55·9	55·0	47·4 (48·3)	58·3 (56·9)	48·3	46·2	52·8	49·2	47·1	56·3
3	26·1 (26·1)	25·9	26·1	23·5	25·3 (27·9)	21·6 (19·7)	24·7	25·6	21·9	24·6	25·4	21·7
4	32·6 (31·6)	32·8	32·5	28·7	22·8 (22·6)	30·8 (29·4)	26·6	23·9	31·3	25·4	22·8	29·3
5	33·1 (32·9)	33·3	33·1	28·5	31·6 (31·6)	26·3 (25·0)	30·4	31·9	26·6 [b]	30·2	31·4	*c*
6	25·9 (26·5)	25·9	25·7	25·0	20·9 (21·2)	26·1 (26·3)	23·1	21·1	25·9	22·4	20·6	26·3
7	25·8 (25·9)	25·9	25·7	22·0	25·7 (26·6)	19·6 (20·4)	24·2	25·9	20·2	24·2	25·2	19·5
8	30·4 (31·5)	30·1	30·9	25·4	15·6 (20·4)	29·3 (30·2)	21·2	16·0	29·1	21·7	18·5	*c*
8a	69·3 (71·5)	65·2	65·6	62·9	60·6 (63·0)	63·4 (63·9)	58·9	57·9	57·2	61·1	61·9	57·9
4a	41·9 (42·0)	42·1	42·2	37·0	36·0 (34·1)	36·3 (33·7)	36·5	36·0	36·8	36·0	35·1	36·7
N-CH_3	42·6 (44·1)			42·9	42·4 (45·6)	43·2 (44·1)						
N-CH_2		46·4	52·8							55·0	54·6 [d]	*c*
N-CD_2							*c*	*c*	*c*			
C-CH_3		9·1					11·3	12·5	6·0			
CF_3			*c*							126·4 [e]		

[a] Solvent $CDCl_3$–$CFCl_3$. [b] Tentative. [c] Not seen clearly. [d] Quartet $J_{^{13}C-F}$ 30 Hz. [e] Quartet $J_{^{13}C-F}$ 281 Hz.

the conformations involved. The problem was solved by carbon-13 spectroscopy. The noise decoupled ^{13}C spectrum of (1 ⇌ 2; R = Me) at 337 K showed the expected ten lines (see Table 2), although the signal for C-8 was still very broad, as a result of the relatively large difference in chemical shift of this carbon in the two conformations. For the same reason, the signal for C-2 was quite broad at 337 K. At reduced temperatures, considerable broadening of the ^{13}C signals occurred before the slow exchange limit, with sharp signals, was reached at 243 K. No changes occurred on further cooling to 223 K. The noise-decoupled spectrum at 223 K showed 20 lines, corresponding to each carbon atom in the two conformations (1; R = Me) and (2; R = Me). Ten of the lines were considerably stronger than the remaining ten, corresponding to unequal proportions of (1) and (2). Assignments were made in the following way. The approximate ratio of from ^1H decoupling are not necessarily the same for each carbon nucleus. Secondly, carbons having different spin–lattice relaxation times (T_1) will give different intensities, unless relatively long pulse intervals are used. Fortunately, NOE in noise-decoupled ^{13}C spectra depend largely on the dipole–dipole interactions between carbon and the directly attached protons. Moreover, experiments with several *cis*-decahydroquinolines have given T_1 values which are independent of position in the ring system but which depend only on the number of attached hydrogen atoms.[10] Consequently, relative molecular abundances should be given correctly by a comparison of integrals for identically substituted carbon atoms (*cf.* ref. 11).

Integration of the ^{13}C signals in the spectrum of

[10] H. Booth and M. L. Jozefowicz, in preparation.
[11] H-J. Schneider, R. Price, and T. Keller, *Angew. Chem., Internat. Edn.*, 1971, 730.

(1 ⇌ 2; R = Me) at 223 K gave the ratio of major to minor conformations as 2·4 ± 0·2 : 1. The calculated shifts allowed confident assignment of the strongest signals to the carbon atoms of conformation (2; R = Me). Thus, at 223 K, 1-methyl-*cis*-decahydroquinoline consists of 70% (2; R = Me) and 30% (1; R = Me).

The calculated shifts for (1; R = Me) and (2; R = Me) were based on observed or calculated shifts for *cis*-decahydroquinoline,[3] modified by the *N*-methyl parameters calculated from the ^{13}C spectra of piperidines and 1-alkylpiperidines.[3] The shift of C-8 in (1; R = Me) was derived from the calculated shift of C-8 in conformation (1) of *cis*-decahydroquinoline, modified by a parameter (−6·6 p.p.m.) deduced from the shifts of the axial methyl carbons in *cis*-1,2-dimethylcyclohexane (11·8 p.p.m.) and in methylcyclohexane (18·4 p.p.m.).[9,11] The *N*-methyl ^{13}C shift in (1; R = Me) was based on that of the 1-methyl carbon in 1,4-dimethylpiperidine, modified by a parameter (−1·1 p.p.m.) deduced from the shifts of the equatorial methyl carbons in *cis*-1,2-dimethylcyclohexane (21·1 p.p.m.) and in methylcyclohexane (22·2 p.p.m.).

The ^1H spectrum of 1-ethyl-*trans*-decahydroquinoline (5; R = CH_2Me) at 220 MHz ($CDCl_3$) gave the expected ill defined resonance at high field, and only the signals listed in Table 1 could be assigned with confidence. Carbon-13 shifts for this molecule appear in Table 2, assignments being made from off-resonance experiments and by comparison with shifts for the 1-methyl compound.

1-(αα-Dideuterioethyl)-*cis*-decahydroquinoline (1 ⇌ 2; R = CD_2Me) was synthesised to produce spectral simplification. The derived ^1H spectrum at 303 K ($CDCl_3$; 220 MHz) showed a singlet for the methyl protons at τ 9·0, a multiplet at 7·35 (8a-H), and a rather narrow multiplet at 7·55 (2*eq*- and 2*ax*-H). The remaining protons gave a complex envelope of overlapping signals at τ 8—9. The signal for 8a-H was a doublet (separation *ca.* 9·0 Hz), each portion being a triplet (separations *ca.* 3·5 Hz). This pattern is consistent with a preponderance of type 1 conformation (1; R = CD_2Me) in a mixture of (1) and (2). Approximate proportions of (1; R = CD_2Me) and (2; R = CD_2Me) were deduced from the ^1H spectrum recorded at 210 K, where relatively slow exchange occurred. The spectrum was complex but two methyl singlets, of relative areas 4·0 : 1, were seen at τ 8·92 and 9·11 respectively. It was concluded that the mixture consisted of *ca.* 80% (1; R = CD_2Me) and 20% (2; R = CD_2Me) at 210 K. Firm supporting evidence came from the noise-decoupled carbon-13 spectrum; this showed only 10 lines at 328 K, because of the relatively long spin-lattice relaxation time of the deuteriated carbon, which in any case is expected to form a quintet owing to [12] C–D coupling. At 218 K, nineteen of the expected twenty signals for (1; R = CD_2Me) and (2; R = CD_2Me) were clearly seen, comprising ten relatively strong signals, and nine relatively weak signals. A comparison of the integrals of signals due to structurally identical carbon atoms gave the relative proportions of conformations as 86 : 14. Lines were assigned to individual carbon atoms by off-resonance experiments and by assuming that shifts would be little different from those in the conformations of the corresponding 1-methyl-*cis*-decahydroquinoline. In addition, spectra were recorded at intermediate temperatures, where differential line-broadening could be noted. Comparison of these spectra with the spectra at fast and slow exchange limits allowed a correlation of major and minor signals for each carbon nucleus. Comparison of the shifts (Table 2) with those of the 1-methyl derivative showed conclusively that the major component (86%) was conformation (1; R = CD_2Me), the minor component (14%) being conformation (2; R = CD_2Me). Of particular diagnostic value are the chemical shifts of C-8 in the two conformations. Thus the position of conformational equilibrium has been altered dramatically by the replacement of (N)Me by (N)CH_2Me.

The ^1H and ^{13}C chemical shifts of 1-(βββ-trifluoroethyl)-*trans*-decahydroquinoline (5; R = CH_2CF_3) are listed in Tables 1 and 2 respectively. The ^{19}F spectrum showed a simple 1 : 2 : 1 triplet, the coupling constant of 10·2 Hz being the interaction of the equivalent fluorine nuclei with the vicinal hydrogen nuclei. The ^1H spectrum of the corresponding *cis*-molecule (1 ⇌ 2; R = CH_2CF_3) at 220 MHz ($CDCl_3$) was complex and gave no stereochemical information because the signals due to 2*eq*-, 2*ax*-, and 8a-H overlapped within a three proton multiplet at τ 7·15—7·41. A lowering of temperature only served to increase the complexity of the spectrum. The tetradeuterio-derivative (6) ⇌ (7) was therefore prepared; the synthesis involved treatment of 2,2-dideuterio-*cis*-decahydroquiniline with trifluoroacetic anhydride, followed by reduction with $LiAlD_4$. The ^1H spectrum of (6) ⇌ (7) gave the usual uninterpretable envelope (13 protons) at high field (τ 8—9), but the signal of the angular 8a-H was now clearly exposed at low field. This signal was a doublet (separation 9·3 Hz), each part being a triplet (separation 3·5 Hz), a coupling pattern consistent with a preponderance of (6) in a mixture of (6) and (7). This conclusion gained support from a variable temperature study of the carbon-13 spectrum of (1 ⇌ 2; R = CH_2CF_3). At 208 K, this spectrum showed clearly 17 of the 22 signals expected for a mixture of (1) and (2) at the slow exchange limit. Ten of the signals belonged to the more abundant conformation, and the remaining seven resulted from a minor conformation, the relative proportions being given by integration as 84 and 16% respectively. The line assignments given in Table 2 depend on the observed multiplicities in an off-resonance spectrum, and on a comparison of chemical shifts with those in the conformations of 1-methyl-*cis*-decahydroquinoline. The assignments for C-2 and $NCH_2(CF_3)$ were confirmed when the noise-decoupled ^{13}C spectrum of the tetradeuterio-derivative (6) ⇌ (7)

[12] K. Kametani and H. Nemoto, *Chem. and Pharm. Bull.* (*Japan*), 1968, **16**, 1696.

at room temperature gave signals at 55 and 49·5 p.p.m. which were multiplets, owing to spin–spin coupling of the ^{13}C with D. The analysis confirms the conclusion, based on the ^{1}H spectrum, that 1-(βββ-trifluoroethyl)-*cis*-decahydroquinoline at 208 K consists of 84% conformation (1; R = CH_2CF_3) (type 1) and 16% conformation (2; R = CH_2CF_3) (type 2). A more accurate assessment of the composition came from the low temperature ^{19}F spectrum, which at 213 K gave two well shifted triplets, the proportions being 83% (1; R = CH_2CF_3) and 17% (2; R = CH_2CF_3).

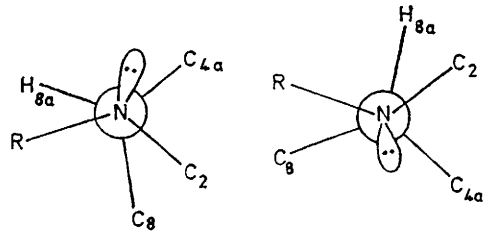
The next stage in the investigation involved a careful determination of the activation energy E_a for the rate process responsible for the spectral changes of (1 ⇌ 2; R = CH_2CF_3) at various temperatures. The ^{19}F spectrum of (1) ⇌ (2) was ideal for this purpose, since the fast exchange limit showed a 1 : 2 : 1 triplet, whilst the slow exchange limit showed two 1 : 2 : 1 triplets which were well separated. Full details of the determination appear in the Experimental section. The presence in the *cis*-amine of *ca.* 6% of the related *trans*-compound (5; R = CH_2CF_3) was put to good use in the accurate determination of the temperature of the sample, and in the assessment of the values of the spin–lattice relaxation time T_2 required in the line-shape analysis. The 1 : 2 : 1 triplet observed for the *trans*-amine was unaltered as the temperature was varied between 200 and 330 K, although its shift relative to that of $CFCl_3$ moved in a linear manner with temperature change. The activation energies E_a of 68·1 (1 → 2; R = CH_2CF_3) and 63·6 kJ mol^{-1} (2 → 1; R = CH_2CF_3) are similar to those which have been reported for the ring inversion process in derivatives of *cis*-decalin.[6] This evidence gives strong support to our contention that the exchanges observed in this investigation are ring inversion processes.

TABLE 3

Position of conformational equilibrium in 1-alkyl-*cis*-decahydroquinolines (1) ⇌ (2) and associated free energy differences ΔG

R	T/K	%(1)	%(2)	ΔG/kJ mol^{-1} (1) → (2)
H	199	6·5	93·5	−4·4
Me	223	30	70	−1·6
$MeCD_2$	218	86	14	+3·3
CF_3CH_2	213	83	17	+2·8

The best values for the position of equilibrium in those 1-alkyl-*cis*-decahydroquinolines studied in this work are summarised in Table 3, which also gives the corresponding free energy differences ΔG. The clear preference for conformation (2), which is the case when R = H, gives way to an increasing preference for conformation (1), as the size of the 1-alkyl group is increased. This trend can be explained in a qualitative way by recalling that the C–N bond length (1·47 Å) is rather shorter than the C–C bond length (1·54 Å), leading to a greater puckering in a piperidine ring than in a cyclohexane ring. The puckering is expected to be most significant around the nitrogen atom, and a puckering equivalent to an alteration in dihedral angles of 5° is expected to have a marked effect on attractive and repulsive interactions. Thus, the Newman projections, for a view along the N–C(8a) bond, are shown



in (8) and (9) for conformations (1) and (2) respectively. With R = H or Me, the dominant repulsive interaction is evidently that between C-2 and C-8, leading to a preference for (9), *i.e.* type (3) conformation. As R increases in size, the repulsive interaction between R and C-8 becomes dominant, leading to a preference for (8), *i.e.* type (1) conformation, as observed for R = $MeCD_2$ and CF_3CH_2.

Finally, spectral data for protons in the 1-acyl-*cis*- and -*trans*-decahydroquinolines, prepared during this work, are summarised in Table 4. At room temperature or above, the 1-acyl-*trans*-decahydroquinolines gave ^{1}H chemical shifts corresponding to an average of those for

TABLE 4

Spectral data for protons in 1-acyldecahydroquinolines (220 MHz; $CDCl_3$)

Isomer	Substituent	T/K	Chemical shifts (τ) 2*eq*-H	2*ax*-H	8a-H	8*eq*-H	Me
trans	COMe	307	6·31	6·84	6·72	7·92	7·94
trans	$COCF_3$	286	6·40	6·65	6·65	7·86	
cis	COMe	308	5·49, 6·43	7·42, 6·90	6·28, 5·35		7·91, 7·94
cis	$COCF_3$	308	5·64, 6·26	7·18, 6·86	6·11, 5·49		

Isomer	Substituent	Approximate coupling constants (Hz) J_{2eq2ax}	J_{2ax3eq}	J_{2ax3ax}	J_{8a8ax}	J_{8eq4ax}	J_{8eq8ax}
trans	COMe	13·5	5		11 [a]	11 [a]	
trans	$COCF_3$	13·5					10
cis	COMe	13·5		13·5	12		
cis	$COCF_3$	13·5		13·5	12		

[a] Mean of J_{8a8ax} and J_{8a4ax}.

the rotational isomers considered with respect to rotation about the N–C(=O) linkage. The clearly observed signals assigned to 2*eq*-, 2*ax*-, 8*eq*-, and 8a-H underwent broadening when the temperature was lowered. As in previous work,[2] 8*eq*-H in both the acetyl and trifluoroacetyl derivatives is deshielded by the acyl function and the signal is clearly exposed at relatively low field. The ^{1}H spectra of the *cis*-amines showed *two* sets of signals for each of 2*eq*-, 2*ax*-, and 8a-H, corresponding to different but equally populated conformations with respect to rotation about the N–C(=O) bond. In line with earlier results,[2] both these conformations preferred the twin-chair conformation (1) to the twin-chair conformation (2), as in both cases the angular 8a-H signal was a doublet in character, with a splitting of *ca.* 12 Hz.

EXPERIMENTAL

M.p.s were measured on a Kofler block. ^{1}H and ^{19}F n.m.r. spectra were determined using a Varian HA-100 spectrometer fitted with an extended locking facility. For ^{1}H spectra the lock was Me_4Si, for ^{19}F spectra $CFCl_3$. Some spectra were measured on the S.R.C. Varian HR-220 spectrometer both at Runcorn and, later, at Harwell. ^{13}C Spectra were measured at 25·15 MHz in the pulsed mode on a JEOL PS-100 spectrometer interfaced to a Nicolet 20 K 20-bit 1085 computer. Free induction decays were accumulated over 2500 or 3000 Hz using a pulse width of 3 μs (25° tip) and were sampled using 8 K data points.

For preparative g.l.c. Varian Aerograph series 712, and Varian Aerograph Autoprep (model A-700) instruments were used. For analytical g.l.c. a Pye series 104 instrument was employed.

1-*Methyl*-trans-*decahydroquinoline*.— *trans*-Decahydroquinoline (3·4 g) was converted into 1-methyl-*trans*-decahydroquinoline (3·0 g, 81%) by the usual Eschweiler–Clarke procedure. The picrate had m.p. 172·5—173° (lit.,[13] 173°).

1-*Methyl*-cis-*decahydroquinoline*.—A similar method converted *cis*-decahydroquinoline [2] (3·0 g) into 1-methyl-*cis*-decahydroquinoline (2·6 g, 79%). The picrate had m.p. 198—199° (lit.,[13] 199—200°).

1-*Ethyl*-trans-*decahydroquinoline*.—A mixture of *trans*-decahydroquinoline (2·8 g), acetic anhydride (20 ml), and acetic acid (20 ml) was heated under reflux for 6 h. The mixture was poured into water (200 ml), basified with sodium carbonate solution, and extracted several times with ether. The combined extracts were washed successively with hydrochloric acid (10%) and water, before being dried ($CaSO_4$). Filtration and distillation gave 1-acetyl-*trans*-decahydroquinoline (2·0 g, 55%), b.p. 76° at 0·05 mmHg. The product (1·4 g), in dry ether (20 ml) was added to a slurry of lithium aluminium hydride (0·5 g) in dry ether (30 ml). The mixture was heated under reflux for 4 days, decomposed with wet ether, and then sodium hydroxide solution (30 ml; 10%). The ethereal layer, after drying ($CaSO_4$), gave 1-*ethyl*-trans-*decahydroquinoline* (1·1 g, 85%), b.p. 228° at 760 mmHg. The *picrate* had m.p. 112—113° (from ethanol) (Found: C, 51·2; H, 6·4; N, 14·1. $C_{17}H_{24}N_4O_7$ requires C, 51·5; H, 6·1; N, 14·1%).

1-(αα-*Dideuterioethyl*)-cis-*decahydroquinoline*.— *cis*-Decahydroquinoline (2·8 g) was converted in the way described above into 1-acetyl-*cis*-decahydroquinoline (1·25 g, 48%), b.p. 79° at 0·08 mmHg. Reduction of this amine (300 mg) with lithium aluminium deuteride, as described above, gave 1-(αα-*dideuterioethyl*)-cis-*decahydroquinoline* (200 mg, 72%), b.p. 229·5° at 761 mmHg (Found: M^+, 169·180. $C_{11}H_{19}D_2N$ requires M, 169·180). The derived *picrate* had m.p. 147·5—148·5° (from ethanol) (Found: C, 51·0; H, 6·3; N, 13·8. $C_{17}H_{22}D_2N_4O_7$ requires C, 51·4; H, 6·3; N, 14·1%).

1-(βββ-*Trifluoroethyl*)-trans-*decahydroquinoline*.— A solution of *trans*-decahydroquinoline (3·5 g) in dry ether (15 ml) was mixed with trifluoroacetic anhydride (10 ml) in dry ether (15 ml) at 0°. The mixture was allowed to warm to room temperature and remain at this temperature during 12 h. Evaporation, followed by several distillations with carbon tetrachloride, allowed removal of both ether and unused anhydride, which codistils with carbon tetrachloride. Distillation of the residue gave 1-trifluoroacetyl-*trans*-decahydroquinoline (5·7 g, 97%), b.p. 64° at 0·02 mmHg, 261° at 760 mmHg (Found: M^+, 235·119. Calc. for $C_{11}H_{16}F_3NO$: M, 235·118). The amide (3 g), in dry ether (30 ml) was reduced by lithium aluminium hydride (0·5 g) in dry ether (30 ml) during 10 days of heating under reflux. The usual work-up gave approximately equal quantities of *trans*-decahydroquinoline and the 1-trifluoroethyl derivative. Preparative separation on a 35 ft × ¼ in column of Carbowax 20M (20%) on alkali-washed Chromosorb W gave 1-(βββ-*trifluoroethyl*)-trans-*decahydroquinoline* as a liquid (Found: M^+, 221·138. $C_{11}H_{18}F_3N$ requires M, 222·137). The derived *picrate* had m.p. 136—137° (from ethanol) (Found: C, 45·0; H, 4·6; N, 12·2. $C_{17}H_{21}F_3N_4O_7$ requires C, 45·3; H, 4·7; N, 12·4%).

1-(βββ-*Trifluoroethyl*)-cis-*decahydroquinoline*.— The method described above was followed in order to convert *cis*-decahydroquinoline (3·5 g) into 1-trifluoroacetyl-*cis*-decahydroquinoline (5·5 g, 82%), b.p. 243° (Found: M^+, 235·118. Calc. for $C_{11}H_{16}F_3NO$: M, 235·118). Reduction of the amide with lithium aluminium hydride in ether gave a liquid thought to be a mixture of *cis*-decahydroquinoline and the 1-trifluoroethyl derivative, although g.l.c. failed to produce a separation. The mixture (1 g) in dry ether (5 ml) was added to trifluoroacetic anhydride (3 ml) in dry ether (5 ml) at 0°. The solution was kept at room temperature for 3 h before the excess of anhydride was removed at 25° and 15 mmHg. The residue was dissolved in ether and extracted several times with hydrochloric acid (10%). The acid extracts were combined, washed with water, and basified with sodium hydroxide solution (30%). The liberated amine was recovered by extraction into ether. Evaporation of the dried ether extracts gave 1-(βββ-*trifluoroethyl*)-cis-*decahydroquinoline*. The derived *picrate* had m.p. 148—149·5° (Found: C, 45·2; H, 4·6; N, 12·3. $C_{17}H_{21}F_3N_4O_7$ requires C, 45·3; H, 4·7; N, 12·4%).

cis- *and* trans-2,2-*Dideuterio*-1-(αα-*dideuterio*-βββ-*trifluoroethyl*)*decahydroquinoline*.—3,4-Dihydroquinolin-2(1*H*)-one (8·0 g) [13] was reduced with lithium aluminium deuteride (2·5 g) in ether (300 ml), the deuteride being contained in a Soxhlet thimble and continuously extracted during 5 days. The usual method of treatment gave 2,2-dideuterio-1,2,3,4-tetrahydroquinoline (5·7 g, 78%) (Found: M^+, 135·101. Calc. for $C_9H_9D_2N$: M, 135·101). The 100 MHz ^{1}H n.m.r. spectrum ($CDCl_3$) showed τ 2·9—3·6 (4H,

[13] M. Ehrenstein and W. Bunge, *Ber.*, 1934, **67**, 1715.

m, aromatic), 6·30br (s, NH), and 7·17—8·20 (4H, m, AA^1BB^1 aliphatic). The amine (4 g) in concentrated hydrochloric acid (30 ml) was hydrogenated at room temperature and 70 atm in a stainless steel bomb having a glass liner, the catalyst being platinum black (500 mg). After 4 days, the solution was filtered, basified with aqueous sodium hydroxide (40%), and extracted several times with ether. The combined extracts were dried and distilled; a mixture of *cis*- and *trans*-2,2-dideuteriodecahydroquinoline (3·1 g) was obtained, b.p. 27° at 0·03 mmHg. The product was cooled to 0° for 12 h, and a quantity of the crystalline *trans*-amine was removed by filtration. The residue (2·6 g) contained approximately 65% *cis*-2,2-dideuteriodecahydroquinoline (analysis by ^{13}C n.m.r. spectroscopy) (Found: M^+, 141·147. Calc. for $C_9H_{15}D_2N$: M, 141·148). The low-field portion of the ^1H n.m.r. spectrum (100 MHz; $CDCl_3$) showed only a singlet ($W_{1/2}$ 10 Hz) for 8a-H. Reaction of the amine (2·15 g) with trifluoroacetic anhydride, as described earlier, gave *cis*- and *trans*-1-trifluoroacetyl-2,2-dideuteriodecahydroquinoline (2·9 g, 81%) as a liquid, b.p. 61° at 0·03 mmHg (Found: M^+, 237·130. Calc. for $C_{11}H_{14}D_2F_3NO$: M, 237·130).

(a) *Temperature.* The design of the HA-100 variable temperature probe imposes limitations on the accuracy with which the temperature of the sample can be accurately determined. Initially, 17 temperature readings (between 213 and 323 K) of the variable temperature accessory were calibrated against thermocouple readings, a chromel–alumel thermocouple being immersed in chloroform in a stationary n.m.r. tube in the probe. Next, the ^{19}F chemical shifts of the fluorine in the conformationally rigid *trans*-amine (the impurity) were measured at temperatures corresponding to those used in the initial calibration. A plot of the ^{19}F shifts against temperature was practically linear, and the best straight line was drawn. A strict linearity was then assumed, so that the easily measured ^{19}F shift of the fluorine in the *trans*-amine impurity was used to determine the temperature of a sample of the *cis*-amine.

(b) *Chemical shifts* (ν_1 *and* ν_2). These are the ^{19}F shifts of the fluorine in the two conformations (1; R = CH_2CF_3) and (2; R = CH_2CF_3) at the slow exchange limit. The use of these parameters was complicated by the marked temperature dependence of the shifts [15] in the region of direct observation of both conformations (200—260 K). When the observed shifts were calculated relative to the shift of the *trans*-amine impurity, and then plotted against temperature, the result was a straight line for the major conformation and a smooth curve for the minor. The ^{19}F shifts for each conformation at higher temperatures (260—320 K) were then obtained by extrapolation.

(c) p_1 *and* p_2. These are the fractional populations of the conformations (1) and (2) respectively at a given temperature. At low temperatures, where the signals of both conformations were visible, p_1 and p_2 were obtained directly, and the values obtained by integration and planimetry were averaged. At higher temperatures, where a single resonance was seen, p_1 and p_2 were calculated from

TABLE 5

Data at 94 MHz from the line-shape analysis of the ^{19}F spectrum of 1-(βββ-trifluoroethyl)-*cis*-decahydroquinoline (1 ⇌ 2; R = CH_2CF_3)

T/K	$10^4T^{-1}/K^{-1}$	Fractional population of (1)/p_1	Shift difference $(\nu_1 - \nu_2)$/Hz	10^4 Exchange parameter τ/s	$\ln k_{2\rightarrow1}$
246·7	40·54	0·7646	485	150·00	3·93
245·5	40·08	0·7599	483	80·00	4·55
259·1	38·60	0·7446	478	40·00	5·22
262·0	38·18	0·7401	477	25·00	5·69
263·3	37·98	0·7395	476	20·00	5·91
268·8	37·20	0·7299	473	15·00	6·18
270·2	37·01	0·7278	472	12·00	6·40
271·5	36·82	0·7262	471	8·00	6·81
278·5	35·91	0·7163	468	3·00	7·77
278·5 *	35·91	0·7163	468	2·00	8·18
282·6	35·39	0·7103	465	3·00	7·76
286·8	34·87	0·7042	463	2·50	7·94
293·7	34·05	0·6955	459	1·30	8·58
293·7 *	34·05	0·6955	459	1·30	8·58
302·2	33·11	0·6844	455	0·45	9·62
303·4	32·96	0·6826	454	0·40	9·74
303·4 *	32·96	0·6826	454	0·50	9·52
307·5	32·52	0·6776	452	0·35	9·87
307·5 *	32·52	0·6776	452	0·20	10·43
311·7	32·08	0·6721	450	0·13	10·85

* Duplicated measurements.

Reduction of the amide (2·8 g) with lithium aluminium deuteride, as described earlier, gave *cis*- and *trans*-2,2-dideuterio-1-(αα-dideuterio-βββ-trifluoroethyl)decahydroquinoline as a liquid (1·3 g, 49%) (Found: M^+, 225·164. Calc. for $C_{11}H_{14}D_4F_3N$: M, 225·163).

Line-shape Analysis of the ^{19}F *Spectrum of* 1-(βββ-*Trifluoroethyl*)-cis-*decahydroquinoline.*—The sample contained as impurity *ca.* 5% of the *trans*-amine. The mixture was dissolved in $CDCl_3$ in an n.m.r. sample tube, $CFCl_3$ was added for 'locking' purposes, and the tube was sealed after expulsion of air with a stream of nitrogen.

The computer program described by Binsch [14] was modified to make it compatible with the available computer, an English Electric KDF9. The program was also modified to take into account the presence of the vicinal H–F coupling. The following parameters were required for the line-shape analysis.

[14] G. Binsch, *Topics Stereochem.*, 1968, **3**, 97.

[15] *Cf.* L. D. Hall and D. L. Jones, *Canad. J. Chem.*, 1973, **51**, 2914.

ν_1, ν_2, and the observed averaged chemical shift. A plot of $-\ln p_1/p_2$ against T^{-1} gave a straight line, from which p_1 and p_2 could be obtained at any required temperature. This plot gave the enthalpy difference (ΔH) for the two conformations as 4·5 kJ mol^{-1} and the entropy difference (ΔS) as 8·45 J K^{-1} mol^{-1}.

(d) $T_2(1)$ *and* $T_2(2)$. These are the spin–spin relaxation times for the ^{19}F nuclei in the two conformations, and they include both spin exchange and effects due to inhomogeneities in H_0, the magnetic field. The values used were 0·1 s in each case, obtained from expression (1) where $W_{1/2}$

$$T_2(1) = T_2(2) = (\Pi W_{1/2})^{-1} \quad (1)$$

is the half-intensity width of the ^{19}F signal of the *trans*-amine impurity. In practice, variation in T_2 by a factor of 10 caused little change in the simulated spectra, provided that only those spectra were used in which the vicinal H–F coupling had been washed out by exchange broadening.

(e) *Exchange parameter* τ. This parameter is related to the rate constants $k_{1\rightarrow2}$ and $k_{2\rightarrow1}$ by expressions (2)—(4).

$$\tau = \tau_1 p_2 = \tau_2 p_1 \quad (2)$$

$$k_{1\rightarrow2} = \tau_1^{-1} \quad (3)$$

$$k_{2\rightarrow1} = \tau_2^{-1} \quad (4)$$

In the line-shape analysis, the exchange parameter τ was varied until, for each temperature, there was a complete match between the observed spectrum and the computer-simulated spectrum. The relevant data are given in Table 5.

The Arrhenius plot of $\ln k_{2\rightarrow1}$ against reciprocal temperature gave a straight line, from which was obtained 63·6 kJ mol^{-1} for E_a for the conversion (2 ⟶ 1; R = CH_2CF_3). The corresponding E_a for (1 ⟶ 2; R = CH_2CF_3) is 68·1 kJ mol^{-1}.

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