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PREFERENCE FOR A CONFORMATION WITH AXIAL *t*-BUTYL GROUP : 8β-*t*-BUTYL-*cis*-DECAHYDROQUINOLINE

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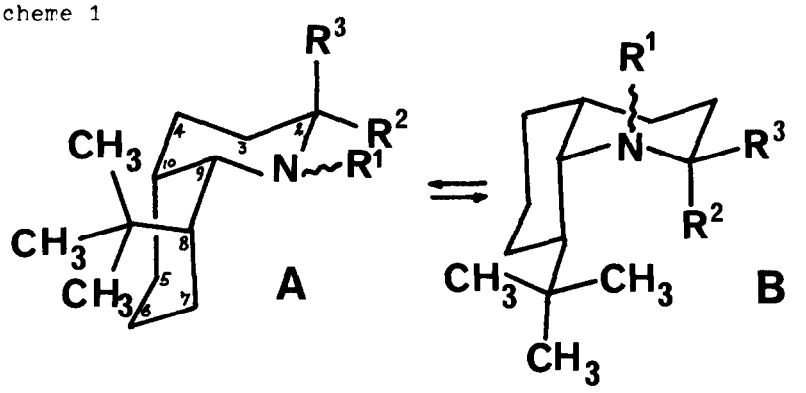
Summary: At -75°C only the signals of the conformation with axial *t*-butyl group are detected in the ^{13}C-NMR spectrum of 8β-*t*-butyl-*cis*-decahydroquinoline. Of the N-methyl derivative 62% exist in the analogous form at -80°C.

Axially *t*-butyl substituted cyclohexane rings are hardly ever observed if the molecule has the chance to avoid the resulting strain by adopting different conformations. A single crystal refraction analysis of a cyclohexylidene derivative with such a group has been reported.[1] The predominant conformation of *trans* 1,2-di-*t*-butylcyclohexane has been calculated to be the diaxially substituted one.[2] Recently, the X-ray structure of 1-phenyl-*cis*-4-*t*-butyl-*r*-cyclohexylpiperidine hydrochloride has shown it to occupy the *t*-butyl-axial conformation in the crystal, but the *t*-butyl is equatorial in solution.[3] In the *trans*-decahydroquinoline system, where ring inversion cannot take place, NMR-data and X-ray analysis for an axial *t*-butyl group have been reported in 8β-*t*-butyl-*trans*-decahydroquinoline.[4]

The corresponding *cis*-compound, 8β-*t*-butyl-*cis*-decahydroquinoline (1) can exist in two double chair conformations, A and B (see Scheme 1). In unsubstituted *cis*-decahydroquinoline, A has been found[5] to be more stable by 3.8 to 4.4 kJ mol^{-1}. In *t*-butylcyclohexane, the preference of the *t*-butyl group for the equatorial position has been calculated[2] to be ~20 kJ mol^{-1}. Compound 1 might thus be expected to exist largely in conformation B, with the trans gauche interaction between $C(CH_3)_3$ and N the determining factor.

The ^{13}C-NMR data of 1 at +27°C and at -75°C are listed in Table 1. Only one set of 11 signals is seen at low temperature, indicating that no second conformation is present to >3% (ring inversion of the *cis*-decahydroquinoline system is frozen at that temperature[5]; cf. also 1m). The calculated chemical shifts of conformations 1A and 1B are also reported. These values were obtained by correcting the low temperature ^{13}C shift data[6] of compounds 2 (as model for 1A) and 3 (as model for 1B) for the shift effects of an equatorial methyl group at C-2 (α_e: +5.04 ppm; β_e: +7.69 ppm;[7] other effects were neglected). A comparison of the -75°C shift values of 1 with 2 and 3 show that the signals must belong to 1A, with axial *t*-butyl group, and not to 1B. While the assignments of a number of signals might be exchanged, carbon atoms C-2, C-8 and C-10 could be assigned

Scheme 1



	R^1	R^2	R^3	A : B	°C	ΔG° (kJ mol^{-1})
1	H	H	H	>97 : <3	-75	<-5.7
1m	CH_3	H	H	62 : 38	-80	-0.8
2	H	CH_3	H	>99 : <1	-70	<-7.8
3	H	H	CH_3	<2 : >98	-65	>+6.7

unambiguously because of their position and their appearance in the off-resonance decoupled spectrum. Each of these signals allows definitely to exclude conformation 1B.

Additional evidence comes from the ^{1}H-NMR spectrum. The signals of the protons at C-2 appear at nearly the same position as in *cis*-decahydroquinoline and show the same coupling pattern (R^2 = H: 2.98 ppm; d, 12, of m; R^3 = H: 2.64 ppm; d, 12, of d, 10, of d, 3). The hydrogen atom at C-9 (at 2.75 ppm) shows a narrow signal (apparent triplet, J = 3.2) due to the small gauche couplings with the protons at C-8 and C-10, whereas in conformation B a large (anti) coupling must lead to a broad resonance. The coupling behaviour of these protons is also indication for largely undisturbed chair conformations of the two rings : any major deformation should lead to an increased coupling for H-9.

The reason for the preference for 1A must be seen in a severe interaction between the *t*-butyl group and the nitrogen in conformation B. Assuming undisturbed geometry of the *cis*-decahydroquinoline ring system, this interaction must amount to >22 kJ mol^{-1} to offset the calculated preference for 1B (20 - 4 kJ mol^{-1}) and explain the observed result (see Scheme 1).

The room temperature ^{13}C-NMR spectrum of the N-methyl derivative of 1 (1m) shows only seven sharp signals. If the probe temperature is raised to +60°C, resonances for all twelve different carbon atoms are observed, with three of them still broadened. At -75°C signals for both conformations 1mA and 1mB are detected; integration of the areas of matching peaks gives a ratio of 62 ± 2 %

Table 1. ^{13}C-NMR Chemical Shifts [a]

C-Atom	1 (A⇌P) [b]	1A [c]	1A calc [d]	1B calc [e]	1m (A⇌P) [f]	1mA [g]	1mB [g]
2	46.5_9	47.9_7	48.0_8	38.2_6	51.3 [h]	59.3_0	46.1_5
3	22.9_1	21.2_5	21.3_3	26.7_3	20.9_{1_i}	21.0_0	19.9_5
4	29.3_0	29.5_6	29.7_7	24.9_2	29.2_7 [i]	29.8_6	26.1_7
5	24.4_8	22.0_0	23.2_4	31.4_2	28.3_1	24.4_8	32.1_7
6	21.6_1	20.7_4	21.8_3	20.8_4	21.8_{2_i}	21.2_3	21.4_6
7	22.5_5	20.9_9	20.4_6	27.3_0	25.8 [i]	21.7_8	28.2_7
8	50.2_3	52.0_1	51.2_4	39.6_7	42.2_0	42.2_4	40.2_9
9	57.2_1	56.6_7	56.4_3	57.3_1	64.6_0	64.9_9	63.2_7
10	32.3_9	30.5_0	30.0_0	37.0_5	30.3_8	31.1_4	27.9_4
quart.	33.4_6	33.4_0	33.6_4	32.6_1	33.7_0	33.4_6	33.3_8
CH_3	28.5_7	28.3_0	28.5_1	28.6_4	29.2_2	29.4_1	28.6_7

[a] In ppm; solvent $CDCl_3$ + 2% Me_4Si at the temperatures indicated. Recorded at 62.89 MHz. [b] ± t +27°C. [c] At -75°C. [d] From 2 at -70°C. [e] From 3 at -65°C. [f] At +60°C because signals were too broad at ambient temperature. [g] At -80°C. [h] Signal still very broad. [i] Signal still broad.

1mA, 38 ± 2 % 1mB. In the ^{1}H-NMR spectrum, the single resonance for N-CH_3 at +60°C (2.37 ppm) is split into two singlets at -75°C for the axial methyl of 1mB (2.49 ppm) and the equatorial one of 1mA (2.28 ppm). The peaks are superimposed on other resonances, but the ratio is ≈3 : 7. That 1mA is the major conformer is clear from the resonances of C-2 in the low temperature ^{13}C-spectrum, and from the chemical shift (3.01 ppm) and coupling (d, 10, of m) of the equatorial proton at C-2 (R^2 = H) in 1mA.

It is surprising that the equilibrium in 1m is less in favor of conformation A compared to 1. The conformational equilibrium at nitrogen in N-methylpiperidine has been determined 10 kJ mol^{-1} (in $CHCl_3$) in favor of the methyl-equatorial conformer.[8] Since the methyl group on nitrogen in 1mB is forced into an axial position to avoid the more serious interaction with the *t*-butyl, the equilibrium for 1m might have been expected to be more on the side of conformation A than in 1, as was the case in the analogous 8β-methyl compounds.[5a,9] The result can be rationalized by assuming some deformation of the cyclohexane ring in 1mA due to an outward bending of the *t*-butyl group.[5b] This could increase the interaction between C-8 and the N-methyl group (which cannot be avoided except by the methyl becoming syn-axial to C-5 and C-7), thus destabilizing 1mA. Alternatively (but less likely), the deformations caused by the equatorial *t*-butyl in 1mB might cause the N-methyl-axial interaction to be smaller than in N-methylpiperidine. To get evidence for either argument, attempts will be made to obtain X-ray analyses of the picrates of 1 - 3 and 1m - 3m.

Compounds investigated : 1 was obtained by equilibration of N-nitroso-8β-*t*-butyl-*trans*-decahydroquinoline[10] with potassium-*t*-butoxide in DMSO at +90°C to give N-nitroso-8β-*t*-butyl-*cis*-decahydroquinoline (mp 77-79°C), which was denitrosated by bubbling dry hydrogen chloride through the solution in anhydrous benzene boiling to reflux. Mp of picrate 171-173°C. Methylation with HCHO / HCOOH gave 1m; mp of picrate 162-163°C. Compounds 2 and 3 have been reported.[11]

Variable temperature NMR spectra were recorded on a Bruker WM 250 spectrometer, purchased under grant Nr. 4009 of the F.z.F.d.w.F.

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