Conformational Analysis. 33.[1] Carbon-13 Nuclear Magnetic Resonance Spectra of Saturated Heterocycles. 5.[2] *cis*-Decahydroquinolines

Friedrich W. Vierhapper and Ernest L. Eliel*

William Rand Kenan, Jr., Laboratories of the University of North Carolina, Chapel Hill, North Carolina 27514

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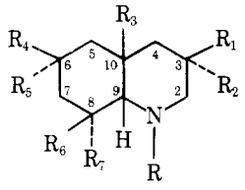
The ^{13}C NMR spectra of *cis*-decahydroquinoline, its two epimeric 3-, 6-, and 8-methyl, as well as its 10-methyl, 3α,10-, 3β,10-, and 8α,10-dimethyl homologues and the corresponding *N*-methyl compounds were recorded. Configurational and conformational assignments have been made on the basis of ^{13}C and ^{1}H NMR spectra. The parent, 10-methyl, 6β-methyl, and 8β-methyl compounds are conformationally heterogeneous; conformational equilibria were determined by low-temperature ^{13}C NMR spectroscopy. Signals in the ^{13}C spectra were assigned on the basis of those of the parent compounds[3a-c] with the help of parameters previously established[2] in the *trans*-decahydroquinoline series. The previously reported[2] upfield shift due, formally, to an antiperiplanar lone pair on nitrogen bearing alkyl [*anti*-:N(Me)-C–C] as well as the downfield shift caused by steric compression of syn-axial methyl groups were confirmed. Groups to which syn-axial substituents are attached are also shifted downfield. Shift parameters of the type introduced by Grant and co-workers[2,4,5] are tabulated for the *cis*-decahydroquinoline series. The ^{13}C spectra of $\Delta^{1,9}$-octahydroquinoline and several of its methyl homologues have been recorded. Conformational equilibria in variously substituted *cis*-decahydroquinolines are discussed.

In a previous paper[2] we have discussed the ^{13}C NMR spectra of a number of methyl-substituted *trans*-decahydroquinolines. Here we report the spectra of 11 *cis*-decahydroquinolines, **1–11** (R = H), and of the corresponding *N*-methyl homologues **1m–11m** (R = CH_3). The spectra of the parent compounds **1** and **1m** have already been published by Booth and Griffiths[3] and are included for completeness only; the remaining spectra are new.[3d]



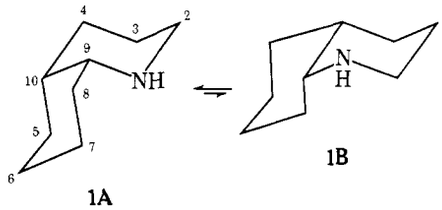
1–11, R = H
1m–11m, R = CH_3

1, R_1–R_7 = H
2, R_1, R_2, R_4–R_7 = H; R_3 = CH_3 (10-CH_3)
3, R_1, R_3–R_7 = H; R_2 = CH_3 (3α-CH_3)
4, R_2–R_7 = H; R_1 = CH_3 (3β-CH_3)
5, R_1–R_4, R_6, R_7 = H; R_5 = CH_3 (6α-CH_3)
6, R_1–R_3, R_5–R_7 = H; R_4 = CH_3 (6β-CH_3)
7, R_1–R_6 = H; R_7 = CH_3 (8α-CH_3)
8, R_1–R_5, R_7 = H; R_6 = CH_3 (8β-CH_3)
9, R_1, R_2, R_4–R_6 = H; R_3 = R_7 = CH_3 (8α,10-di-CH_3)
10, R_1, R_4–R_7 = H; R_2 = R_3 = CH_3 (3α,10-di-CH_3)
11, R_2, R_4–R_7 = H; R_1 = R_3 = CH_3 (3β,10-di-CH_3)

In Table I are summarized all pertinent chemical shifts for compounds **1–11**, in Table II those for **1m–11m**. The spectra were first recorded at 30 °C but because a number of signals for the conformationally heterogeneous compounds **1, 2, 6,** and **8** and their *N*-methyl analogues **1m, 2m, 6m,** and **8m** were exchange-broadened at that temperature, their spectra were also recorded at 55 °C or (in the case of **1**) 65 °C. At these temperatures exchange was fast enough to lead to sharpening of all the signals. At low temperatures (−68 °C) the spectra of the eight conformationally heterogeneous compounds decoalesced into two sets of lines in each case (Tables I and II) which could be assigned to the two contributing conformations. The spectra of the other 14 compounds did not change appreciably upon cooling (except for a slight temperature dependence of the chemical shifts); these compounds are presumably conformationally homogeneous.

In the sequel we shall discuss the spectral assignments for each of the compounds studied, the salient features of the ^{13}C NMR spectra, and, for the conformationally heterogeneous compounds, the position of equilibrium and rationale therefor.

^{13}C Spectra. Except for closely coincident signals (shown in parentheses in Tables I and II to denote that they may have to be interchanged) assignments were made relatively easily by a combination of off-resonance decoupling, analogy with *cis*-decalins,[4] analogies with the *trans*-decahydroquinolines,[2] known[5] effects of methyl substituents in six-membered rings, and, above all, on the basis of the earlier assignment[3] of the parent compounds **1** and **1m** which was confirmed in the present study. Individual compounds will be discussed below; in all cases the carbons next to nitrogen (C-2, C-9, and, where pertinent, NCH_3) displayed signals at lowest field and were distinguished from each other by off-resonance decoupling. At next lowest field was usually found C-10, except in those cases where C-4 and C-5 were downfield shifted by the β_e effect[5] of an appropriately located equatorial methyl group; in all cases the assignment of C-10 was confirmed by off-resonance decoupling which also served to identify signals of *C*-methyl groups, if any.



1A **1B**

1mA, 1mB,
NCH_3 instead of NH

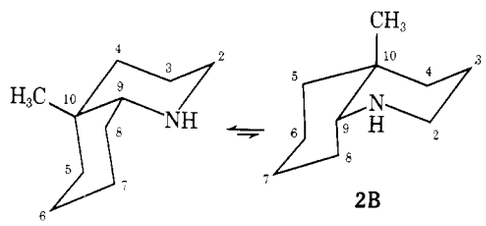
The spectral assignments for this conformer mixture have been made previously.[3a] Our signals agree with those reported, though only moderately well, deviations of 0.5 ppm being common, probably because of the broadness of the lines. At low temperature (Table I) two sets of sharp lines are seen whose shifts are in excellent agreement with those reported[3a,c] (generally within 0.1 ppm). The major set of low-temperature signals is assigned to conformer **1A**, which predominates in a ratio of 90:10 (lit.[3a] 93.5:6.5 at −74 °C). Similar arguments apply to **1m**, which has also been studied previously.[3b] In concordance with the earlier study[3b] we find a diminished percentage of **1mA** (71%, nearly identical with the percentage reported[3b] at −50 °C) compared to **1A**. With one or two exceptions, our signal positions both at 55 and −68 °C agree with

Table I. ^{13}C Chemical Shifts[a] for *cis*-Decahydroquinolines

Compd[b]	Temp[c]	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9[d]	C-10[d]	CH_3
Parent, **1**	30	46.58	22.73	29.82	26.57	25.56	21.64	31.87	55.03	35.85	
Parent, **1**	65	46.76	23.07	30.09	26.87	25.79	21.85	32.18	55.39	36.30	
Parent, **1A**[e]	−68	47.73	21.18	30.60	24.98	26.32	20.34	32.75	54.79	35.13	
Parent, **1B**[e]	−68	39.74	*f*	23.97	31.66	*f*	*f*	*f*	53.87	35.60	
10-CH_3, **2**	30	46.46	(23.10)	38.21	31.29	(21.87)	21.16	28.31	60.12	32.27	26.52
10-CH_3, **2**	55	46.69	(23.32)	38.50	31.62	(22.13)	21.36	28.66	60.48	32.50	26.63
10-CH_3, **2A**[g]	−68	47.25	(22.48)	39.19	28.94	(21.42)	19.93	28.01	59.66	31.99	26.22
10-CH_3, **2B**[g]	−68	*f*	*f*	*f*	40.26	*f*	25.90	*f*	58.58	32.36	27.30
3α-CH_3, **3(B)**	30	47.78	33.38	33.54	31.74	20.65	(26.09)	(25.88)	53.80	36.45	19.78
3β-CH_3, **4(A)**	30	55.53	26.59	40.07	26.15	26.59	20.66	32.63	54.69	36.05	19.65
6α-CH_3, **5(A)**	30	48.11	21.62	30.85	34.25	33.16	29.29	33.16	54.62	35.75	22.76
6β-CH_3, **6**	30	41.69	(26.44)	(26.44)	38.93	26.76	32.97	(26.13)	54.55	35.11	21.57
6β-CH_3, **6**	55	41.97	(26.58)	(26.72)	38.93	26.93	32.99	(26.34)	54.76	35.20	21.49
6β-CH_3, **6A**[h]	−68	47.50	20.92	(30.08)	(32.42)	*f*	(28.37)	*f*	54.79	(30.08)	17.90
6β-CH_3, **6B**[h]	−68	39.53	27.23	24.80	40.45	26.17	34.35	25.17	53.65	35.91	22.60
8α-CH_3, **7(A)**	30	48.17	22.05	31.14	24.80	26.52	28.48	36.65	60.44	37.22	18.65
8β-CH_3, **8**	30	43.31	25.10	27.81	29.47	21.16	31.49	30.65	61.17	34.10	18.37
8β-CH_3, **8**	55	43.50	25.20	28.00	29.54	21.24	31.55	30.95	61.39	34.28	18.38
8β-CH_3, **8A**[i]	−68	47.84	21.49	(30.38)	25.16	20.44	26.18	34.85	60.41	(30.08)	17.54
8β-CH_3, **8B**[i]	−68	38.98	26.75	24.77	32.05	21.04	34.53	26.63	60.64	35.65	18.85
8α,10-Dimethyl, **9(A)**	30	47.89	(22.86)	40.22	28.99	(22.08)	28.28	30.75	65.62	33.36	18.98 (8) 26.14 (10)
3α,10-Dimethyl, **10(B)**	30	47.55	28.27	38.16	40.74	21.72	(26.38)	(26.69)	58.87	33.50	19.98 (3) 28.39 (10)
3β,10-Dimethyl, **11(A)**	30	55.41	28.03	49.39	30.43	21.97	20.27	28.33	59.84	32.85	19.56 (3) 26.29 (10)

[a] In $CDCl_3$, from internal Me_4Si, ppm. Parentheses indicate that assignments are not unambiguous. [b] *cis*-Decahydroquinoline. For conformations A and B see formula schemes in text. "α" means "substituent is on the opposite side as the hydrogen at C-10," "β" means "on the same side of the ring as this hydrogen." [c] °C. Only when compounds were found to be conformationally inhomogeneous at room temperature, were low and high temperature ^{13}C NMR spectra recorded. [d] **9** and **10** are used rather than **8a** and **4a** to allow exclusive use of "a" for "axial." [e] 90% **1A**; 10% **1B**. [f] Not observed because either overlaid by a signal of the major component or too small to be discerned. [g] 94% **2A**; 6% **2B**. [h] 11% **6A**; 89% **6B**. [i] 41.5% **8A**; 58.5% **8B**.

those reported[3b] to within 0.2 ppm (average deviation 0.1 ppm).



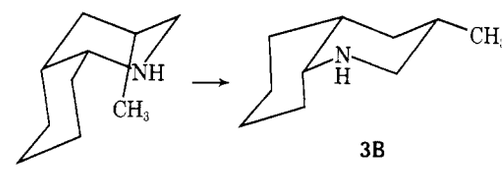
2A **2B**

2mA, 2mB,
NCH_3 instead of NH

Since compound **2**[3d] is conformationally heterogeneous, assignments in the low-temperature spectrum of **2A** are discussed first. Signals for C-2 and C-7 are essentially unchanged from the parent compound **1A.** C-4 is shifted nearly 9 ppm downfield by the β_e effect of the methyl substituent, C-5 is shifted 4 ppm downfield by a β_a effect. Signals for C-6 and C-8 are shifted upfield by the axial methyl group (steric shift) by 4.5–5 ppm. In the minor isomer **2B** only CH_3, C-5, C-7, C-9, and C-10 were seen. Integration indicates 94% of the major isomer and 6% of the minor. The room temperature spectrum can be assigned by its general similarity with that of the major conformer. The steric compression effect of the axial methyl group shifts from the cyclohexane ring (C-6, C-8) to the piperidine ring (C-3) as one passes from **2A** to **2B,** whereas that of the axial methylene and NH groups of the ring junctions passes from C-3, C-5, and C-7 to C-2, C-4, C-6, and C-8. The effects at C-3, C-6, and C-8 should roughly compensate each other, but C-4 and C-2 should move upfield in **2B** and therefore in the mixture **2** whereas C-5 and C-7 should move downfield; these changes are indeed observed. (The upfield shift for C-4 is enhanced by a change from the larger downfield shifting β_e to the smaller β_a whereas the downfield shift of C-5 is enhanced by the opposite change as one proceeds from **2A** to **2B.**)

The assignments in the *N*-methyl analogues **2mA** and the conformer mixture **2m** were made analogously by comparison with **1mA** and **1m.** In this case, most of the signals for the minor isomer **2mB** were recorded and the predicted effects on C-2, C-4, C-5, and C-7 (vide supra) as one passes from **2mA** to **2mB** can be individually verified. C-8 in **2mB** is 7.5 ppm upfield from C-8 in **2mA** and the conformer mixture at 55 °C also shows a substantial upfield shift of C-8 compared to its position in the major isomer **2mA.** Part of this shift is no doubt due to the change of the Me–N–C(9)–C(8) segment from the e,e to the e,a conformation.[5] However, this conformational change may be insufficient to account for the total effect; we shall return to this point later.

The ratio of **2mA** to **2mB,** obtained by integration of several peaks belonging to each conformer, is 77:23 at −68 °C.



3A **3B**

3mA, 3mB,
NCH_3 instead of NH

Compound **3** displays a sharp spectrum at room temperature, indicating conformational homogeneity; conformer **3A** should be greatly destabilized by a CH_3/CH_2 syn-axial interaction. Thus **3** exists entirely as **3B.** Its signals correspond closely to those in **1B** where comparison[3a] is possible except for C-3 and C-2, C-4 which are affected by α_e and β_e effects, respectively. C-6, C-7, and C-8 were not seen in **1B;** the assignment of C-6 is unequivocal[3b] but C-7 and C-8 are too close

Table II. ^{13}C Chemical Shifts[a] for *N*-Methyl-*cis*-decahydroquinolines, and Shift Effects[b] upon Introduction of Equatorial or Axial *N*-Methyl Groups

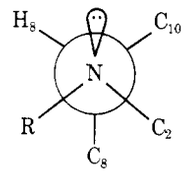
Compd[c]	Temp[d]	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	CCH_3	NCH_3
N-CH_3, **1m**	+30	55.8[e]	23.35	28.44	28.44	25.01	21.86	25.9[e]	62.89	36.94		42.91
N-CH_3, **1m**	+55	55.17	23.46	28.91	28.56	25.18	22.00	25.73	63.00	37.13		42.87
N-CH_3, **1mA**[f]	−68	58.38	21.71	30.83	26.41	26.13	19.65	29.39	63.42	36.47		43.22
(Effect of N-Me		+10.65	+0.53	+0.23	+1.43	−0.19	−0.69	−3.36	+8.63	+1.34)		
N-CH_3, **1mB**[f]	−68	47.47	25.39	22.88	31.67	20.94	[g]	15.65	60.69	36.14		42.53
(Effect of N-Me		+7.73		−1.09	+0.01				+6.82	+0.54)		
N,10-Dimethyl, **2m**	+30	55.3[e]	22.01	36.5[e]	34.3[e]	22.18	21.83	21.53	68.18	33.49	27.27	43.32
N,10-Dimethyl, **2m**	+55	54.75	22.14	36.00	34.61	22.30	21.91	21.31	68.18	33.62	27.33	43.27
N,10-Dimethyl, **2mA**[h]	−68	58.15	(21.66)	39.52	29.86	(21.51)	19.20	23.23	68.66	32.84	26.58	43.47
(Effect of N-Me		+10.90	−0.82	+0.33	+0.92	+0.09	−0.73	−4.78	+9.00	+0.85	+0.36)	
N,10-Dimethyl, **2mB**[h]	−68	47.37	[g]	27.95	40.64	[g]	25.39	15.70	65.85	33.61	26.83	42.88
(Effect of N-Me					+0.38		−0.51		+7.27	+1.25	−0.47)	
N,3α-Dimethyl, **3m(B)**	+30	55.75	31.46	32.59	31.81	21.10	25.63	16.55	60.53	35.96	19.71	42.31
(Effect of N-Me		+7.97	−1.92	−0.95	+0.07	+0.45	−0.46	−9.33	+6.73	−0.49	−0.07)	
N,3β-Dimethyl, **4m(A)**	+30	66.23	26.73	40.09	27.40	26.79	19.85	29.29	63.20	37.55	19.97	43.04
(Effect of N-Me		+10.70	+0.14	+0.02	+1.25	+0.20	−0.81	−3.34	+8.51	+1.50	+0.32)	
N,6α-Dimethyl, **5m(A)**	+30	58.58	21.99	31.07	35.48	33.41	28.52	29.64	63.09	37.16	22.63	43.07
(Effect of N-Me		+10.47	+0.37	+0.22	+1.23	+0.25	−0.77	−3.52	+8.47	+1.41	−0.13)	
N,6β-Dimethyl, **6m**	+30	48.74	25.64	24.81	40.17	27.08	33.56	16.82	61.27	35.94	22.23	42.68
N,6β-Dimethyl, **6m**	+55	49.21	25.60	25.26	40.17	27.26	33.56	17.41	61.58	35.88	22.11	42.73
N,6β-Dimethyl, **6mB**[i]	−68	47.32	25.89	23.56	40.28	26.66	33.71	15.30	60.32	36.24	22.60	42.51
(Effect of N-Me		+7.79	−1.34	−1.24	−0.17	+0.49	−0.64	−9.87	+6.67	+0.33	0.00)	
N,8α-Dimethyl, **7m(A)**	+30	59.56	21.64	30.85	26.61	26.40	28.42	39.98	68.80	39.80	23.24	45.31
(Effect of N-Me		+11.39	−0.41	−0.29	+1.81	−0.12	−0.06	+3.33	+8.36	+2.58	+4.59)	
N,8β-Dimethyl, **8m**	+30	56[e]	21.29	29.74	28.19	20.54	28.5[e]	30.43	69.16	28.75	18.13	43.16
N,8β-Dimethyl, **8m**	+55	55.47	21.43	29.68	28.49	20.71	28.71	30.25	69.23	28.94	18.26	43.15
N,8β-Dimethyl, **8mA**[j]	−68	58.66	21.28	30.48	26.17	19.79	24.85	29.56	70.00	28.08	17.39	43.38
(Effect of N-Me		+10.82	−0.21	+0.10	−1.01	−0.65	−1.33	−5.29	+9.59	−2.00	−0.15)	
N,8β-Dimethyl, **8mB**[j]	−68	45.66	(20.71)	[g]	31.74	(20.71)	35.57	(27.36)	67.41	(28.32)	19.45	41.71
(Effect of N-Me		+6.68	−6.04		−0.31	−0.33	+1.04	+0.73	+6.77	−7.33	+0.60)	
N,8α,10-Trimethyl, **9m(A)**	+30	59.38	22.11	39.75	30.81	22.48	28.26	31.93	73.93	35.39	23.42 (8)	45.38
(Effect of N-Me		+11.49	−0.75	−0.75	+1.82	+0.40	−0.02	+1.18	+8.31	+2.03	+4.44 27.42 (10) +1.28	
N,3α,10-Trimethyl, **10m(B)**	+30	55.75	27.43	37.31	41.09	21.72	25.79	16.10	65.75	34.48	19.97 (3)	42.74
(Effect of N-Me		+8.20	−0.84	−0.85	+0.35	±0.0	−0.59	−10.59	+6.88	+0.98	−0.01 29.06 (10) +0.67	
N,3β,10-Trimethyl, **11m(A)**	+30	66.28	26.63	49.48	31.45	22.11	19.53	23.74	68.51	33.83	19.75 (3)	43.33
(Effect of N-Me		+10.87	−1.40	+0.09	+1.02	+0.32	−0.74	−4.59	+8.67	+0.98	+0.19 26.63 (10) +0.34	

[a] See footnote *a*, Table I. [b] Data in parentheses; calculated for pairs of conformationally homogeneous compounds. $\delta_{mA} - \delta_A$, or $\delta_{mB} - \delta_B$; a plus sign indicates that the signal is downfield shifted upon introduction of the NCH_3 group. Position of NCH_3 is not definite in **1mB**, **3mB**, and **6mB** (see Discussion). [c] See footnote *b*, Table I. [d] See footnote *c*, Table I. [e] Signal was extremely broad. [f] 71% **1mA**, 29% **1mB**. [g] See footnote *f*, Table I. [h] 77% **2mA**, 23% **2mB**. [i] >95% **6mB**; only the signal for C-9 (63.59) of **6mA** could be observed. [j] 89.5% **8mA**, 10.5% **8mB**.

for unambiguous assignment, since C-7, which is 1.4 ppm downfield of C-8 in *cis*-decalin (low-temperature spectrum),[4] is shifted upfield[2] by replacement of the $CH_2\gamma$ group by NH. The equatorial methyl group in **3B** is shifted upfield from its normal[5] position by the anti-periplanar nitrogen.[6]

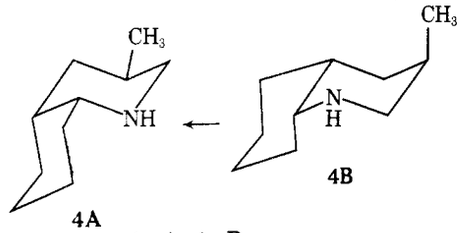
Compound **3m** is similarly conformationally homogeneous. Accordingly, all its signals correspond closely to those[3b] of **1mB** save those at C-3 (α_e effect) and C-2 and C-4 (β_e effect). C-8 is found at very high field similarly as in **1mB** and **2mB.** Comparison of C-8 in **3mB** with C-8 in **3B** (a corresponding comparison could not be made for **1** or **2**) indicates a −9.3 ppm (upfield) shift in the *N*-methyl compound. In the carbocyclic analogues, the computed[5b] upfield shift (combination of gauche and buttress effects) is −6.8 ppm and the observed[4] shift from *cis*-decalin to 1β-methyl-*cis*-decalin is −6.5 ppm. We have reported elsewhere[7a] that enhanced upfield shifts occur when there is a combination of an anti-periplanar lone pair and a methyl group on amine nitrogen (Chart I). It is not

Chart I



C-8 is shifted upfield when R = CH_3 but not when R = H

clear whether the effect is actually caused by the lone pair or whether it is simply an enhanced compression effect. However, the latter alternative is unlikely because the effect does not operate in reverse: the upfield shift of an axial *N*-methyl group[2] by introduction of an equatorial methyl gauche to it[7a,c] is only −7.7 ppm.

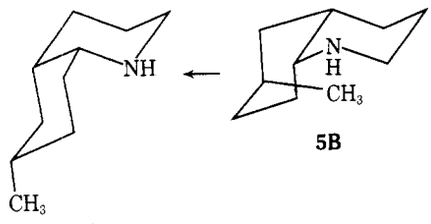


4A **4B**

4mA, 4mB,
NCH_3 instead of NH

The signals in **4**[3d] are sharp at room temperature, pointing to conformational homogeneity. In this case the intrinsic preference for the **A** isomer (cf. discussion of **1** above) is reinforced by the fact that **4B** would have an axial methyl group. The signals for C-2, C-3, and C-4 in **4A** are shifted downfield from those in **1A** by the expected α_e and β_e effects. The equatorial methyl group is shifted upfield by the anti-periplanar nitrogen[6] as discussed above for **3B.**

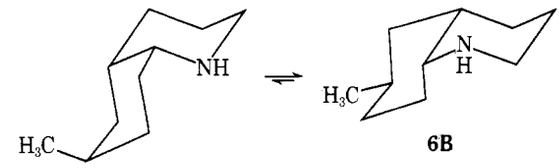
Compound **4m** similarly exists in conformation **4mA** with the expected downfield shifts, relative to **1mA** at C-2, C-3, and C-4. The complete coincidence of C-8 with that in **1mA** confirms the absence of the **4mB** isomer in which, as discussed above, C-8 would have shifted strongly upfield.



5A **5B**

5mA, 5mB,
NCH_3 instead of NH

Compound **5** also shows a sharp ^{13}C spectrum at room temperature: conformer **5B** with its methyl group syn-axial to C-4 is not viable. Comparison of **5A** (= **5**) with **1A** discloses essentially unchanged shifts in the piperidine ring; in the cyclohexane ring C-6, C-5, and C-7 experience the expected downfield α_e and β_e shifts of the methyl substituent which, itself, displays the normal shift. The situation in **5m** (= **5mA**) is entirely analogous.

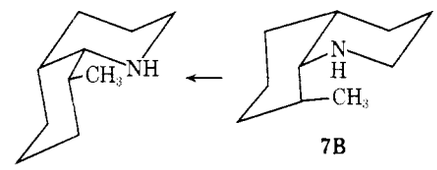


6A **6B**

6mA, 6mB,
NCH_3 instead of NH

Compound **6,** the diastereomer of **5,** is conformationally heterogeneous as indicated by its broad spectrum at room temperature which sharpens only on warming to 55 °C. At −68 °C two spectra are seen, that of the major isomer **6B** (89%) and that of the minor isomer **6A** (11%). Assignments in the minor isomer are based on comparison with **1A** with little shift occurring at C-2, C-3, C-4, and C-9. The remaining assignments are uncertain because two of the expected signals were not seen and off-resonance decoupling could not be performed on the rest, which are all expected to fall in the same region of the spectrum. The position of the axial methyl group is normal. Assignment of the signals in **6B** is straightforward through comparison with **1B**[3a] and **3B** taking into account the α_e and β_e effects of the methyl substituent at C-6,5,7. We note, however, that the position of C-3 in **6B** (27.23 ppm) is 2.2 ppm upfield from that published[3a] for **1B** (29.4 ppm). A similar discrepancy is found between **8B** (see below: C-3 at 26.75 ppm) and **1B;** we have already indicated[3c] that we could not find a resonance for **1B** at the position reported. (We do find a weak signal in the low-temperature spectrum of **1** at ca. 27.1 ppm but this signal may be caused by *trans*-decahydroquinoline impurity which, at room temperature, displays C-3 at 27.29 ppm.[2]) In the conformer mixture **6** at 55 °C, assignments are based on similarity of signal positions with those in the major conformer **6B;** C-4, C-8, and C-3 are, however, too close to each other for individual assignment.

The situation in **6m** is similar to that in **6** except that the minor conformer is reduced to less than 5% and only one of its carbons (C-9, at 63.59 ppm) could be seen. The peaks of the major conformer (and hence of the conformer mixture **6m**) are readily assigned by comparison with **1mB.**



7A **7B**

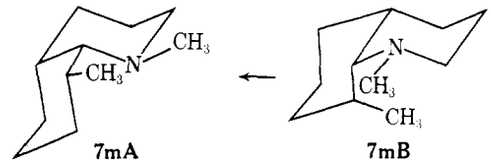
Conformation **7B,** with the methyl group syn-axial to C-2 and C-4, will not contribute and therefore **7** displays a sharp spectrum at room temperature. Assignments of peaks, by comparison with the parent compound **1A,** is straightforward. C-2, C-3, C-4, C-5, and C-6 are little affected by the methyl substituent. The relatively large downfield shift of C-10 comes from the $\beta_g\gamma_t$ effect[4] (corresponding to the $\beta_a\gamma_e$ effect[5b] in monocyclic systems) introduced by the combination of N-1 (β_g) and Me-8 (γ_t). C-8 shifts downfield by only ca. 3.9 ppm (Table III), considerably less than the α carbon in the other

Table III. Effects[a] of Methyl Substitution on ^{13}C Chemical Shifts in *cis*-Decahydroquinolines[b]

Effect[c,d]	Ring atom	Value Found	Value Calcd[c]	Compd[b]
α_e	3	(+5.4)	+6.0	**4(A)**
α_e	3	(+6.2[e])	+6.0	**3(B)**
α_e	6	(+6.8)	+6.0	**5(A)**
α_e	6	(+5.5[f])	+6.0	**6B**
α_e	3	(+5.6[g])	+6.0	**11(A)**
$\alpha_e + \alpha_e\beta_a$	8	(+3.9)	+3.1	**7(A)**
$\alpha_e + \alpha_e\beta_a$	8	(+2.7[g])	+3.1	**9(A)**
$\alpha_e + \alpha_e\beta_e$	8	(+0.8[f])	+3.5	**8B**
β_e	2	(+7.8)	+9.0	**4(A)**
β_e	2	(+8.0)	+9.0	**3(B)**
β_e	4	(+9.5)	+9.0	**4(A)**
β_e	4	(+9.6)	+9.0	**3(B)**
β_e	5	(+9.3)	+9.0	**5(A)**
β_e	5	+8.8	+9.0	**6B**
β_e	7	(+9.0)	+9.0	**5(A)**
β_e	7	(+8.3[f])	+9.0	**6B**
β_e	7	(+8.4[f])	+9.0	**8B**
β_e	2	(+8.2[g])	+9.0	**11(A)**
β_e	4	(+10.2[g])	+9.0	**11(A)**
$\beta_e + \beta_e\gamma_a$	7	(+8.1)	+8.2	**7(A)**
$\beta_e + \beta_e\gamma_a$	7	(+8.4[g])	+8.2	**9(A)**
$\beta_e + \alpha_a\beta_e$	9	(+5.7)	+5.6	**7(A)**
$\beta_e + \alpha_a\beta_e$	9	(+6.0[g])	+5.6	**9(A)**
$\beta_e + \alpha_e\beta_e$	9	+6.8	+6.5	**8B**
$\beta_e + G_\beta$	4	+8.6	+7.7	**2A**
$\beta_e + G_\beta$	4	+9.1[h]	+7.7	**9(A)**
$\beta_e + G_\beta$	4	+9.3[i]	+7.7	**11(A)**
$\beta_e + G_\beta$	5	+8.6	+7.7	**2B**
$\beta_e + G_\beta$	5	+9.0[j]	+7.7	**10(B)**
α_a	8	+2.1	+1.4	**8A**
α + Q-T + 2V$_g$[k]	10	−3.1	−3.2[k]	**2A**
α + Q-T + 2V$_g$[k]	10	−3.2	−3.2[k]	**2B**
α + Q-T + 2V$_g$[k]	10	−3.9[h]	−3.2[k]	**9(A)**
α + Q-T + 2V$_g$[k]	10	−3.0[j]	−3.2[k]	**10(B)**
α + Q-T + 2V$_g$[k]	10	−3.2[i]	−3.2[k]	**11(A)**
β_a	7	+5.8	+5.4	**8A**
β_a	9	+5.6	+5.4	**8A**
$\beta_a + G_\beta$	4	+4.6[j]	+4.1	**10(B)**
$\beta_a + G_\beta$	5	+4.0	+4.1	**2A**
$\beta_a + G_\beta$	5	+4.2[h]	+4.1	**9(A)**
$\beta_a + G_\beta$	5	+4.3[i]	+4.1	**11(A)**
$\beta_a + G_\beta$	9	+4.9	+4.1	**2A**
$\beta_a + G_\beta$	9	+4.7	+4.1	**2B**
$\beta_a + G_\beta$	9	+5.2[h]	+4.1	**9(A)**
$\beta_a + g_\beta$	9	+5.1[j]	+4.1	**10(B)**
$\beta_a + G_\beta$	9	+5.2[i]	+4.1	**11(A)**
γ_a	6	−5.9	−6.4	**8A**
$\gamma_a + G_\gamma$	3	−5.1[j]	−4.4	**10(B)**
$\gamma_a + G_\gamma$	6	−4.9	−4.4	**2A**
$\gamma_a + G_\gamma$	6	−4.4[h]	−4.4	**9(A)**
$\gamma_a + G_\gamma$	6	−4.6[i]	−4.4	**11(A)**
$\gamma_a + G_\gamma$	8	−4.7	−4.4	**2A**
$\gamma_a + G_\gamma$	8	−5.9[h]	−4.4	**9(A)**

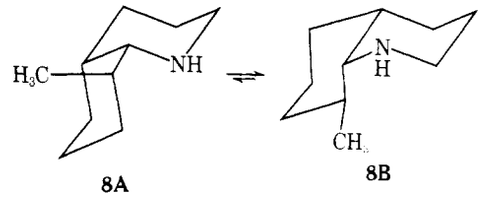
[a] Reference: **1A** or **1B** unless otherwise indicated. Where room temperature signals (of **3, 4, 5, 7,** and **9**) are compared with the signals at −68 °C in **1A, 1B** (or in other low temperature spectra as indicated), the effects are placed in parentheses. Disregard of the temperature change leads to inaccuracies of 0.1–0.9 ppm (see text). [b] Similar results are obtained on comparison of NCH_3 compounds (**mA** vs. **1mA,** and **mB** vs. **1mB**), except for **7mA** and **9mA** [syn-axial $CH_3(1)/CH_3(8)$] and **8mB** [axial $CH_3(1)$ compared to equatorial in **1mB**]. [c] Parameters of Table IV, ref 5b, were used if not otherwise indicated. [d] $\delta_A - \delta_{1A}$, or $\delta_B - \delta_{1B}$, if not otherwise indicated. A positive sign indicates that the signal is downfield in the methyl substituted compound. [e] Corresponding signal was not seen in **1B;** the signal in **6B** (−68 °C) was used instead. [f] Corresponding signal was not seen in **1B;** the signal in **3**(B) (30 °C) was used instead. [g] Compared with **2A.** [h] Compared with **7(A).** [i] Compared with **4(A).** [j] Compared with **3(B).** [k] Since no comparable parameters are given in ref 5b, the values from ref 4 are used.

methyl derivatives, because the usual α_e effect is, in the present situation, complemented by an $\alpha_e\beta_a$ effect (Me-8, N-1).[2,5b] Similarly, the β_e effect is ca. 8.2 ppm (see Table III) at C-7 but the downfield shift at C-9, where an $\alpha_a\beta_e$ effect (of N-1 and Me-8) contributes,[5b] is much smaller. The *C*-methyl group, though equatorial, resonates at relatively high field because of gauche interaction with N-1.[6]



7mA **7mB**

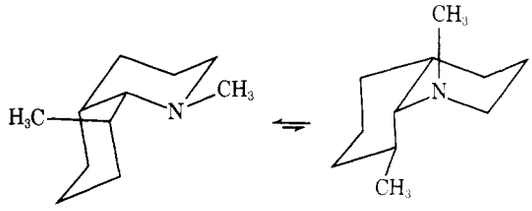
The conformational situation in **7m** is more complex. The syn-axial N-Me/C-Me interaction in **7mA** cannot be relieved by making the *N*-methyl group axial, since even more serious congestion would result. Conformer **7mB** is excluded for the reasons mentioned for **7B;** thus **7m** seems to exist entirely in conformation **7mA** (compare signals at C-3, C-4, C-5, and C-6 with **1mA**). The distortion which no doubt occurs in this rather strained species reflects itself in downfield shifts at C-2 and C-10 (ca. 1.2 and 3.3 ppm relative to **1mA**—the corresponding shift differences of **7A** vs. **1A** are ca. 0.4 and—vide supra—2.1 ppm; in contrast, the shift differences at C-7 and C-9 are similar for **7** and **7m**). Most notable is the mutual downfield shifting of the methyl groups in **7mA:** C-Me from 18.65 ppm in **7** to 23.24 ppm in **7m;** N-Me from 43.22 ppm in **1mA** to 45.31 ppm in **7mA.** This effect is similar to that seen by Stothers and co-workers for Me syn-axial to OH.[9] Also remarkable is the large downfield shift of C-8 relative to **1mA** (10.6 ppm) and to **7A** (3.3 ppm—the γ-gauche upfield shift of the N-Me group is evidently overwhelmed); similar downfield shifts are seen in other systems[2,9] for ring carbons which bear syn-axial substituents.



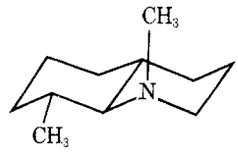
8A **8B**

Of the compounds studied, **8** is the conformationally most heterogeneous. At room temperature, most of its signals were quite broad, though a sharp spectrum was obtained at 55 °C. At −68 °C the spectrum was resolved into that of a major conformer **8B** (59%) and of a minor one, **8A** (41%) whose signal assignments rest on those of **1A,** and of **1B** and **3B,** respectively. The signals of **8A** remote from the methyl group agree well with those of **1A** and the shifts engendered by the methyl are satisfactorily explained in terms of the usual α_a, β_a, and γ_a effects. Agreement of **8B** with **1B** and **3B** is less good, possibly due to a shifting of the NH from the normal[10] equatorial to the axial position caused by Me-8. Particularly to be noted is the anomalously small $\alpha_e + \alpha_e\beta_e$ effect of the methyl group (itself normal in shift) on C-8 of only 0.75 ppm.

The signals of the conformer mixture at 55 °C are readily assigned from those of the two components and knowledge of their relative proportions.

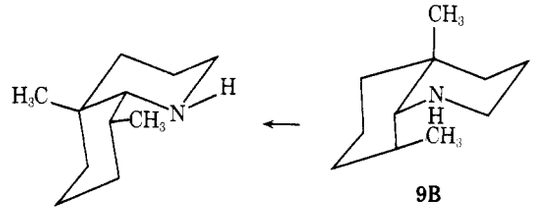


8mA **8mB**



12

In the *N*-methyl derivatives **8m** the conformational proportions are reversed from those of the corresponding NH compounds **8**. Conformer **8mA** now clearly predominates (89.5%) with **8mB** contributing but 10.5%. The signals of **8mA** are readily assigned from those of **1mA** with reasonable agreement after application of the usual α_a, β_a, and γ_a shifts. However, the signals of **8mB** are not comparable to those of **1mB**[3b] because model considerations indicate that the N-Me group in **8mB** is sterically prevented from occupying its normal[7b] equatorial position. Shifting it to the axial position will bring about changes at C-2, C-3, C-9, and C-10, as well as at C-8 which is now no longer anti-periplanar to the lone pair and thus no longer experiences the upfield shifting effect from either that cause or that of a buttressing gauche substituent (vide supra). Nevertheless, the assignment of the low-field signals to C-2 and C-9 is straightforward. The position of C-3 can be estimated by its similarity with C-3 in the trans analogue **12**;[2] C-4 is not much affected by the position of the *N*-methyl group and should be close to its normal position (**1mB, 6mB**) of 25.5 ppm; both signals are overlaid by signals of the major conformer **8mA**. C-5 and C-6 are assigned from the spectrum of **1mB**, C-7 from the spectrum of **12**. C-10 is expected at 28 ppm (correcting the value of 35.65 in **8B** by a γ_a effect[2] of −7.5 ppm). C-8 might be expected at 26.6 ppm, its shift in **8B**; signals are found at 28.32 and 27.36 ppm. Both the signals of C-8 and of NCH_3 are at lower field than predicted: in **12**, NCH_3 resonates at 33.23, and correction for the gauche and buttressing effects[5b] of C-8 6.77 ppm) which are absent in **8mB** brings the expected value to 40 ppm. It would appear from the literature[11] that the 1,2-anti-periplanar arrangement of two groups causes an additional downfield shift of about 1.5 ppm which may account for the lower than expected field position of the signals for C-8 and N-Me. Me-8 in **8mB** agrees well in shift with 8-Me in **12**.

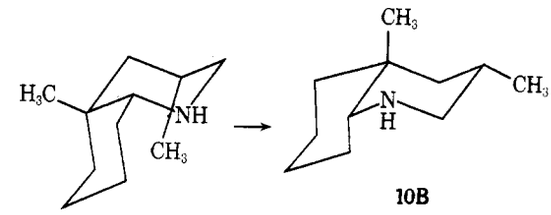


9A **9B**

9mA, 9mB,
NCH_3 instead of NH

Compound **9** shows the sharp spectrum of a conformationally homogeneous species (**9A**): **9B** suffers from the same methyl–methylene syn-axial interactions as **7B**. Assignment of signals in **9A** is straightforward on the basis of the analogy with **2A** and **7A**. As in **2A**, C-3 and C-6 are too close to each other for unequivocal assignment.

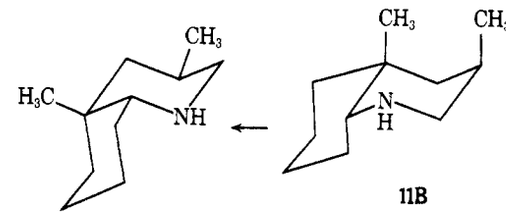
The spectrum of **9m** similarly points to conformational homogeneity in the form **9mA**. C-8, C-10, and the methyl groups can be assigned easily from the off-resonance decoupled spectrum, the rest of the signals by analogy with **7m(A)** and **2mA**.



10A **10B**

10mA, 10mB,
NCH_3 instead of NH

The 3α,10-dimethyl-*cis*-decahydroquinoline (**10**) exists exclusively in conformation **10B** because of a CH_3/C-5 syn-axial interaction in the **A** conformation. Assignment of signals is facile by comparison with **3** and use of parameters for methyl substitution,[2] except for C-7 and C-8, which are too close for unambiguous assignment. Compound **10m** is also conformationally homogeneous (**10mB**); in this compound the NCH_3 group must be exclusively in the equatorial position through the biasing influence of the CH_3-10 group, as in **2mB**. Again C-8 resonates at very high field.



11A **11B**

11 mA, 11mB,
NCH_3 instead of NH

Compound **11**, finally, exists in conformation **A** whose natural predominance is further enhanced by the CH_3/CH_3 syn-axial interactions in **B**. The same is true for **11m** (= **11mA**). Assignment of signals is unambiguous by comparison with **4(A)**, **2A** and **4m(A)** and **2mA**, respectively.

The various shift parameters which may be derived from the observed shifts in the *cis*-decahydroquinoline series are collected in Table III. Because of temperature dependence of ^{13}C shifts (found, in some *trans*-decahydroquinolines, to range from 0.1 to 0.9 ppm over a 100 °C temperature range, with a

Table IV. Conformational Equilibria in Mobile *cis*-Decahydroquinolines[a]

	R = H			R = CH_3 (m series)		
Compd	A, %	B, %	$\Delta G°_{205}$, kcal/mol	A, %	B, %	$\Delta G°_{205}$, kcal/mol
1	90 ± 1[b]	10 ± 1[b]	0.90 ± 0.05[b]	71 ± 2[c]	29 ± 2[c]	0.36 ± 0.04
2	94.5 ± 1	5.5 ± 1	1.16 ± 0.08	77 ± 1	23 ± 1	0.49 ± 0.03
6	11 ± 1	89 ± 1	−0.85 ± 0.04	<5	>95	<−1.2
8	41 ± 2	59 ± 2	−0.15 ± 0.04	89.5 ± 1.5	10.5 ± 1.5	0.87 ± 0.07

[a] In $CDCl_3$ at −68 °C (205 K). For enumeration of signals used in integration, see Experimental Section. [b] Lit.[3a] 93.5% **A**, 6.5% **B** at −74 °C, $\Delta G°$ = 1.05 kcal/mol. [c] Lit.[3b] 70% **A**, 30% **B** at −50 °C, $\Delta G°$ = 0.38 kcal/mol.

mean of 0.46 ppm) some of these parameters, where room temperature data are compared with the low temperature values of the parent compounds **1A** and **1B**, are of low accuracy. Such values are marked as such in Table III and are included only for the sake of completeness. For the same reason, standard deviations are not indicated in the table.

The most salient aspect of the data in Table III is the generally very close agreement of the parameters in the *cis*-decahydroquinoline series with the Grant parameters[4,5] in cyclohexane. This feature had been previously observed in *trans*-decahydroquinolines.[2]

Conformational Analysis. In Table IV are shown the percentages of the two conformers (**A** and **B**) for **1, 2, 6,** and **8** and their *N*-methyl derivatives **1m, 2m, 6m,** and **8m,** along with the corresponding free-energy differences, at −68 °C, for the equilibrium **A** ⇌ **B** (cf. the earlier diagrams). These percentages were obtained by integration of the C-13 signals in the low-temperature spectra. While it is known that there are pitfalls in the procedure—unequal NOE effects and relaxation times may cause the signals not to be proportional in area to the number of nuclei—in the present instance the chances for systematic error are reduced because except in the case of **6m,** several different sets of signals belonging to the two conformers were integrated (see Experimental Section). In addition, Booth and Griffiths[3b] have cited evidence relating to T_1 measurements in *cis*-decahydroquinolines which suggests that at least the CH_2 groups should provide reliable integrals in a mixture of isomers or conformers.

The position of equilibrium for 1 and **1m** has been determined previously[3a] and interpreted[3b] in a straightforward way. In **1A** two of the butane-gauche interactions of *cis*-decalin are replaced by the less unfavorable[12] propylamine-gauche interactions. In **1B** one of the butane-gauche interactions is replaced by a *more* unfavorable C–N–C–C gauche interaction (more unfavorable because the C–N distance is shorter than C–C). Quantitatively speaking one may compare the situation in **1A** to that in axial *N*-methylcyclohexylamine, which is[13] about 1 kcal/mol less stable than the equatorial isomer, the difference between its conformational equilibrium and that of methylcyclohexane ($-\Delta G_{Me}$ = 1.7 kcal/mol) being 0.7 kcal/mol. (Complete agreement between this figure and the 0.90 kcal/mol difference between **1A** and **1B** cannot be expected, for whereas the conformational situation in **1A** is similar to that in the axial conformation of *N*-methylcyclohexylamine, the equatorial conformer of this amine has possibilities of rotational isomerism which do not exist in **1B.** The qualitative conclusion—that **1B** should be disfavored by more than 0.7 kcal/mol—is indeed borne out.)

Compared to the **1A** ⇌ **1B** case, the equilibrium in **1mA** ⇌ **1mB** is shifted substantially toward the **B** isomer. This has been explained[3b] as being due to a $CH_2(8)/CH_3(N)$ compression in **1mA** which is clearly seen in a Dreiding model. Another way of interpreting this interaction is to say that in a saturated heterocyclic six-membered ring, the region around the heteroatom is usually puckered (torsional angle τ >60°). One result of this puckering is to bring the equatorial/equatorial (e,e) vicinal groups closer together than the equatorial/axial (e,a) ones, contrary to what happens in cyclohexane[14] where $\tau_{e,e}$ (≈65°) > $\tau_{e,a}$ (≈55°).

We note that ΔG in **1m** is similar to the value determined previously[15] by an indirect method in solvent methanol (0.47 kcal/mol) but quite different from the value[15] in glyme, 1.3 kcal/mol.

The N-Me(a) ⇌ N-Me(e) equilibrium in **1m** requires mention. Axial *N*-methyl cannot contribute in **1mA** because of the syn-axial interactions with C-5 and C-7. However, **1mB** (and, thus, also **3mB** and **6mB**) may exist in part with axial *N*-methyl. In **2mB** and **10mB** the NCH_3 must be purely equatorial (N-Me/10-Me syn-axial interactions in the N-Me axial form), in **8mB** purely axial (N-Me/8-Me syn-axial interaction in the equatorial form). In **1mB** the axial NCH_3 conformation has two Me/H syn-axial interactions whereas the conformation with equatorial N-Me has only one; the difference thus amounts to one syn-axial N-Me/H. The magnitude of this interaction has been variously estimated as ½ × 1.8 = 0.9 kcal/mol[7b] or ½ × 3.0 = 1.5 kcal/mol.[8b] The former value would indicate the presence of 18% of the N-Me(a) conformation at 30 °C and 10% at −68 °C; the latter 7.5% at 30 °C and 2.5% at −68 °C. Accurate experimental information is, unfortunately, hard to come by: the axial N-Me in **8mB** and the equatorial ones in **2mB** and **10mB** (Table II) are too close in shift to permit reliable interpolation for the cases of **1mB, 3mB,** and **6mB.** One can use the shift changes of C-3, C-10, and C-8 upon addition of an *N*-methyl group as an indicator, if the signals can be seen in both NH and NCH_3 derivatives of equatorially biased (**2mB, 10mB**), axially biased (**8mB**), and "mobile" (**1mB, 3mB, 6mB**) compounds (Table II). The changes at C-8 are most telling, since this C atom is shifted strongly upfield by equatorial N-methylation (**10B** → **10mB:** −10.6 ppm), but downfield by axial N-methylation (**8B** → **8mB:** +0.7 ppm). Use of the corresponding shift differences at 30 °C (**3B** → **3mB:** −9.3 ppm) and at −68 °C (**6B** → **6mB:** −9.9 ppm) allows estimation of the conformational population in the "mobile" systems. The results are 11.5% NCH_3 axial at 30 °C (K = 7.7; $\Delta G°$ = 1.2 kcal/mol) and 6% NCH_3 axial at −68 °C (K = 15.1; $\Delta G°$ = 1.1 kcal/mol). This suggests that the NCH_3 axial conformation may be disregarded even in the **mB** series (except in the case of **8mB,** vide supra) and that the N-Me/H syn-axial interaction is higher than we have reported previously.[7b] In an investigation independent of ours[7b] and Robinson's,[8a,b] $-\Delta G°$ for N-Me was indeed found to be ≥2.7 kcal/mol.[8c]

The conformational equilibria in **2**[3d] and **2m** are surprising. One might have expected that the methyl group at C-10 finds itself in a less favorable environment in conformation **A** (methyl syn-axial to two hydrogen atoms in the cyclohexane ring) than in conformation **B** (methyl syn-axial to one hydrogen and one lone pair in the piperidine ring—a situation found more favorable for the methylene group in **1B** as compared to **1A**). If that were so, equilibrium in **2** and **2m** should have been shifted toward conformer **B** compared to 1 and **1m** contrary to what is observed: both the equilibria between **2A** and **2B** and between **2mA** and **2mB** are actually slightly shifted toward the **A** side compared to the **1A** ⇌ **1B** and **1mA** ⇌ **1mB** equilibria. The best rationalization we can suggest is one based on a reflex effect:[16] the very close approach of H_a-8 and H_a-2 in **1B** (which, as implied earlier,[3b] is partially responsible for the lesser stability of the **B** form) leads to a substantial bending apart of C-8 and C-2 which, in turn, forces together Me_a-10 and H_a-3 in the **B** conformer, thus enhancing their interactions. This effect is reciprocal, of course, and another way of expressing it is to say that Me-10 in the **B** conformer prevents minimization of the strain caused by the C-2/C-8 compression (Scheme I). An additional possibility is that the 10-methyl group in the **B** conformer prevents the NR group from occupying the axial position and thus destabilizes **B** through loss of entropy of mixing. This effect, while plausible for **2,** is not likely to be important for **2m,** for the reasons discussed above.

Scheme I

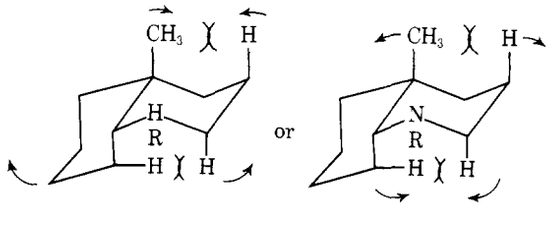


Table V. Pertinent ^{1}H Chemical Shifts[a] of *cis*-Decahydroquinolines (1–11) and *N*-Methyl-*cis*-decahydroquinolines (1m–11m)[b]

Registry no.	Substance[c]	H_{2e}	H_{2a}	H_9	NCH_3	CCH_3
10343-99-4	Parent, **1**	3.02 (d, 11 of m)	2.64 (t, 12 of d, 3)	2.82 (s, ½-width 8)		
45846-78-4	10-CH_3, **2**	3.04 (d, 12 of m)	2.58_5 (d, 12 of d, 10 of d, 3)	2.41 (t, 3)		0.94 (s)
60490-03-1	3α-CH_3, **3(B)**	2.68 (d, 12 of d, 4)	2.37_5 (d, 12 of d, 10)	2.84 (d, 12 of t, 4)		0.85 (d, 6)
60166-53-2	3β-CH_3, **4(A)**	3.04_5 (d, 11 of d, 4 of d, 2)	2.25 (t, 11)	2.78 (s, ½-width 7)		0.78 (d, 6)
60490-04-2	6α-CH_3, **5(A)**	3.10 (d, 11 of m)	2.65 (t, 11 of d, 3.5)	2.81 (s, ½-width 7)		0.92 (d, 6)
60490-05-3	6β-CH_3, **6**	2.80 Multiplet, not resolved				0.86_5 (d, 6.3)
60490-06-4	8α-CH_3, **7(A)**	3.11 (d, 12 of m)	2.57 (t, 12 of d, 4)	2.63 (s, overlaid with H_{2a})		0.91 (d, 6.5)
60490-07-5	8β-CH_3, **8**	2.75 Multiplet, not resolved		2.43 (d, 6.5 of d, 3.5)		0.94_5 (d, 7)
60490-08-6	8α,10-Dimethyl, **9(A)**	3.14 (d, 11 of m)	2.53 (t, 11 of d, 3)	2.24 (d, 3)		0.88 (d, 6.5)[d] 0.92 (s)[e]
60490-09-7	3α,10-Dimethyl, **10(B)**	2.69 (d, 12.5 of d, 5)	2.37 (d, 12.5 of d, 11)	2.38 (d, 12 of d, 3.5)		0.79 (d, 6)[f] 1.08 (s)[e]
60490-10-0	3β,10-Dimethyl, **11(A)**	3.01_5 (d, 11 of d, 4 of d, 2)	2.16 (t, 11)	2.34 (s, ½-width 7)		0.76 (d, 6.5)[f] 0.92 (s)[e]
16726-25-3	*N*-Methyl, **1m**	2.67 (broad m)	Not resolved		2.20	
60490-11-1	*N*,10-Dimethyl, **2m**	2.70 (broad m)	Not resolved		2.22	1.00 (s)
60490-12-2	*N*,3α-Dimethyl, **3m(B)**	2.45 (d, 10.5 of d, 4)	2.05_5 (t, 10.5)	2.71_5 (d, 10.5 of t, 4)	2.37	0.88 (d, 6)
60490-13-3	*N*,3β-Dimethyl, **4m(A)**	2.80 (d, 10.5 of d, 3.5 of d, 2)	1.60 (t, 10.5)	Not resolved	2.16_5	0.79_5 (d, 6)
60490-14-4	*N*,6α-Dimethyl, **5m(A)**	2.87 (d, 9 of m)	Not resolved	1.93 (s, ½-width 7)	2.16	0.93 (d, 6)
60490-15-5	*N*,6β-Dimethyl, **6m**	2.40 Overlaid with NCH_3, not resolved		2.65 (d, 11 of t, 4)	2.35	0.84 (d, 6)
60490-16-6	*N*,8α-Dimethyl, **7m(A)**	2.74 (d, 11 of m)	Not resolved	1.97 (s, ½-width 6)	2.22_5	1.12_5 (d, 6.5)
60490-17-7	*N*,8β-Dimethyl, **8m**	2.89 (d, 10 of m)	Not resolved		2.28	0.97_5 (d, 7)
60490-18-8	*N*,8α,10-Trimethyl, **9m(A)**	2.78_5 (d, 11 of m)	2.18 (t, 11 of d, 3)	1.68 (d, 3)	2.28_5	1.11 (d, 7)[d] 0.95 (s)[e]
60490-19-9	*N*,3α,10-Trimethyl, **10m(B)**	Not resolved			2.31_5	0.84 (d, 6)[f] 1.12_5 (s)[e]
60490-20-2	*N*,3β,10-Trimethyl, **11m(A)**	2.78 (d, 10.5 of d, 3.5 of d, 2)	1.60_5 (d, 11.5 of d, 10.5)	Not resolved	2.17_5	0.77_5 (d, 6.5)[f] 0.95 (s)[e]

[a] In $CDCl_3$, ppm, from Me_4Si; the reported shift values are centers of groups of signals in the spectra. [b] The parenthesized data are multiplicity and coupling constants (in hertz). [c] Substituted *cis*-decahydroquinoline. [d] CH_3-8. [e] CH_3-10. [f] CH_3-3.

Conformational equilibria in **6** and **6m** are readily accounted for by assuming additivity of ΔG in the equilibria for **1** or **1m** with ΔG for the methyl group at C-6 (−1.7 kcal/mol[17]). The calculated ΔG for **6** is then 0.90 − 1.7 = −0.80 kcal/mol vs. −0.85 found; the corresponding value for **6m** is 0.37 − 1.7 = −1.33 kcal/mol, too negative for accurate experimental determination by low-temperature ^{13}C NMR (which, however, supports $\Delta G < -1.2$ kcal/mol).

The equilibrium for **8** allows one to calculate the CH_3–C–C–N gauche interaction. Conformer **8A** is destabilized compared to **1A** by 1.7 kcal/mol (two CH_3/H syn-axial interactions). If this were all, ΔG for **8** should be −0.80 kcal/mol, as calculated for **6** above, or −0.85 kcal/mol, as observed. The experimental value, −0.15 kcal/mol, indicates an offsetting interaction of 0.65–0.70 kcal/mol in **8B** ascribable to gauche Me–C–C–N. The small difference (0.15 kcal/mol) between this figure and the butane-gauche (CH_3–C–C–C) interaction (0.85 kcal/mol in cyclic compounds) contrasts with that (½ × 0.90 = 0.45 kcal/mol) found in **1** (vide supra). This may be because in **8B** the gauche interaction is either of the Me–C–C–NH (rather than Me–C–C–N:) type or else the hydrogen on nitrogen in **8B** must be forced into the less favorable[10] axial position.

The situation in **8m** is substantially different because the N-Me group in **8mB** is forced, by Me-8 to become axial (or else there would be a very severe Me/Me syn-axial interaction). This increases the number of N-Me/H syn-axial interactions from one (with H_e-8) to two (with H_a-3 and H_a-10). The calculated ΔG for **8mA** ⇌ **8mB**, starting with the value of 0.37 kcal/mol for **1m** and adding the increments discussed in the previous paragraph plus the new increment of 0.9[7b] or 1.5[8b] kcal/mol, is 0.37 − 1.7 + 0.7 + 0.9 (or 1.5) = 0.27 or 0.87 kcal/mol, compared to the experimentally found +0.87. Once again the larger value for the N-Me(a)/H syn-axial interaction gives the better agreement with experiment.

Compounds **3(B)**, **5(A)**, **7(A)**, **9(A)**, **10(B)**, and **11(A)** and the corresponding methyl derivatives **3m(B)**, **5m(A)**, **7m(A)**, **9m(A)**, **10m**, and **11m** are conformationally homogeneous because the alternative conformers (**3A, 5B, 7B, 9B, 10A, 11B, 3mA, 5mB, 7mB, 9mB, 10mA, 11mB**) would have severe methyl/methylene syn-axial interaction (see also the earlier discussion regarding **9mB**). Compounds **4** and **4m** exist as the **A** conformers because the intrinsic preference for the **A** conformation is, in these cases, reinforced by the presence of the axial methyl groups in **4B** and **4mB.**

Synthesis, Configurational Assignments, and ^{1}H NMR Spectra. The compounds investigated were prepared by hydrogenating either the parent quinoline or 5,6,7,8-tetrahydroquinoline[18] over platinum in concentrated hydrochloric acid at elevated temperature and 50 psi pressure of hydrogen, or by hydrogenating the corresponding $\Delta^{1,9}$-octahydroquinoline[19] over Raney nickel in ethanol, at room temperature and 50 psi pressure of hydrogen.

Both methods have advantages and drawbacks. While hydrogenation of quinolines in strongly acidic medium proceeds quite readily to the 5,6,7,8-tetrahydro stage even at room temperature,[18] further reduction to the decahydro stage is extremely slow, especially in hydrochloric acid. Use of different acids (e.g., 12 N H_2SO_4) shortens the reaction time somewhat, but also increases the amount of trans fused decahydro product, whereas in hydrochloric acid one obtains very high proportions of *cis*-decahydroquinolines.[20] Hydrogenation at ~70 °C and use of increased amounts of catalyst cuts the reaction time to a reasonable length.

Hydrogenation of $\Delta^{1,9}$-octahydroquinolines proceeds readily with a variety of catalysts, but leads to mixtures with varying proportions of trans products. In contrast to quinoline reduction, use of an acid medium seems to increase the amounts of trans products formed; in strongly acidic medium (concentrated HCl) hydrogenation times again become very long, without leading to an increase in the yield of cis-fused product. The highest proportions of cis-decahydroquinolines were obtained with Raney nickel in anhydrous ethanol. While some *trans*-decahydroquinolines are always formed (more so in 95% than in absolute ethanol), this method has the advantage of short reaction times; moreover, it permits the synthesis of 10-methyl substituted *cis*-decahydroquinolines.[21]

The structure of the *cis*-decahydroquinolines follows, in the first instance, from that of their quinoline or octahydroquinoline precursors. Trans isomers, if any, formed as by-products were removed by preparative gas chromatography; the epimeric cis compounds were similarly separated. Since the trans isomers were readily identified by comparison with earlier prepared[19] samples, this left only the problem of assignment of the two cis epimers in the case of the 3- (**3, 4**), 6- (**5, 6**), 8-methyl (**7, 8**), and 3,10-dimethyl (**10, 11**) homologues. The strongest evidence for configurational and conformational assignment rests on the ^{13}C NMR spectra, which have already been discussed in detail. The ^{1}H NMR spectra tabulated in Table V were generally less definitive than in the conformationally homogeneous trans series;[19] however, the **B** conformation in the case of **3, 3m,** and **10** was characterized by the large coupling constant for H_9 ($J_{H_9/H_{8a}}$). Compound **8,** which exists as a conformational mixture, showed an intermediate coupling constant for H_9 whereas those compounds existing in the **A** conformation (notably **4, 5, 11, 5m, 7m**) displayed H_9 as a relatively narrow unresolved multiplet, except in the case of **9A** and **9mA** where the expected doublet ($J_{e,a}$ = 3 Hz) is resolved. In the case of the equatorial *N*-methyl compounds (i.e., excluding **8mB**) H_{2a} is anti axial to the lone pair on the nitrogen of the N-Me group, a situation which causes a strong upfield shift.[19] Unfortunately the signal is resolved only in **4m** and **11m,** where indeed it is at very high field (1.60 ppm) and shows a large apparent triplet splitting (combination of J_{gem} ≈ and approximately equal J_{aa}). The same triplet is seen in **3m,** still much upfield from H_{2e}, but not at quite as high field as in **4m** because of the countervailing downfield shift by the syn-axial C-8 in the **3mB** conformation. Characteristic coupling constants are also seen for H_{2a} in **5, 7, 9, 9m, 10,** and **11,** and for H_{2e} in **3, 4, 5, 9, 10,** and **11** and **3m, 4m, 5m,** and **11m.** Finally, **7mA** and **9mA,** earlier mentioned as having a C-Me/N-Me syn-axial interaction, display the CH_3-8 protons at unusually low field (1.1, 1.12 ppm).

In summary, we feel that the combination of arguments based on conformational analysis, ^{13}C, and (to a lesser extent) ^{1}H chemical shifts leaves no doubt on the assignment of the epimers **3/4, 5/6, 7/8,** and **10/11.**

Octahydroquinolines. In Table VI are summarized the C-13 spectra of several $\Delta^{1,9}$-octahydroquinolines prepared in the course of this investigation. Signal assignments for the parent compound are supported by the spectra of the *8,8,10-d_3* analogues prepared by exchange with NaOEt/EtOD. The remaining assignments were made on a parametric basis.

Experimental Section

Melting points were determined on an Electrothermal variable temperature heating block. Analytical gas–liquid chromatography was carried out with a Hewlett-Packard 5750 research chromatograph, equipped with a thermal conductivity detector, on 0.125-in. columns. Columns used were a 12-ft, aluminum, 20% Carbowax 20M + 10% KOH on Chromosorb W, 80/100 mesh; a 20-ft, aluminum, 20% QF-1 on Chromosorb W, 80/100 mesh; and a 10-ft, stainless steel, 30% SE-30 on Chromosorb W, 60/80 mesh, at temperatures between 100 and 200 °C. A Varian Aerograph Series 2700 and a Varian Aerograph Model 960, with 0.375-in. aluminum columns with matching phase on Chromosorb A were used for preparative VPC.

NMR spectra were recorded on a Varian XL-100 pulsed Fourier transform nuclear magnetic resonance spectrometer. ^{1}H NMR spectra

Table VI. ^{13}C Chemical Shifts[a] of $\Delta^{1,9}$-Octahydroquinolines

Compd[b]	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	CH_3
Parent[c]	49.64	21.42	27.54	35.04	26.01	28.02	39.34	173.21	38.72	
Parent[c,d]	47.54	19.99	28.74	36.16	25.50	25.87	38.30	199.46	41.58	
6-CH_3	49.72	21.45	27.97	43.44	32.34	35.74	38.79	172.82	37.81	21.80
8α-CH_3[e]	49.92	21.22	28.14	35.76	25.99	36.90	41.69	174.90	38.94	16.85
8β-CH_3[e]	49.56	21.58	28.06	35.18	20.44	33.01	41.61	176.98	34.21	18.41
10-CH_3	49.98	19.43	36.95	41.93	21.85	27.97	36.02	175.97	36.73	24.45
8,10-Dimethyl	50.41	19.47	37.56	42.28	21.85	37.21	36.98	177.36	36.79	17.44 (8) 25.14 (10)
3α,10-Dimethyl[f]	57.96	25.53	45.69	42.20	21.65	27.80	35.67	175.17	38.07	19.46 (3) 25.66 (10)
3β,10-Dimethyl[f]	57.54	24.38	46.24	41.07	22.14	28.69	35.67	177.26	36.67	19.11 (3) 24.64 (10)

[a] In parts per million, from internal Me_4Si. Solvent $CDCl_3$, if not otherwise indicated. [b] $\Delta^{1,9}$-Octahydroquinoline. [c] Shifts of $\Delta^{1,9}$-octahydroquinoline in $CDCl_3$ and CF_3COOH are slightly different from values reported earlier[17] because of using 25.16 MHz rather than 25.2 for calculation of parts per million. [d] In CF_3COOH; lock signal in this case was F. [e] Mixture of isomers; from integration of corresponding signals ratio was determined as 75% 8α-CH_3 and 25% 8β-CH_3. [f] Assignment of structures was made by comparison with matching decahydro compounds (Table I); see Experimental Section.

were recorded in the cw mode, in 5-mm o.d. tubes. ^{13}C NMR spectra were measured at 25.16 MHz, in the pulsed mode, in 10-mm o.d. tubes. Solvent in both cases was $CDCl_3$, with 2–5% Me_4Si admixed as internal reference; the deuterium of the solvent provided the internal lock signal. Integration of corresponding signals in the low-temperature ^{13}C spectra was effected by counting squares of the signal areas, and by multiplying signal height with half width, after expanding electronically as much as resolution and noise level permitted. The following signals (numbers refer to position of carbon atoms) were integrated and gave (parenthesized) percentages (only one conformer of each pair is reported): **1A,** 2 (91), 4 (89), 9 (90); **1mA,** 2 (73), 4 (72), 8 (72), 9 (72), NCH_3 (68); **2A,** 5 (95), 7 (95), 9 (94), 10 (94), CH_3 (95); **2mA,** 2 (76), 4 (76), 5 (77), 7 (77), 8 (79), 9 (78), NCH_3 (76); **6A,** 2 (11), 3 (11), 7 (12), 9 (12), CH_3 (8); **8A,** 2 (41), 5 (43), 6 (41), 7 (40), 9 (41), CH_3 (39); **8mA,** 2 (90), 3 (89), 9 (91), 10 (89), CCH_3 (90), NCH_3 (88).

Microanalyses were carried out by Galbraith Laboratories, Inc.

Starting Materials. The synthesis of the various quinolines, 5,6,7,8-tetrahydroquinolines,[18] and $\Delta^{1,9}$-octahydroquinolines[19] has been described elsewhere in detail. Quinolines obtained commercially were purified previous to hydrogenation by heating with Raney nickel in ethanol and distillation.[18,20]

trans-Decahydroquinolines, formed as by-products in the hydrogenations, were identified by VPC comparison with the authentic samples[19] on the columns described above.

3,10-Dimethyl-$\Delta^{1,9}$-octahydroquinolines were prepared in a way analogous to the synthesis of 10-methyl-[19,21] and 8,10-dimethyl-$\Delta^{1,9}$-octahydroquinoline.[19]

2-(2′-Cyanopropyl)-2-methylcyclohexanones (13). 2-Methylcyclohexanone was washed with dilute alkali and water, dried over $MgSO_4$, and distilled. To 260 g (2.32 mol) of the ketone and 7 g of Triton B, 39.3 g (0.58 mol) of freshly distilled methacrylonitrile was added dropwise with stirring. The reaction vessel was cooled intermittently to keep the temperature below 35 °C. After addition was complete the mixture was stirred at room temperature overnight, diluted with ether, neutralized with dilute HCl, washed with a saturated solution of NaCl, and dried over $MgSO_4$. The ether was evaporated at reduced pressure and the residue distilled to give unreacted 2-methylcyclohexanone and **13,** bp 119 °C (0.5 mm), yield 77.3 g (74%). Gas chromatography (SE-30) shows ~8% by-product, presumably 2-(2′-cyanopropyl)-6-methylcyclohexanone.

2-(2′-Cyanopropyl)-2-methyl-1,1-ethylenedioxycyclohexanes (14). A solution of **13** (72 g, 0.4 mol), ethylene glycol (30 g), and 0.5 g of toluenesulfonic acid in 250 ml of benzene was heated to reflux and the water formed was separated with a Dean-Stark trap. After 48 h the solvent was evaporated and the residue dissolved in ether and washed three times with water. The ether solution was dried, the ether removed at reduced pressure, and the residue distilled, bp 114 °C (0.5 mm), yield 89.2 g (92%).

2-(2′-Methyl-3′-aminopropyl)-2-methyl-1,1-ethylenedioxycyclohexanes (15). A solution of 80.6 g (0.36 mol) of **14** in 200 ml of anhydrous ether was slowly added to 14.6 g of $LiAlH_4$ in 1 l. of anhydrous ether and the mixture heated to reflux overnight. The excess $LiAlH_4$ was carefully decomposed with water, the ether layer separated, and the residue washed repeatedly with ether. The combined ether phases were concentrated without drying and the products (**15**) were used without purification.

3α,10- and 3β,10-Dimethyl-$\Delta^{1,9}$-octahydroquinoline (16α, 16β). Compounds **15** were dissolved in 200 ml of 2 N HCl and the solution was heated to reflux for 1 h, cooled, made strongly basic with a 50% solution of NaOH, and extracted repeatedly with petroleum ether. The extract was dried, the solvent and then the residue distilled, bp 106–110 °C (12 mm), yield 49.5 g (83% from **14**). Gas chromatography (Carbowax–KOH) shows two strongly overlapping peaks of **16α** and **16β** (together 93%) and ~7% by-product (presumably 3,8-dimethyl-$\Delta^{1,9}$-octahydroquinolines). Picrate, mp 117–122 °C.

Anal. Calcd for $C_{17}H_{22}N_4O_7$: C, 51.77; H, 5.62. Found: C, 51.60; H, 5.80.

NMR: ^{13}C see Table VI. Assignment of signals was possible by comparison with the spectrum of material recovered after hydrogenation (see below), which proved to be a pure isomer. Assignment of configurations was made on the basis of comparison with the corresponding 3,10-dimethyl-*cis*-decahydroquinolines **10** and **11,** but is only tentative.

^1H of **16α** (recovered after hydrogenation): CH_3(3) 0.89 ppm (d, 6.5 Hz); CH_3(10) 1.17 ppm; H_{2a} 2.90 ppm (d, J = 17 Hz, of d, J = 10 Hz, of d, J = 3 Hz); H_{2e} 3.70 ppm (d, J = 17 Hz, of m).

16β (from spectrum of mixture): CH_3(3), CH_3(10) as **16α**; H_{2a} 2.83 ppm; H_{2e} 3.66 ppm. Overlap with the signals of **16α** prevented a more detailed analysis.

Reduction of 16α and 16β with Sodium–Ethanol. A solution of 6.6 g of **16α** + **16β** in 80 ml of anhydrous ethanol was reduced with 20 g of sodium as previously reported.[19] The mixture of products was separated by preparative gas chromatography (Carbowax–KOH). Products in order of increasing retention times were as follows.

3β,10-Dimethyl-*cis*-decahydroquinoline (11), 46%. Picrate, mp 180–182 °C.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10. Found: C, 51.70; H, 6.00.

NCH_3 derivative: picrate, mp 147–148 °C.

3α,10-Dimethyl-*trans*-decahydroquinoline (17), 51%, mp 28–29 °C. Picrate, mp 193 °C.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10. Found: C, 51.55; H, 6.14.

^1H NMR CH_3(3) 0.77 ppm (d, J = 6.5 Hz); CH_3(10) 0.92 ppm (s); H_9 2.13 ppm; H_{2a} 2.22$_5$ ppm (t, J = 11.5 Hz); H_{2e} 3.02 ppm (d, J = 11.5 Hz, of d, J = 4 Hz, of d, J = 2 Hz).

NCH_3 derivative: picrate, mp 212–213 °C.

3β,10-Dimethyl-*trans*-decahydroquinoline (18), 3%. No derivatives of **18** were prepared because of the extremely small amount of isolated material.

^1H NMR CH_3(3) 1.14 ppm (d, J = 7.2 Hz); CH_3(10) 1.00 ppm (s); H_9 2.17$_5$ ppm; H_{2e}, H_{2a} 2.87 ppm (AB near degenerate).

Hydrogenation of 16α and 16β. The mixture of **16α** + **16β** was hydrogenated over Raney nickel in anhydrous ethanol in the manner described below. Products were **11** (41%), **18** (4.5%), and and **3α,10-dimethyl-*cis*-decahydroquinoline** (**10**), 30.5%, which could not be separated from 10% of **17.** Picrate of the mixture: mp 155–158 °C.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10. Found: C, 51.66; H, 6.18.

Table VII. Hydrogenations[a] of Quinolines, Tetrahydroquinolines, and $\Delta^{1,9}$-Octahydroquinolines[b]

Registry no.	Substance reduced (catalyst, temp)	Solvent (redn time[c])	%	Product[d]
91-22-5	Quinoline	HCl concd	90	*cis*-[e]
	(Pt, ~70 °C)	(72 h)	8	*trans*-[f]
			2	$\Delta^{1,9}$-Octahydro-
	Quinoline	H_2SO_4 12 N	60	*cis*-[e]
	(Pt, R.T.)	(20 h)	40	*trans*-[f]
1074-06-2	$\Delta^{1,9}$-Octahydroquinoline	C_2H_5OH, anhyd	78	*cis*-[e]
	(Raney nickel, R.T.)	(12 h)	22	*trans*-[f]
	$\Delta^{1,9}$-Octahydroquinoline	C_2H_5OH, anhyd	65	*cis*-[e]
	[Pd (5%) on C, R.T.]	(12 h)	35	*trans*-[f]
	$\Delta^{1,9}$-Octahydroquinoline	CH_3COOH (5% HCl)	50	*cis*-[e]
	(Pt, R.T., 1 atm)	(7 h)	50	*trans*-[f]
611-32-5	8-Methylquinoline	HCl concd	<1	8α-Methyl-*trans*-[f]
	(Pt, ~70 °C)	(100 h)	66	8α-Methyl-*cis*-[g]
			19[i,j]	8β-Methyl-*trans*-[f] / 8β-Methyl-*cis*-[h]
			14	8-Methyl-$\Delta^{1,9}$-octahydro
	8-Methylquinoline	CH_3COOH–HCl[k]	18	8α-Methyl-*trans*-[f]
	(Pt, ~70 °C)	(24 h)	44	8α-Methyl-*cis*-[g]
			23[i]	8β-Methyl-*trans*-[f] / 8β-Methyl-*cis*-[h] (little)
			15	8-Methyl-$\Delta^{1,9}$-octahydro
52761-53-2	8-Methyl-$\Delta^{1,9}$-octa-	HCl concd	29	Starting material
	hydroquinoline	(24 h[l])	29	8α-Methyl-*trans*-[f]
	(Pt, ~70 °C[l])		44	8α-Methyl-*cis*-[g]
			27	8β-Methyl-*trans*-[f]
	8-Methyl-$\Delta^{1,9}$-octa-	C_2H_5OH, anhyd	5	8α-Methyl-*trans*-[f]
	hydroquinoline	(12 h)	75	8α-Methyl-*cis*-[g]
	(Raney nickel, R.T.)		25[i]	8β-Methyl-*trans*-[f] / 8β-Methyl-*cis*-[h] (little)
91-62-3	6-Methylquinoline	HCl concd	26	6β-Methyl-*cis*-[m]
	(Pt, ~70 °C)	(24 h)	4	6α-Methyl-*trans*-[f]
			70	6α-Methyl-*cis*-[n]
52601-67-9	6-Methyl-$\Delta^{1,9}$-octa-	C_2H_5OH, anhyd	45	6α-Methyl-*trans*-[f]
	hydroquinoline	(12 h)	55	6α-Methyl-*cis*-[n]
	(Raney nickel, R.T.)			
612-58-8	3-Methylquinoline	HCl concd	91.5	3α-Methyl-*cis*-[o]
	(Pt, ~70 °C)	(24 h)	8.5	3β-Methyl-*cis*-[h]
28712-62-1	3-Methyl-5,6,7,8-	HCl concd	90	3α-Methyl-*cis*-[o]
	tetrahydroquinoline	(24 h)	10	3β-Methyl-*cis*-[h]
	(Pt, ~70 °C)			
37442-12-9	10-Methyl-$\Delta^{1,9}$-octa-	C_2H_5OH, anhyd[p]	85	10-Methyl-*cis*-[q]
	hydroquinoline	(12 h)	15	10-Methyl-*trans*-[f]
	(Raney nickel, R.T.)			
55905-40-3	8,10-Dimethyl-$\Delta^{1,9}$-	C_2H_5OH, anhyd	86	8α,10-Dimethyl-*cis*-[r]
	octahydroquinoline	(12 h)	14	8α,10-Dimethyl-*trans*-[f]
	(Raney nickel, R.T.)			
60490-22-4	3,10-Dimethyl-$\Delta^{1,9}$-	C_2H_5OH, anhyd	41	3β,10-Dimethyl-*cis*-[s]
	octahydroquinoline[s]	(100 h)	30.5	3α,10-Dimethyl-*cis*-[s]
	(Raney nickel, R.T.)		10	3α,10-Dimethyl-*trans*-[s]
			4.5	3β,10-Dimethyl-*trans*-[s]
			14	3α,10-Dimethyl-$\Delta^{1,9}$- octahydroquinoline[s]

[a] At 50 psi pressure of hydrogen, if not otherwise indicated. [b] For starting materials see ref 19. [c] Hydrogenations were continued for additional 3–8 h after noticeable hydrogen uptake had ceased. [d] Determined by VPC and listed in order of increasing retention times; products are decahydroquinolines if not otherwise indicated. [e] Picrate, mp 144–145 °C (lit.[20] 144–144.5 °C). [f] For identification of trans compounds see ref 19. [g] Picrate, mp 147 °C. Anal. Calcd for $C_{16}H_{22}N_4O_7$: C, 50.26; H, 5.80. Found: C, 50.17; H, 5.80. NCH_3 derivative: picrate, mp 201–202 °C. [h] Because of the extremely small amounts of pure compound isolated, no derivatives were prepared. [i] Considerable overlapping of signals in VPC on all columns available prevented determination of exact ratio. [j] Integration of NMR signals gave the relative ratio of 8β-methyl-*trans*:8β-methyl-*cis* of 30:70. [k] 42.5% CH_3COOH, 42.5% H_2O, 15% HCl concd. [l] After hydrogenation at R.T. for 24 h, only 24% of the starting material had reacted. The experiment was continued at elevated temperature for an additional 24 h. [m] Picrate, mp 136–137 °C. Anal. Calcd for $C_{16}H_{22}N_4O_7$: C, 50.26; H, 5.80. Found: C, 50.19; H, 5.69. NCH_3 derivative: picrate, mp 185–186 °C. [n] Hydrochloride, mp 266–268 °C (lit.[22] 263–264 °C for 6-methyl-*cis*-decahydroquinoline of otherwise unspecified configuration). Picrate, mp 175–176 °C. NCH_3 derivative: picrate, mp 191–192 °C. [o] Picrate, mp 155.5–156.5 °C. Anal. Calcd for $C_{16}H_{22}N_4O_7$: C, 50.26; H, 5.80. Found: C, 50.55; H, 5.81. NCH_3 derivative: picrate, mp 136–137 °C. [p] An identical isomer ratio was found after 48-hr hydrogenation time. Use of 96% aqueous ethanol gave ~60% cis, ~40% trans after 48 h hydrogenation. Picrate, mp 193 °C (lit.[21] 190–192 °C). NCH_3 derivative: picrate, mp 227–228 °C. [r] Picrate, mp 205–207 °C. Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10. Found: C, 51.66; H, 6.06. NCH_3 derivative: picrate, mp 217–218 °C. [s] See text.

NCH_3 derivative: picrate, mp 162–168 °C.

3α,10-Dimethyl-$\Delta^{1,9}$-octahydroquinoline (**16α**), pure by ^{13}C spectrum, 14%. Picrate: mp 126–127 °C.

Configuration of products **10, 11, 17,** and **18** was assigned by comparison of their ^{13}C and ^{1}H spectra with known spectra[2,19] of 3- and 10-methyldecahydroquinolines (see also Discussion).

Hydrogenations. These were carried out in a Parr low-pressure shaker type hydrogenation apparatus at 50 psi pressure of hydrogen. A wrap-around bottle heater was used where elevated temperatures were required.

Fifty millimoles of starting material was dissolved in a 500-ml Parr bottle in 50 ml of ice-cold acid (see Table VII) or in anhydrous ethanol; 2.5 g of platinum[23] or 5 g of Raney nickel[24] or 1.5 g of palladium (5%) on C was added, the bottle connected to the hydrogenator, the air removed, and the bottle heated to the required temperature. Hydrogenation was continued for 3–8 h after detectable hydrogen uptake had ceased. The solution was brought to room temperature and the catalyst was filtered off.

Acidic solutions were chilled in ice, made strongly basic with 50% NaOH solutions, and extracted repeatedly with petroleum ether. The combined extracts were dried over Na_2SO_4, the solvent was distilled off, and the residue was purified by total distillation at reduced pressure (without fractionation) by means of a Kugelrohr unit, using bulbs with ground glass joints. The distilled products were checked by VPC, using the columns described above. Compositions given in Table VI were determined this way.

Solutions in ethanol were worked up by distilling off the solvent, followed by total distillation of the residue and determination of the composition by VPC as described above.

Products were isolated by preparative VPC on the columns described above, and identified by their ^{1}H (Table V) and ^{13}C (Tables I and II) NMR spectra. *N*-Methyl derivatives were prepared by the usual Clark–Eschweiler procedure using HCOOH and HCHO; the melting points of the picrates of the NH precursors and of the *N*-methyl derivatives are listed in Table VII.

Compounds **1** and **1m** have been described previously.[3,20] The configuration of **2**[3d] had been deduced[21] from the analogy of its formation to the formation of *cis*-decahydroquinoline upon hydrogenation of the corresponding $\Delta^{1,9}$-octahydroquinoline. Compound **5** proved to be identical with a 6-methyl-*cis*-decahydroquinoline previously described[22] without specification of configuration of the methyl group. The remaining NH and NCH_3 *cis*-decahydroquinolines (with the exception of **4**[3d]) are new.

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Registry No.—**2m** picrate, 60490-21-3; **3** picrate, 60490-23-5; **3m** picrate, 60490-24-6; **5** HCl, 60490-25-7; **5** picrate, 60490-26-8; **5m** picrate, 60490-27-9; **6** picrate, 60490-28-0; **6m** picrate, 60490-29-1; **9** picrate, 60490-30-4; **9m** picrate, 60490-31-5; **10** picrate, 60490-32-6; **11** picrate, 60490-33-7; **13** (*R**,*R**), 60490-34-8; **13** (*R**,*S**), 60490-35-9; **14** (*R**,*R**), 60490-36-0; **14** (*R**,*S**), 60490-37-1; **15** (*R**,*R**), 60490-38-2; **15** (*R**,*S**), 60490-39-3; **16α**, 60490-40-6; **16α** picrate, 60490-41-7; **16β**, 60490-42-8; **16β** picrate, 60490-43-9; **17** picrate, 60490-45-1; **17** (NCH_3) picrate, 60490-47-3; **18,** 60490-48-4; 2-methylcyclohexanone, 583-60-8; methacrylonitrite, 126-98-7.

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