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(52) Double intensity in noise-decoupled spectrum.

Reduction of 5,6,7,8-Tetrahydroquinolines and 2,3,4,5,6,7,8,10-Octahydroquinolines to *trans*-Decahydroquinolines†

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The reduction of the title compounds with sodium in ethanol gives largely (~90%) *trans*-decahydroquinolines. When alkyl substituents or fused rings are present in the starting materials, the decahydroquinoline juncture of the product is still largely trans, but two (or more) epimers at the point of alkyl substitution (or fused ring juncture) result; they are separated readily by preparative gas chromatography. Similar reduction of 5,6,7,8-tetrahydroisoquinoline gives mainly $\Delta^{9,10}$-octahydroisoquinoline (58%) with lesser amounts of *cis*- (20%) and *trans*-decahydroisoquinoline (22%). Reduction of 5,6,7,8-tetrahydroquinoline with sodium in ethanol-*O*-*d* surprisingly gives mainly 2,3,3,4,9,10-hexadeuterio-*trans*-decahydroquinoline with some deuteration also occurring at position 8. Evidently exchange at an intermediate reduction stage is involved. Similar reduction of pyridine gives 2,3,3,4,5,5,6-heptadeuteriopiperidine. Reduction of $\Delta^{1,9}$-octahydroquinolines with sodium in ethanol provides an alternative path for the synthesis of *trans*-decahydroquinolines, including compounds with methyl substituents at C-10. The synthesis of certain deuterated analogs is also described. The ^{1}H NMR spectra of the compounds synthesized (including the deuterated analogs) as well as of their *N*-methyl, *N*-ethyl, and *N*-isopropyl derivatives are described in some detail.

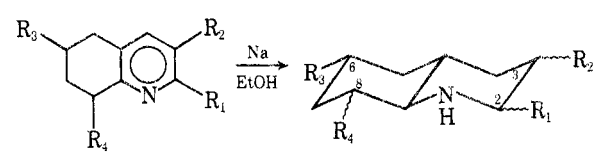
As explained in the accompanying paper,[1] there is a dearth of convenient known syntheses for the trans isomers of decahydroquinoline and decahyd oisoquinoline. Catalytic hydrogenation of quinolines and isoquinolines normally leads to the cis products, or at best (under special conditions) to mixtures in which the trans isomer may predominate. While the separation of *cis*- and *trans*-decahydroquinolines and decahydroisoquinolines by modern gas-chromatographic methods presents no insuperable difficulty, the problem is aggravated when there are alkyl substituents in the ring, in which case *four* diastereoisomers are formed: the α and β isomers[2] (referring to the stereochemical placement of the alkyl group) in both the cis and trans ring-fused series.

Chemical Reduction of 5,6,7,8-Tetrahydroquinolines. Having devised a convenient synthesis[1] of 5,6,7,8-tetrahydroquinolines and -isoquinoline by hydrogenation of the corresponding quinoline or isoquinoline over platinum oxide in strongly acidic medium, we decided to explore the sodium–ethanol[4,5] reduction of the benztetrahydro compounds as a means to obtaining the *trans*-decahydro compounds which we required in another investigation.[6] The results are summarized in Table I.

5,6,7,8-Tetrahydroquinoline (1) is reduced to *trans*-decahydroquinoline (90%) along with 10% of the cis isomer (Scheme I). In the case of the 2- (2), 3- (3), 6- (4), and 8-substituted (5) homologs, again the combined yield of the *trans*-decahydro product adds up to 90%, but in this case two diastereoisomers, α and β, result. Except in the case of the 6-methyl compound (9), where only the α (equatorial) isomer was isolated, the α and β isomers were cleanly separated by gas chromatography and identified by elemental

† This paper, and the preceding one, is dedicated by F.W.V. to Professor Dr. K. Kratzl on the occasion of his 60th birthday.

Scheme I



1	$R_1 = R_2 = R_3 = R_4 = H$	6	
2	$R_1 = CH_3$; $R_2 = R_3 = R_4 = H$	7	(α, β)
3	$R_2 = CH_3$; $R_1 = R_3 = R_4 = H$	8	(α, β)
4	$R_3 = CH_3$; $R_1 = R_2 = R_4 = H$	9	(α only)
5	$R_4 = CH_3$; $R_1 = R_2 = R_3 = H$	10	(α, β)

analysis, ^{1}H NMR (see below), and ^{13}C NMR[7] spectral study. In the tricyclic series, 1,2,3,4,5,6,7,8-octahydroacridine[1] (11) was reduced in high yield to *trans-syn-trans*-perhydroacridine (12, Scheme II).[8] The stereoisomeric mixture of 5,6,6a,7,8,9,10,10a-octahydrobenzo[*h*]quinolines (13) obtained by catalytic hydrogenation of the aromatic precursor[1] was reduced to a mixture of three perhydrobenzo[*h*]quinolines (14–16) in which the juncture of the piperidine to the adjacent cyclohexane ring was trans and the decalinoid ring fusion displayed the two possible cis junctures and one of the possible trans junctures (Scheme II).[8]

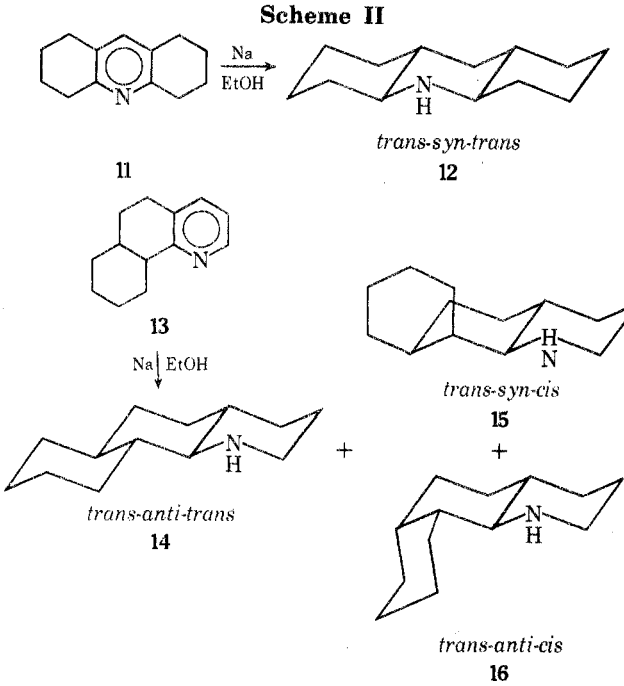
Unfortunately, 5,6,7,8-tetrahydroisoquinoline (17) is reduced in the main (58%) to the 1,2,3,4,5,6,7,8-octahydro compound[9] (18) with only minor amounts of *cis*- (20) and *trans*-decahydroisoquinoline (19) being formed (Scheme III). Apparently the sequence of reduction steps is such that the last of the three double bonds to be reduced ends up in the 9,10 position, where it is, of course, inert to further reduction.[10] A plausible though unproven sequence of events is suggested in Scheme IV. It should be noted that in the reduction of the tetrahydroquinoline analog (discussed below), even if a double bond remained in the 9,10

Table I
Reduction of 5,6,7,8-Tetrahydroquinolines and Related Compounds with Sodium in Ethanol

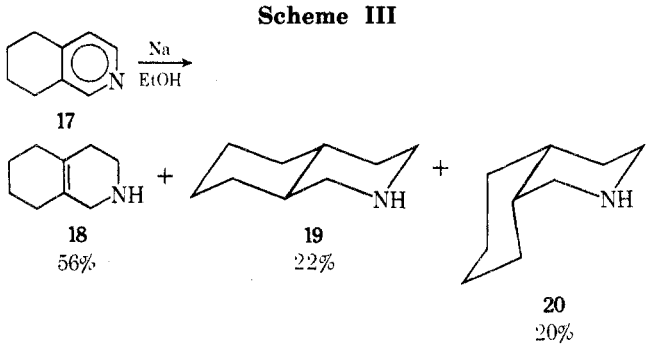
Starting material[a]	Products, composition, %[b,c]
5,6,7,8-Tetrahydroquinoline (1)	*trans*-Decahydroquinoline[d] (6), ~90
	cis-Decahydroquinoline,[e] ~10
2-Methyl-5,6,7,8-tetrahydroquinoline (2)	2β-Methyl-*trans*-decahydroquinoline[f] (7β), 54.5
	2α-Methyl-*trans*-decahydroquinoline[g] (7α), 41.5
	Two substances (cis?), unidentified, 4
3-Methyl-5,6,7,8-tetrahydroquinoline (3)	3α-Methyl-*trans*-decahydroquinoline[h] (8α), 60
	3β-Methyl-*trans*-decahydroquinoline[i] (8β), 30
	Other substance, unidentified,[j,k] 10
6-Methyl-5,6,7,8-tetrahydroquinoline (4)	6α-Methyl-*trans*-decahydroquinoline[l] (9α), 91
	One other substance, unidentified, 9
8-Methyl-5,6,7,8-tetrahydroquinoline (5)	8α-Methyl-*trans*-decahydroquinoline[m] (10α), 48
	8β-Methyl-*trans*-decahydroquinoline[n] (10β), 51
	8α-Methyl-*cis*-decahydroquinoline,[k] traces
5,6,7,8-Tetrahydroisoquinoline (17)	*trans*-Decahydroisoquinoline[o] (19), 22
	cis-Decahydroisoquinoline[p] (20), 20
	$\Delta^{9,10}$-Octahydroisoquinoline[q] (18), 58
1,2,3,4,5,6,7,8-Octahydroacridine (11)	*trans-syn-trans*-Perhydroacridine[r] (12), >90
	Other products, not identified, <10
5,6,6a,7,8,9,10,10a-Octahydrobenzo[*h*]-quinoline (13)	*trans-anti-trans*-Perhydrobenzo[*h*]quinoline[s] (14), ~30
	trans-anti-cis-Perhydrobenzo[*h*]quinoline[t] (16), ~18
	trans-syn-cis-Perhydrobenzo[*h*]quinoline[t] (15), 52

[a] For synthesis of starting materials see ref 1. [b] For nomenclature, see ref 2. [c] Analysis by gas chromatography. For columns used see Experimental Section. [d] Mp 48° (lit.[19] mp 48–48.5°); because of slight overlap of peaks the percent values are only approximate. [e] By comparison with an authentic sample, prepared according to ref 19. [f] Hydrochloride, mp 292–293° (lit.[22] mp 293–294°). [g] Hydrochloride, mp 284–285° (lit.[22] mp 284–285°). [h] Mp 81° (from petroleum ether; a melting point of 70–71° is reported for an unspecified mixture of 3-methyldecahydroquinolines.[4] Picrate, mp 179°. [i] Because of the extremely small amounts of material isolated, no derivatives were prepared. [j] From the ^{1}H NMR spectrum, one substance was assigned the structure of 3-methyl-$\Delta^{3,4}$-octahydroquinoline. Insufficient material was isolated for further identification. Based on comparison of retention times, the other two substances are believed to be 3α- and 3β-methyl-*cis*-decahydroquinoline. [k] Cis compounds for comparison were synthesized according to ref 19; synthesis and characterization is described elsewhere.[7] [l] Mp 68–69° [lit. for 6-methyl-*trans*-decahydroquinoline without specification of configuration of the methyl group, 68–69°: S. Fujise and M. Iwakiri, *Bull. Chem. Soc. Jpn.*, 11, 293 (1936)]. [m] Anal. Calcd for $C_{10}H_{19}N$: C, 78.37; H, 12.50. Found: C, 78.82; H, 12.20. Picrate, mp 193–194°. Hydrochloride, mp 247–248° dec. *N*-Benzoyl-8α-methyl-*trans*-decahydroquinoline, mp 48°. [n] Anal. Calcd for $C_{10}H_{19}N$: C, 78.37; H. 12.50. Found: C, 78.42; H, 12.35. Picrate, mp 148.5–149.5°. Hydrochloride, mp 279–280° dec. *N*-Benzoyl-8β-methyl-*trans*-decahydroquinoline, mp 127–128°. [o] Picrate, mp 174–175° [lit. mp 175–176°: W. L. F. Armarego, *J. Chem. Soc. C*, 377 (1967)]. [p] Picrate, mp 149–150° (lit.[o] mp 149–150°). [q] Picrate, mp 176–176.5° (lit.[9] mp 172°). Hydrochloride, mp 149° (lit.[9] mp 150°). [r] Mp 89° (petroleum ether) [lit. mp 90.5–91.5°: H. Adkins and H. L. Coonradt, *J. Am. Chem. Soc.*, 63, 1563 (1941)]. [s] Mp 41–42° (from petroleum ether). Anal. Calcd for $C_{13}H_{23}N$: C, 80.76; H, 11.99. Found: C, 80.74; H, 11.83. [t] Mp 76° (from petroleum ether). Anal. Calcd for $C_{13}H_{23}N$: C, 80.76; H, 11.99. Found: C, 80.69; H, 11.82.

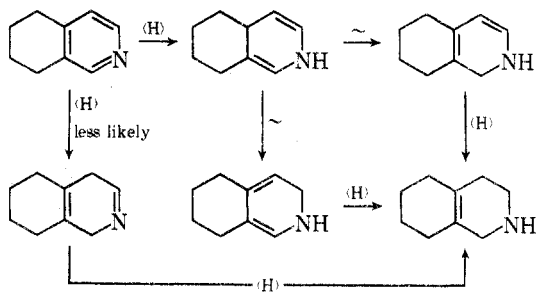
Scheme II



Scheme III



Scheme IV



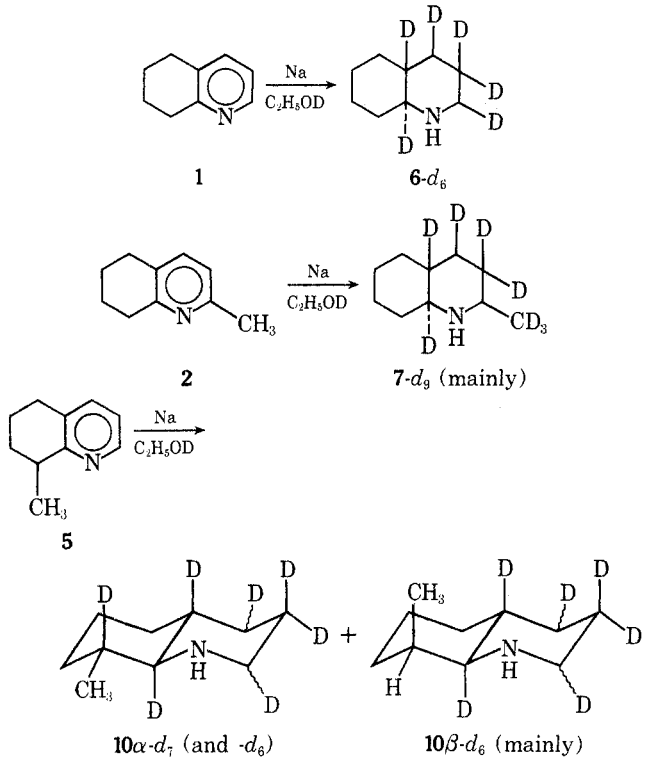
position, it would be enaminic and thus subject to further reduction.

Reduction of 5,6,7,8-Tetrahydroquinoline with Sodium in Ethanol-*O*-*d*. To obtain deuterated analogs of some of the above-described *trans*-decahydroquinolines for a ^{13}C NMR study, we reduced the benztetrahydro compounds with sodium in ethanol-*O*-*d*. This reduction, shown in Scheme V for **1**, provided a surprise in that both the ^{13}C NMR and the mass spectrum of the product indicated it to be largely a hexadeuterio (rather than the expected 2,3,4,9,10-pentadeuterio) species, containing also some heptadeuterated material. The ^{13}C NMR spectrum unequivocally indicated that the extra deuterium was at C-3, since the ^{13}C NMR signal of C-3 was suppressed, owing to the missing nuclear Overhauser effect[11] of the absent proton there. The additional deuteration occurred at C-8, which displayed a triplet superimposed upon a singlet in the ^{13}C NMR spectrum. In Scheme VI are shown two alternative sequences for the reduction of **1** with sodium in ethanol. Both proceed via the 1,4,5,6,7,8-hexahydro intermediate,[12] which is then assumed to rearrange to either the 3,4,5,6,7,8-hexahydro or the 4,10,5,6,7,8-hexahydro derivative. The former would exchange, in the presence of EtOD–EtO^-, at C-3, the latter at C-8, the exchange involving a HC–C=N– proton in either case. Further reduction would lead to $\Delta^{1,9}$ compound in the former case (with subsequent exchange at C-8) and to the $\Delta^{1,2}$ (with subsequent exchange at C-3) in the latter, with ultimate reduction to the partially deuterated decahydro species in either case. Since the dienoid species (C=N–C=C) is probably more fleeting than the enamine species, so that exchange is more likely to occur in the latter, and since the proton at C-3 is much more extensively exchanged than that at C-8, we prefer the reaction path via the 4,10,5,6,7,8-hexahydro intermediate.

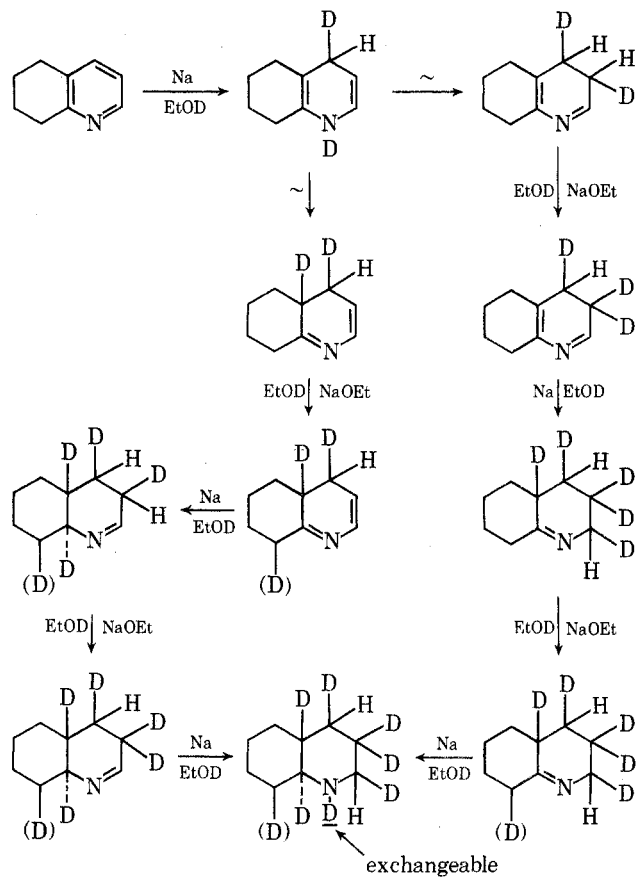
The reductions are summarized in Table II.

When the 2-methyl homolog **2** was similarly reduced (Scheme V), the ^{13}C NMR and ^1H NMR spectra of the product (deuterated **7**) indicated extensive H–D exchange in the methyl group (which passes through a N=C–CH_3 intermediate in the course of the reaction). This is further evidence that the last intermediate may be the $\Delta^{1,2}$-octahydro derivative.

Scheme V



Scheme VI



Reduction of the 8-methyl homolog **5** was particularly interesting because of different degrees of deuterium incorporation in **10α** and **10β** (Scheme V). The **10β** epimer contained six deuterium atoms only, whereas **10α** was appreciably heptadeuterated, with the extra deuterium at C-8. The α isomer (Scheme V) has an equatorial C-8 methyl group and an axial C-8 hydrogen; in the intermediate $\Delta^{1,9}$-imine intermediate, the corresponding carbanion is well disposed for p–π overlap with the C=N double bond[13] and thus presumably prone to ready H–D interchange. In contrast, the β isomer has an equatorial C-8 hydrogen which, in the imine precursor, is nearly in the plane of the double bond and thus ill disposed for p–π overlap in the anion. Exchange of this proton is presumably so slow as to be negligible in the time period of survival of the imine.

We also reduced pyridine with sodium–ethanol-*O*-*d* and showed by mass spectral, ^1H NMR, and ^{13}C NMR analysis that the product formed (85.5%) is piperidine-*2,3,3,4,5,5,6-d*$_7$, as would be expected on the basis of the analogy with Scheme IV.

Reduction of 2,3,4,5,6,7,8,10-Octahydroquinolines. A few cases of reactions of $\Delta^{1,9}$-octahydroquinolines with sodium in ethanol are summarized in Scheme VII and the product compositions are shown in Table III. Except for the case of the 9-methyl compounds **26** and **27α** (which cannot, of course, be obtained from quinoline precursors), the lengthy (see below) route via the $\Delta^{1,9}$-octahydroquinolines offers no advantages over the shorter and more convenient two-stage reduction of quinolines, especially since the product compositions in the two cases are quite similar (compare Table III with Table I).

Table II
Reductions of Tetrahydro- and Octahydroquinolines with Sodium and Ethanol-*O*-*d*

Starting material	Product[a]
Pyridine	Piperidine-*2,3,3,4,5,5,6*-d_7[b]
5,6,7,8-Tetrahydroquinoline (**1**)[c]	*trans*-Decahydroquinoline-*2,3,3,4,9,10*-d_6[c,d]
2-Methyl-5,6,7,8-tetrahydroquinoline (**2**)	2β-Methyl-*trans*-decahydroquinoline-*2,3,3,4,9,10,*-α,α,α-d_9[e]
	2α-Methyl-*trans*-decahydroquinoline-*2,3,3,4,9,10,*-α,α,α-d_9[e]
8-Methyl-5,6,7,8-tetrahydroquinoline (**5**)	8α-Methyl-*trans*-decahydroquinoline-*2,3,3,4,9,10*-d_6[d]
	8β-Methyl-*trans*-decahydroquinoline-*2,3,3,4,9,10*-d_6 and -*2,3,3,4,8,9,10*-d_7
5,6,7,8-Tetrahydroisoquinoline (**14**)	$\Delta^{9,10}$-Octahydroisoquinoline-*1,3,4,4*-d_4 and -*1,3,4*-d_3
$\Delta^{1,9}$-Octahydroquinoline (**21**)	*trans*-Decahydroquinoline-*9,10*-d_2[f]
10-Methyl-$\Delta^{1,9}$-octahydroquinoline (**24**)[g]	10-Methyl-*trans*-decahydroquinoline-*8,8,9*-d_3[h]

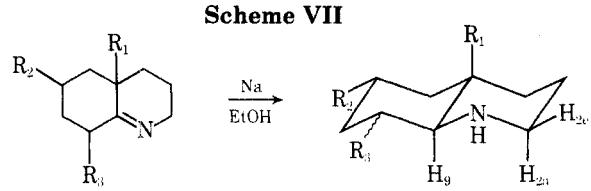
[a] Products isolated; for product composition see Tables I and III, if not otherwise indicated. [b] Crude product contains about 8% starting material but can be purified by preparative gas chromatography. [c] Neither the starting material (1) nor *trans*-decahydroquinoline (6) exchange hydrogen when treated with NaOEt in EtOD. [d] Small amounts of *2,3,3,4,8,9,10*-d_7 product admixed; see Discussion. [e] This is the major product, but there is also some side-chain mono- and dideuterated material and some deuteration at C-8; see Discussion. [f] Ca. 60%; rest is *trans*-decahydroquinoline-*9*-*d* and very little *trans*-decahydroquinoline-*8,9,10*-d_3. [g] Heated to reflux with EtOD and NaOEt for 3 hr, and then reduced with Na. [h] Small amount of *8,9*-d_2 product admixed.

Table III
Reduction of $\Delta^{1,9}$-Octahydroquinolines with Sodium and Ethanol

Starting material ($\Delta^{1,9}$-octahydroquinoline)	Product, composition, %[a-c]
Unsubstituted (**21**)	*trans*-Decahydroquinoline[d,e] (**6**), ~95
	cis-Decahydroquinoline,[d,e] ~5
6-Methyl- (**22**)	6α-Methyl-*trans*-decahydroquinoline (**9**α), 94
8-Methyl- (**23**)	8α-Methyl-*trans*-decahydroquinoline (**10**α), 66
	8α-Methyl-*cis*-decahydroquinoline,[f] 6
	8β-Methyl-*trans*-decahydroquinoline (**10**β), 28
10-Methyl- (**24**)	10-Methyl-*trans*-decahydroquinoline[d,e,g] (**26**), ~90
	10-Methyl-*cis*-decahydroquinoline,[d,e,h] ~10
8,10-Dimethyl- (**25**)	8α,10-Dimethyl-*trans*-decahydroquinoline[i] (**27**α) ~95
	One other substance, unidentified, ~5

[a] For nomenclature see ref 2. [b] Products characterized in Table I are not described further. [c] By gas chromatography; for columns used see Experimental Section. [d] Because of overlap of peaks percent values are only approximate. [e] No formation of cis product by this procedure is indicated in ref 15. [f] By comparison with authentic sample; see ref 7. [g] Picrate, mp 227–228° (lit.[15] mp 224–225°). [h] Picrate, mp 193° (lit.[15] mp 190–192°). [i] Anal. Calcd for $C_{11}H_{23}N$: C, 78.98; H, 12.65. Found: C, 78.76; H, 12.91. Picrate, mp 220–222°.

Scheme VII



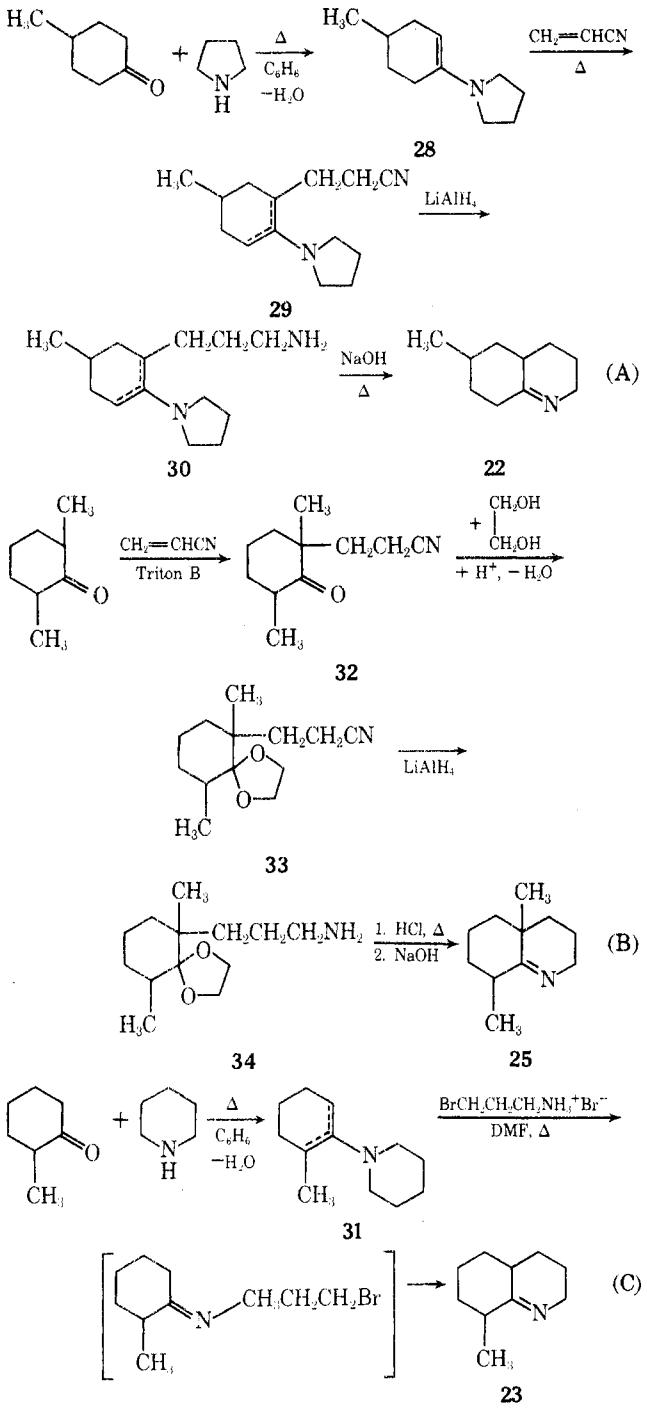
21	$R_1 = R_2 = R_3 = H$	**6**
22	$R_2 = CH_3$; $R_1 = R_3 = H$	**9**α
23	$R_3 = CH_3$; $R_1 = R_2 = H$	**10**α, β
24	$R_1 = CH_3$; $R_2 = R_3 = H$	**26**
25	$R_1 = R_3 = CH_3$; $R_2 = H$	**27**α

The starting materials required for the $\Delta^{1,9}$-octahydroquinoline route were synthesized either from the pyrrolidine enamine of cyclohexanone and acrylonitrile followed by lithium aluminum hydride reduction and hydrolysis[14] (Scheme VIII, A, used for the parent compound[14] and its 6-methyl derivative), or from 2-methylcyclohexanone and acrylonitrile, followed by ketal formation with ethylene glycol, hydride reduction,[15] and acid-catalyzed deketalization and cyclization[15] (Scheme VIII, B used for the 10-methyl[15] and 8,10-dimethyl compounds), or from the piperidine enamine of 2-methylcyclohexanone and 3-bromopropylamine in a one-step reaction[16,17] (Scheme VIII, C used for the 8-methyl compounds).

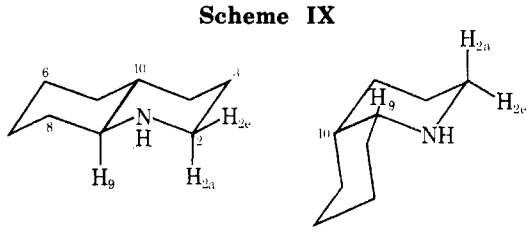
We also studied the reduction of $\Delta^{1,9}$-octahydroquinoline (**21**) and its 10-methyl homolog (**24**) with sodium–ethanol-*O*-*d* (Table II). Reduction of **21** involved partial exchange of the 10 hydrogen prior to reduction; in the case of **24** exchange of the α hydrogens (in this case the two hydrogens located at C-8) was furthered by treating the compound with NaOEt–EtOD before reduction.

Identification of Products. NMR Spectra. Configurational assignment of the products rests both on ^{1}H NMR and on ^{13}C NMR spectra. The ^{1}H NMR spectra of the NH compounds (**6–10**, Scheme I), as well as two of the three perhydrobenzo[*h*]quinolines (**12**, **15**, Scheme II), are summarized in Table IV with emphasis on the downfield protons α to the ring nitrogen (the remaining protons, with the exception of those of the methyl group, are generally not well resolved). The ^{13}C NMR spectra will be reported in detail elsewhere,[7] but we have included in Table IV the *C*-methyl signals which are characteristic of conformation (and configuration): axial methyl groups are upfield from equatorial ones.[18] The spectra for *N*-alkyl derivatives (*N*-methyl, *N*-ethyl, *N*-isopropyl) are reported elsewhere[6] and will be commented on briefly.

Scheme VIII



Scheme IX



The ^1H NMR spectra of *cis*- and *trans*-decahydroquinoline (**6**) have been investigated by Booth and Bostock.[19] Characteristic of the trans isomer is the downfield equatorial proton at C-2 (H_{2e}, Scheme IX) as a doublet (geminal splitting), further split by gauche protons, at 3.04 ppm; a relatively complex, widely split signal for the corresponding axial proton H_{2a} at 2.62 ppm; and a broad, ill-resolved signal for the tertiary axial proton (H_9) at ca. 2.08 ppm. The spectrum (and the other spectra to be discussed in the sequel) may be understood on the following premises: (1) axial protons, especially when α to nitrogen, are shifted upfield, relative to equatorial ones; (2) tertiary protons tend to be downfield from secondary ones; and (3) methyl or methylene substituents (R) on the carbon adjacent to one occupied by the proton under consideration (RC–CH) produce upfield shifts if gauche and downfield shifts if anti to the proton in question.[20] In addition, of course, the usual rules of coupling (large for a,a, small for a,e or e,e) apply.[21] Thus H_9 is upfield from H_{2a} even though the former is tertiary, because of the upfield shifting effect of the methylene groups CH_2-4 and CH_2-5 (gauche). In the cis isomer (Scheme IX, only the major conformer in which syn-axial interactions are minimized is shown) H_9 is shifted downfield to 2.82 ppm, since it is now anti to the methylene group at C-10 rather than gauche. The H_2's are unchanged.

The 6-methyl compound **9** (Scheme I) has essentially the same spectrum as **6**, confirming the trans ring juncture. The position (0.87 ppm) and coupling constant (6 Hz) of the methyl group suggests its equatorial placement which is confirmed by the ^{13}C NMR signal (22.39 ppm).[18]

The 8-methyl compounds, **10**α and **10**β (Scheme I), also have the H_2 protons essentially unchanged; H_9 in **10**α is shifted upfield beyond 1.8 ppm to the point where it almost disappears in the envelope of the cyclohexanoid protons; this is to be expected as the result of the presence of an extra gauche methyl group. In contrast, **10**β has H_9 at 2.23 ppm as a neat double doublet (J_1 = 9, J_2 = 4.5 Hz). The downfield shift (relative to **6**) is consistent with the presence of an anti methyl group and the double doublet results from one axial–axial and one axial–equatorial split. The position and coupling constants for the methyl groups (Table IV) support the assignment, the axial methyl in **10**β being slightly further downfield and having a slightly larger coupling constant. The ^{13}C NMR signals are also in agreement.

In the 3-methyl compounds, **8**α and **8**β (Scheme I), the signal of H_9 is, expectedly, little shifted relative to **6**, thus confirming the trans ring juncture. In **8**α (equatorial Me) H_{2e} is surprisingly at almost the same field (3.00 ppm) as in **6**; the expected upfield shift caused by a gauche methyl group does not occur. It is, however, seen in H_{2a}, which is shifted upfield to 2.25 ppm and appears as a near triplet with $J_{gem} \approx J_{anti}$ (there is no gauche proton). In **8**β, in contrast, H_{2e} and H_{2a} are nearly degenerate at 2.84 ppm, as might be expected as a result of an upfield shift of H_{2e} by the gauche methyl group and a downfield shift of H_{2a} (relative to **6**) by the same methyl group positioned anti. The splittings and chemical shifts of the methyl groups (Table IV) support the assignment of configuration to **8**α (equatorial methyl) and **8**β (axial methyl), as do the ^{13}C NMR signals.

In one of the two 2-methyl compounds (**7**α,β, Scheme I), the β isomer (equatorial CH_3), the shift of H_9 (2.16 ppm) is little changed from that in **6** and the axial H_{2a} shows up as a very broad (multiply split) signal at 2.70 ppm. In **7**α (axial methyl), on the other hand, the syn-axial methyl shifts H_9 downfield to 2.45 ppm, which is characteristic of a van der Waals shift. H_{2e} in **7**α, being equatorial, is narrower than the axial H_{2a} in **7**β and displays a quartet further split narrowly by ring protons (gauche). The methyl proton and ^{13}C NMR signals and the proton splittings (Table IV) support the assignments.[22]

The 10-methyl compound **26** (Scheme VII) has nearly the same H_{2e} and H_{2a} (shifts) as **6**, although H_{2a}, in this case, is a nearly perfect triplet of doublets (J_1 = 12, J_2 = 3.5 Hz) as a result of equal geminal and anti coupling con-

Table IV
Pertinent Chemical Shifts[a] of *trans*-Decahydroquinolines and Perhydrobenzo[*h*]quinolines[b]

Substance[c]	^{1}H H_{2e}	H_{2a}	H_9	CH_3	^{13}C CH_3
Parent (**6**)	3.04 (d, 12)	2.62	2.08		
2α-CH_3 (**7α**)	3.30_5 (q, 7)		2.45	1.20 (d, 7)	18.59
2β-CH_3 (**7β**)		2.70	2.16	1.07 (d, 6)	22.91
3α-CH_3 (**8α**)	3.00 (d, 12)	2.24_5 (t, 10.5)	1.99	0.82 (d, 6)	19.58
3β-CH_3 (**8β**)	2.84		~2	1.09 (d, 7)	17.65
6α-CH_3 (**9α**)	3.07_5 (d, 12)	2.65_5	2.06	0.87 (d, 6)	22.39
8α-CH_3 (**10α**)	3.08 (d, 12)	2.59	<1.8	0.91 (d, 6)	18.56
8β-CH_3 (**10β**)	3.08 (d, 12)	2.63	2.23 (d, 9, of d, 4.5)	0.95 (d, 7)	12.61
10-CH_3 (**26**)	3.06 (d, 12)	2.64 (t, 12, of d, 3.5)	2.21	0.93 (0.5)	15.57
8α,10-Dimethyl (**27α**)	3.14_5 (d, 12)	2.61_5 (t, 12, of d, 3.5)	1.85 (d, 9.5)	0.96[d] 0.85 (d, 6)[e]	16.72[d] 18.92[e]
trans-anti-trans[f] (**14**)	3.11 (d, 12)	2.58_5	<2.0		
trans-syn-cis[f] (**15**)	3.11 (d, 12)	2.63_5	2.21 (d, 9, of d, 4)		

[a] In $CDCl_3$ from Me_4Si; since part of the ABXY pattern of H_{2e} and H_{2a} is not resolved, the reported values are centers of signals in the spectra. [b] The parenthesized data are multiplicity and coupling constants (in hertz); only clearly recognizable patterns are reported. [c] Substituted *trans*-decahydroquinoline, if not otherwise indicated. [d] CH_3-10. [e] CH_3-8. [f] Perhydrobenzo[*h*]quinoline.

Table V
Pertinent Chemical Shifts[a] of Ring-Deuterated *trans*-Decahydroquinolines

R	6-R-*d*		10β-R-*d*			10α-R-*d*		
	H_{2e}	H_{2a}	H_{2e}	H_{2a}	CH_3[b]	H_{2e}	H_{2a}	CH_3[b,c]
H	2.94	2.55_5	2.98_5	2.56	0.93_5 (7 Hz)	3.01	2.53	0.89_5 (6 Hz) 0.88_8
CH_3	2.73_5	1.95_5	2.76	1.95	0.94 (7 Hz)	2.85	2.76	0.92 (6 Hz) 0.91_3
CH_2CH_3	2.78	2.13	2.83_5	2.05	0.94 (7 Hz)	3.10_3	2.53	0.92 (6 Hz) 0.91_3
$CH(CH_3)_2$	2.84	1.97	2.83	1.98	0.92 (7 Hz)	3.18	2.52_3	0.91_3 (6 Hz) 0.90_6

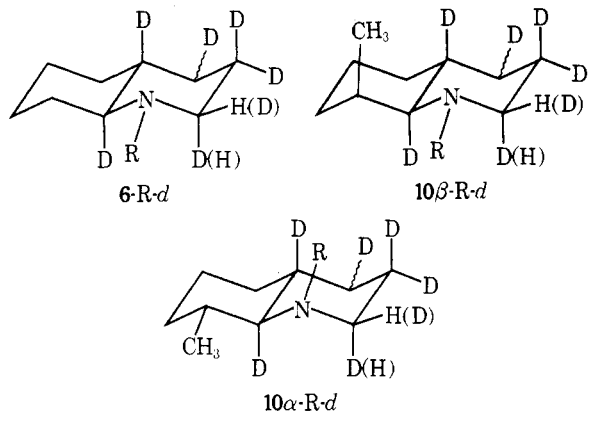
[a] In CF_2BrCF_2Br, from Me_4Si. Chemical shifts of *trans*-decahydroquinoline in this solvent are, H_{2e}, 2.995, H_{2a} 2.585, H_9 2.025; of 8α-methyl-*trans*-decahydroquinoline, H_{2e} 3.045, H_{2a} 2.555, CH_3 0.895. The difference between chemical shifts in Tables IV and V is therefore partly due to a solvent effect, and partly to D isotope effects (see footnote *c*). [b] Parenthesized values: coupling constants. [c] The first set of signals are doublets of the compounds with a proton on C-8; in the second set (shifted upfield by 0.7 Hz by the deuterium) this proton is exchanged against deuterium and the corresponding methyl signal is a singlet.

stants and a much smaller gauche coupling constant, H_9 is shifted downfield by the anti-placed 10-methyl group to 2.21 ppm and is considerably narrower than in **6**, since one of the anti splittings is absent. A long-range coupling of the 10-methyl group, presumably to H_9 (J = 0.5 Hz), could also be discerned. Finally, the 8,10-dimethyl compound **27α** (Scheme VII) is almost identical with **26** in the H_{2e} and H_{2a} region, but H_9 is shifted back upfield to 1.85 ppm by the gauche methyl group at C-8, which is thus shown to be equatorial. Also, H_9 is a clean doublet, J = 9.5 Hz, since it is split by only one proton (at C-8) in anti location. This split is the best indication for the trans ring junction as well as equatorial methyl at C-8; the latter is also supported by the ^{1}H NMR shift and coupling constant and the ^{13}C NMR shift (Table IV).

In the tricyclic series, the trans-anti-trans isomer of the perhydrobenzo[*h*]quinoline **14** (Scheme II) was recognized by the close similarity of its ^{1}H NMR spectrum with that of the analogous 8α-methyl compound (**10α**). In contrast, the trans-syn-cis compound (**15**, Scheme II) bears an extremely close resemblance in both chemical shifts and coupling constants of all three salient protons to **10β**. These two structures are thus established unequivocally by a conformational analogy. ^{13}C NMR spectroscopy[7] confirms the configurations of these two isomers and the third one (**16**), which was not obtained pure enough for ^{1}H spectral investigation.

The ^{1}H NMR spectra of the *N*-methyl derivatives of **6**, **8α**, **8β**, **9α**, **10α**, **10β**, **14**, **15**, **16**, **26**, and **27α** and the *N*-ethyl and *N*-isopropyl derivatives of **6**, **8**, **10α**, **10β**, and **26** have been tabulated elsewhere.[6] These spectra are of lesser interest than those of the NH precursors because the gauche effect of the equatorial *N*-alkyl group is to shift H_{2a} and H_9 upfield to a point where they are largely overlaid with the envelope of the other protons. An exception occurs in the compounds in which the *N*-alkyl group is axial (NCH_3 of

Scheme X



10α, **14** and **16**) or at least largely axial (NCH_3 of **27α**, *N*-ethyl and *N*-isopropyl of **10α**); H_{2a} and H_9 are now shifted downfield by (a) the anti effect of the *N*-alkyl group and (b) by the absence of the upfield shifting axial pair of electrons on nitrogen to the point where they may again be clearly discerned. However, in case of the NCH_3 derivatives of **10α**, **14**, **16**, and **27α**, H_{2e} and H_{2a} have nearly identical chemical shifts, and the ABXY pattern is nearly degenerate and hard to resolve. The methylene protons in the *N*-ethyl compounds are diastereotopic, and the AA′ part of the AA′X_3 appears in the downfield region, partly overlaid with the signal of H_{2e}. This difficulty was overcome by either decoupling the methyl protons of the ethyl group, whereupon the AA′X_3 collapsed to an AA′, or by recording the deuterium noise-decoupled spectra of the NCH_2CD_3 analogs.

Of more interest are the deuterium noise decoupled spectra of *N*-methyl-*trans*-decahydroquinoline-*2,3,3,4,-9,10-d*$_6$ (**6**-Me-*d*) and its 8-methyl homologs (**10β**-Me-*d* and **10α**-Me-*d*) shown in Scheme X (R = Me). It should be noted that these compounds are singly but nonspecifically deuterated at C-2, so that in each case they are mixtures of the 2α-*d* and 2β-*d* epimers. Also, because of dideuteration at C-3, the sole remaining proton at C-2 is an entirely uncoupled singlet[24] which can be clearly discerned even if it falls into the envelope of the rest of the protons. The pertinent chemical shifts for these compounds and the corresponding *N*-ethyl and *N*-isopropyl homologs are shown in Table V and are of interest in that they provide values not only for ν_a and ν_e in the *N*-methyl equatorial (**10β**, R = Me) and mobile (**6**) species, but also in the *N*-methyl axial case (**10α**, R = Me). Shifts in the former situation have previously been seen in appropriately substituted *N*-methylpiperidines[23] and values of $\Delta(\nu_e - \nu_a)$ of 1.19–1.20 ppm in the N-Me(e) and of 1.02 or 1.10 ppm (in CH_2Cl_2 or toluene-d_8 at −80°C) in the mobile series were reported. The values in the decahydroquinoline series (in CF_2BrCF_2Br at room temperature) are somewhat different: $\Delta_{Me(e)}$ = 0.81 ppm (from **10β**-Me-*d*) and $\Delta_{Me(mobile)}$ = 0.78 ppm (from **6**-Me-*d*). In addition, one can determine a value $\Delta_{Me(a)}$ = 0.09 ppm from the shifts in **10α**-Me-*d*. It is interesting that, on the usual assumption[25] that the value for the mobile system is the weighted average of that for the anancomeric (conformationally biased) systems $\Delta_{Me(mobile)} = n_e\Delta_{Me(e)} + n_a\Delta_{Me(a)}$, one may compute $K = m_e/n_a$ = 23 and $-\Delta G°$ = 1.86 kcal/mol, in excellent agreement with values obtained by more accurate methods.[6] It is of interest that the corresponding Δ values in the secondary amines (NH compounds) are nearly constant: **6**-*d*, 0.39 ppm; **10β**-*d*, 0.43 ppm; **10β**-*d*, 0.48 ppm. Thus, if it is true that these values are determined mainly by the position of the lone pair on nitrogen and not by the position of the *N*-methyl group,[23] the equatorial–axial NH equilibria in **6**, **10β**, and **10α** must be similar, with the peri or syn-axial methyl group exercising little if any bias on the NH.

Experimental Section

Melting points were determined on a Sargent Mel-Temp variable temperature heating block and are uncorrected. 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 12 ft, aluminum, 20% Carbowax 20M + 10% KOH on Chromosorb W, 80/100 mesh, and 12-ft stainless steel 30% SE-30 on Chromosorb W, 60/80 mesh, at temperatures between 80 and 200°. A Varian Aerograph Series 2700 instrument with 0.375-in. aluminum column with matching phase on Chromosorb A was used for preparative gas chromatography.

NMR spectra were recorded on a Varian XL-100 instrument equipped with Fourier transform for ^{13}C analysis. Substances for the spectra summarized in Table IV were dissolved in $CDCl_3$, the deuterium-decoupled spectra of the polydeuterated compounds (Table V) were recorded in $C_2F_4Br_2$. The solvents provided the internal lock signal (D or F); 2% Me_4Si was added to the samples as internal reference. ^{13}C spectra in Table IV were recorded in $CDCl_3$.

Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6E. Microanalyses were carried out by Galbraith Laboratories, Inc.

Starting Materials. Syntheses of the various methyl-substituted 5,6,7,8-tetrahydroquinolines (**1–5**), of 5,6,7,8-tetrahydroisoquinoline (**17**), 1,2,3,4,5,6,7,8-octahydroacridine (**11**), and 5,6,6a,7,8,9,10,10a-octahydrobenzo[*h*]quinoline (**13**) have been described in detail elsewhere.[1] $\Delta^{1,9}$-Octahydroquinoline (**21**) was prepared from *N*-1-cyclohexenylpyrrolidine and acrylonitrile as described by Cohen and Witkop.[14] 10-Methyl-$\Delta^{1,9}$-octahydroquinoline (**24**) was synthesized as described by Henshall and Parnell;[15] the intermediate 1-(2-cyanoethyl)-2,2-ethylenedioxy-1-methylcyclohexane was reduced with $LiAlH_4$ (see below for 8,10-dimethyl-$\Delta^{1,8}$-octahydroquinoline).

6-Methyl-$\Delta^{1,9}$-octahydroquinoline (22). *N*-(4-Methyl-1-cyclohexenyl)pyrrolidine (28). 4-Methylcyclohexanone (100.8 g, 0.9 mol), pyrrolidine (85.2 g, 1.2 mol), and benzene (45 ml) were heated to reflux for 5 hr, the water formed being separated with a Dean-Stark trap. When the theoretical amount of water had been collected, solvent and excess pyrrolidine was evaporated at reduced pressure; the product was used without purification.

1-*N*-Pyrrolidinyl-2-(2-cyanoethyl)-4-methylcyclohexene (29). The crude **28** was dissolved in 60 ml of dioxane, 52.5 g (0.99 mol) of freshly distilled acrylonitrile was added, and the mixture was heated to reflux for 2 hr. The solvent was distilled off and the residue was distilled at reduced pressure, yield 153 g (78%), bp 125–130° (0.5 mm).

1-*N*-Pyrrolidinyl-2-(3-aminopropyl)-4-methylcyclohexene (30). The above product (**29**, 65.4 g, 0.3 mol) was dissolved in 150 ml of anhydrous ether and added slowly to 11.5 g (0.3 mol) of $LiAlH_4$ in 650 ml of anhydrous ether. After addition was complete, the suspension was stirred for 1 hr. The excess $LiAlH_4$ was decomposed carefully with ethyl acetate and water, the ether phase was decanted, and the aqueous phase was extracted four times with ether. The combined ether phases were concentrated without drying, and the product was used without purification.

6-Methyl-$\Delta^{1,9}$-octahydroquinoline (22). The above product (**30**) was mixed with 25 ml of aqueous NaOH (2 *N*) and heated under nitrogen for 1 hr on a boiling water bath. After cooling to room temperature the mixture was extracted repeatedly with petroleum ether, and the extracts were combined and dried. The solution was concentrated, and the residue was distilled at reduced pressure. The product (20.4 g, 45% from the nitrile) boiled at 110.5–111° (20 mm); it was pure by VPC. ^1H NMR: δ 0.97 (d, J = 6 Hz, 3 H, CH_3), 3.57 (broad s, 2 H, H-2's), remainder broad, unresolved 0.8–2.5 ppm, 12 H. Picrate, mp 136–137°. Anal. Calcd for $C_{16}H_{20}N_4O_7$: C, 50.53; H, 5.30. Found: C, 50.68; H, 5.52.

8-Methyl-$\Delta^{1,9}$-octahydroquinoline (23). *N*-(2-Methylcyclohexenyl)piperidine (**31**),[26] bp 74–77° (1.2 mm) [lit. bp 48° (1.7 mm)] (0.11 mol), 3-bromopropylamine hydrobromide (0.10 mol), and 30 ml of dimethylformamide were placed in a 250-ml three-necked flask, equipped with a thermometer and heated to 80°, when an exothermic reaction started. The flask was cooled by immersion in an ice bath to keep the temperature of the reaction mixture below 110°. When the reaction subsided, the mixture was heated with magnetic stirring at 100–110° for 12 hr and cooled to

room temperature, and 100 ml of water and 7 ml of concentrated HCl were added. The solution was extracted three times with ether (discarded). The aqueous solution was overlaid with petroleum ether, and was made strongly basic by addition of a concentrated solution of NaOH. The basic solution was extracted repeatedly with petroleum ether, the organic extracts were dried, the solvent was evaporated, and the residue was distilled at reduced pressure. 8-Methyl-$\Delta^{1,9}$-octahydroquinoline (**23**), bp 116–119° (30 mm), was collected. The product was a mixture of two stereoisomers, the major component having the CH_3 group α, the minor β; two methyl signals were visible in the ^1H NMR spectrum, and the ^{13}C spectrum[7] showed two sets of signals. ^1H NMR: δ 1.05 (d, J = 6 Hz, CH_3-α, 2.25 H), 1.14 (d, J = 7.5 Hz, CH_3-β, 0.75 H), 3.54 (broad s, 2 H, H-2's), rest broad, unresolved, 1.0–2.3 ppm. Ratio of CH_3 signals in ^{13}C spectrum:[7] 25% β, 75% α. Picrate, mp 151–152°. Anal. Calcd for $C_{16}H_{20}N_4O_7$: C, 50.53; H, 5.30. Found: C, 50.60; H, 4.89.

8,10-Dimethyl-$\Delta^{1,9}$-octahydroquinoline (25). 2-(2-Cyanoethyl)-2,6-dimethylcyclohexanone (32). 2,6-Dimethylcyclohexanone (mixture of isomers) was washed with dilute alkali and water, dried over $MgSO_4$, and distilled. To 6.35 g (0.5 mol) of the ketone and 2 g of Triton B, 7.5 g (0.14 mol) of freshly distilled acrylonitrile was added dropwise. The reaction vessel was cooled intermittently to keep the temperature below 35°. After addition was complete the mixture was stirred at room temperature overnight, diluted with ether, neutralized with dilute HCl, washed with a saturated aqueous solution of NaCl, and dried over $MgSO_4$. The ether was evaporated at reduced pressure and the residue was distilled, yield 12.65 g (50.5%), bp 117° (0.7 mm).

2-(2-Cyanoethyl)-2,6-dimethyl-1,1-ethylenedioxycyclohexane (33). Compound **32** (12.65 g, 0.071 mol) was dissolved in 50 ml of benzene, 5.2 g of ethylene glycol and 200 mg of *p*-toluenesulfonic acid were added, and the mixture was heated to reflux. The water formed was collected in a Dean-Stark trap. After 48 hr the solvent was evaporated, and the residue was dissolved in ether and washed three times with water. The ether solution was dried over $MgSO_4$, the solvent was removed at reduced pressure, and the residue was distilled, bp 108–112° (0.3 mm), yield 14.2 g (90%).

2-(3-Aminopropyl)-2,6-dimethyl-1,1-ethylenedioxycyclohexane (34). A solution of **33** (14.2 g, 68 mmol), dissolved in 40 ml of anhydrous ether, was added slowly to a suspension of 2.6 g (68 mmol) of $LiAlH_4$ in 150 ml of anhydrous ether, and the mixture was heated to reflux for 4 hr. The excess $LiAlH_4$ was decomposed carefully with ethyl acetate and water, the ether layer was separated, the aqueous phase was extracted repeatedly with ether, and the combined ether phases were concentrated without drying. The product (**34**) was used without further purification.

8α,10-Dimethyl-$\Delta^{1,9}$-octahydroquinoline (25). Compound **34** was dissolved in 40 ml of 2 *N* HCl and the solution was heated to reflux for 1 hr, cooled, made strongly basic with a concentrated solution of NaOH, and extracted repeatedly with petroleum ether. The organic extract was dried and the solvent was distilled. The residue was distilled at reduced pressure in a Kugelrohr distillation apparatus, air bath temperature 140° (22 mm). The product was pure by VPC. ^1H NMR: δ 1.02 (d, J = 6 Hz, 3H, CH_3-8), 1.18 (s, 3 H, CH_3-10), 3.65 (broad s, 2 H, H-2's), rest broad, unresolved 1.0–3.0 ppm. Picrate, mp 185–186°. Anal. Calcd for $C_{17}H_{22}N_4O_7$: C, 51.77; H, 5.62. Found: C, 51.99; H, 5.74.

Reductions with Sodium and Ethanol. These were carried out as described in the literature.[4,15,27] Anhydrous ethanol had to be used for the reduction of pyridine or else the yields of piperidine were drastically lowered.[28]

Reductions with Sodium in Ethanol-*O*-*d*. Ethanol-*O*-*d* was prepared from tetraethyl orthosilicate and D_2O as described by Pasto and Meyer.[29] The uncatalyzed decomposition of the tetraethyl orthosilicate was unsatisfactory: even after prolonged reaction times (5–7 days) at elevated temperatures (reflux) only part of the starting materials had reacted.[30] Addition of small amounts of DCl[30] or $SOCl_2$ led to a very fast and quantitative reaction. The ethanol-*O*-*d* was then heated to reflux for 48 hr with and distilled from crushed CaO.

Piperidine-*2,3,3,4,5,5,6-d*$_7$. Pyridine (4 g) (dried over solid KOH and distilled) was dissolved in 30 ml of ethanol-*O*-*d* and the solution was heated to reflux. Ten grams of sodium (cut in small pieces and stored under anhydrous ether) was gradually added. When part of the sodium was dissolved and sodium ethoxide started precipitating, 20 ml more ethanol-*O*-*d* was gradually added and the mixture was heated until all the sodium had reacted. After addition of 60 ml of water the mixture was distilled until the boiling temperature had reached 100°. The distillate was neutralized with dilute HCl and the solvent was evaporated. The residue was dried in a vacuum desiccator over P_2O_5, yield 5.97 g (97%). One gram of the impure piperidinium-d_7 hydrochloride was dissolved in 2 ml of water, and the solution was covered with petroleum ether and made strongly basic with aqueous NaOH. The basic solution was repeatedly extracted with petroleum ether, the organic extracts were dried over KOH, and the solvent was carefully distilled off. Analytical VPC showed two signals: piperidine (92%) and pyridine (8%). The mixture of amines was separated by preparative VPC (Carbowax 20M KOH column, see above; column temperature 80°), and the mass spectrum of the piperidine-d_7 recorded giving a parent peak of *m/e* 92 (d_7). The ^{13}C spectrum (in $C_2F_4Br_2$) (proton noise-decoupled) showed two triplets: δ 24.91 (J_{CD} = 20 Hz, C-4); 47.34 ppm (J_{CD} = 20 Hz, C-2,6); both triplets were further split by long-range C–D coupling. A very weak and broad signal at ~27 ppm (of C-3 and C-5) was partly overlaid by the signal of C-4. The deuterium noise-decoupled ^1H spectrum in $C_2F_4Br_2$ showed two singlets of equal intensity, H on C-2 and C-6, 2.70 ppm, and NH and H on C-4 at 1.49 ppm.

***trans*-Decahydroquinoline-*2,3,3,4,9,10-d*$_6$.** 5,6,7,8-Tetrahydroquinoline (1.5 g) was dissolved in 25 ml of ethanol-*O*-*d* and reduced by gradual addition of 6 g of sodium and an additional 20 ml of ethanol-*O*-*d* as described above. When all the sodium had reacted, the mixture was poured into water and the resulting aqueous solution was extracted repeatedly with petroleum ether. The petroleum ether extracts were dried over KOH, the solvent was distilled off on a rotary evaporator, and the solid residue was recrystallized three times from small amounts of petroleum ether, yield 1.14 g, mp 47–48°.

Mass spectrum: The strongest peak corresponded to a mass of 145 (d_6), with a signal of approximately half that intensity for d_7 (146) (*trans*-decahydroquinoline-*2,3,3,4,8,9,10-d*$_7$). The signal for C-7 in the ^{13}C spectrum was split into two peaks with a shift difference of 2.4 Hz, the more upfield signal being due to deuterium at C-8. Full details of the ^{13}C spectrum will be reported elsewhere.[7]

In a similar way 2-methyl- and 8-methyl-5,6,7,8-tetrahydroquinoline and 5,6,7,8-tetrahydroisoquinoline were reduced. The products were separated by preparative VPC.

2α-Methyl-*trans*-decahydroquinoline-*d* and 2-β-Methyl-*trans*-decahydroquinoline-*d*. The mass spectra of both compounds had the largest peak at a mass of 162 (d_9), with large peaks at 161 and 160, and a smaller peak at 163. The ^{13}C spectrum indicates that the compound with mass 163 has deuterium in 2, 3, 3, 4, 8, 9, and 10 and three deuterium atoms in the side chain.

8α-Methyl-*trans*-decahydroquinoline-*d*. The largest peak in the low-voltage mass spectrum corresponds to a mass of 159, with a signal of half that intensity at 160. Both the signals of the CH_3 and C-7 in the ^{13}C spectrum are split, the lower intensity upfield signal being due to deuterium at C-8.

8β-Methyl-*trans*-decahydroquinoline-*d*. The largest peak in the low-voltage mass spectrum is at 159; the peak at 160 was small. No second signal for the CH_3 and C-7 in the ^{13}C spectrum could be seen.

$\Delta^{9,10}$-Octahydroisoquinoline-*d*. The mass spectrum shows ca. 60% d_4 product (mass 141) and *ca.* 40% d_3. The ^{13}C spectrum shows triplets for the signals of C-1 (48.52 ppm, 49.18 in the undeuterated analog) and C-3 (43.01, 43.78 in the undeuterated compound). Only a small triplet due to residual proton at C-4 is visible; the larger part (60%) has this proton exchanged (*1,3,4,4-d*$_4$), and the signal is dissipated.

***trans*-Decahydroquinoline-*d*.** $\Delta^{1,9}$-Octahydroquinoline was reduced with Na–EtOD and the *trans*-decahydroquinoline-*d* was isolated as described above for the 5,6,7,8-tetrahydroquinoline. The ^{13}C spectrum showed complete disappearance for C-9 (fully deuterated), two signals for both C-4 and C-5 in a ratio of 4:6, due to exchange of *ca.* 60% of the proton at C-10, a signal for C-8 which was hardly reduced in intensity, and only a very small additional upfield signal for C-7, indicating very little exchange of H at C-8.

10-Methyl-*trans*-decahydroquinoline-*8,8,9-d*$_3$. 10-Methyl-$\Delta^{1,9}$octahydroquinoline (2 g) was added to 25 ml of ethanol-*O*-*d* in which 500 mg of sodium has been dissolved. The solution was heated to reflux for 3 hr under a protective atmosphere of nitrogen. Then 6 g of sodium and 15 ml of ethanol-*O*-*d* were gradually added. When all the sodium was dissolved, the reaction mixture was poured into water, the aqueous solution was extracted with petroleum ether, the petroleum ether extract was dried, and the solvent was distilled. The mixture of 10-methyl-*trans*- (ca. 90%) and -*cis*- (ca. 10%) decahydroquinoline-*d* (1.81 g, isomer ratio by VPC) was dissolved in ether, 3.25 g of picric acid in ether was added, and the picrate was recrystallized twice from ethanol. The recrystallized picrate was decomposed in aqueous NaOH and the 10-

methyl-*trans*-decahydroquinoline-*d* was extracted with petroleum ether. The extract was dried and the solvent was evaporated. The residue was distilled in a Kugelrohr apparatus to yield 950 mg of product, pure by VPC.

The ^{13}C spectrum showed no visible signal for C-9 (completely deuterated), a triplet of weak intensity for C-8 (due to C-8 substituted by a proton and a deuterium; the dideuterio substituted C-8 is not visible) and two signals for C-7 with a shift difference of 2.5 Hz (due to C-8 HD and C-8 D_2). The signal for C-6 was noticeably broadened by the deuterium at C-8.

Exchange Experiments with *trans*-Decahydroquinoline and 5,6,7,8-Tetrahydroquinoline. *trans*-Decahydroquinoline (or 5,6,7,8-tetrahydroquinoline) (1 g) was added to 25 ml of ethanol-*O*-*d* in which 500 mg of sodium had been dissolved. The solution was heated to reflux for 3 hr, cooled to room temperature, and diluted with 100 ml of water. The amine was extracted with petroleum ether, the extracts were dried, and the solvent was evaporated. The residue was distilled in a Kugelrohr apparatus and the distillate was shown to be pure by VPC. Both mass spectrum and ^{13}C spectrum were identical with those of untreated starting material.

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Registry No.—**1**, 10500-57-9; **2**, 2617-98-3; **3**, 28712-62-1; **4**, 52601-65-7; **5**, 52601-66-8; **6**, 767-92-0; **6**-R-*d* (R = H), 55905-17-4; **6**-R-*d* (R = CH_3), 55905-18-5; **6**-R-*d* (R = CH_2CH_3), 55905-19-6; **6**-R-*d* [R = $CH(CH_3)_2$], 55905-20-9; **7***α*, 18609-01-3; **7***β*, 18610-37-2; **8***α*, 52679-13-7; **8***α* picrate, 55905-21-0; **8***β*, 52601-71-5; **9***α*, 55905-22-1; **10**-R-*d* (R = H), 55905-23-2; **10**-R-*d* (R = CH_3), 55905-24-3; **10**-R-*d* (R = CH_2CH_3), 55905-25-4; **10**-R-*d* [R = $CH(CH_3)_2$], 55905-26-5; **10***α*, 52761-68-9; **10***α* picrate, 55905-27-6; **10***α* HCl, 55905-28-7; **10***α* *N*-benzoyl analog, 55905-29-8; **10***β*, 52730-00-4; **10***β* picrate, 55905-30-1; **10***β* HCl, 55905-31-2; **10***β* *N*-benzoyl analog, 55905-32-3; **11**, 1658-08-8; *trans*-**13**, 55905-33-4; *cis*-**13**, 55905-34-5; **14**, 55925-21-8; **15**, 55925-22-9; **16**, 55925-23-0; **17**, 36556-06-6; **18**, 2721-62-2; **21**, 1074-06-2; **22**, 52601-67-9; **22** picrate, 55905-35-6; *cis*-**23**, 55905-36-7; *cis*-**23** picrate, 55905-37-8; *trans*-**23**, 55905-38-9; *trans*-**23** picrate, 55905-39- **24**, 37442-12-9; **25**, 55905-40-3; **26**, 45846-79-5; **27***α*, 55905-41-4; **27***α* picrate, 55905-42-5; **28**, 39716-23-9; **29**, 55905-07-2; **30**, 55905-09-4; **31**, 55905-11-8; **32**, 7647-22-5; **33**, 55905-43-6; **34**, 55905-44-7; piperidine-*2,3,3,4,5,5,6-d*$_7$, 55905-45-8; *trans*-decahydroquinoline-*2,3,3,4,9,10-d*$_6$, 55905-17-4; 4-methylcyclohexanone, 589-92-4; pyrrolidine, 123-75-1; acrylonitrile, 107-13-1; *cis*-2,6-dimethylcyclohexanone, 766-42-7; *trans*-2,6-dimethylcyclohexanone, 766-43-8; ethylene glycol, 107-21-1.

References and Notes

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