Selectivity in the Hydrogenation of 6- and 8-Substituted-quinolines

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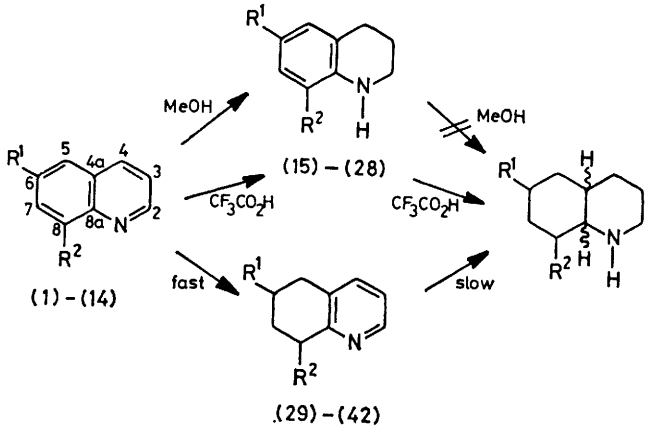
Quinoline (1) and the 6- or 8-substituted-quinolines (2)—(14) (R = Me, Pr^i, Bu^t, Ph, OMe, OH, CF_3, or F) were hydrogenated catalytically on platinum under either weakly basic (solvent MeOH) or strongly acidic (solvent CF_3CO_2H) conditions. In methanol the only product was the corresponding 1,2,3,4-tetrahydro-compound. In trifluoroacetic acid, compounds hydrogenated in the benzene ring were isolated as major products; both electron-withdrawing and electron-donating substituents at C-6 or C-8 cause (sometimes drastic) reduction in yield. The products were characterized by their ^1H and ^{13}C n.m.r. spectra.

SINCE the first attempts of hydrogenation of quinoline (1) and related phenyl-substituted or -condensed pyridines it was generally accepted [1] that saturation takes place at the pyridine ring to give, in the case of (1), 1,2,3,4-tetrahydroquinoline, with further hydrogenation leading to the fully saturated systems. Only recently it has been shown [2] that this only applies to hydrogenation in neutral or weakly acidic medium, whereas in strong acid (12N-HCl, 12N-H_2SO_4, or CF_3CO_2H) the reaction leads to the 5,6,7,8-tetrahydro-, and then (less easily) to mainly *cis*-decahydro-products.



	R^1	R^2		R^1	R^2
(1), (15), (29)	H	H	(8), (22), (36)	OMe	H
(2), (16), (30)	Me	H	(9), (23), (37)	H	OMe
(3), (17), (31)	H	Me	(10), (24), (38)	OH	H
(4), (18), (32)	H	Pr^i	(11), (25), (39)	H	OH
(5), (19), (33)	Bu^t	H	(12), (26), (40)	CF_3	H
(6), (20), (34)	H	Bu^t	(13), (27), (41)	H	CF_3
(7), (21), (35)	H	Ph	(14), (28)	H	F
(42)	H	C_6H_{11}			

When the scope of this change in behaviour towards hydrogenation of quinoline was investigated,[2b] a number of questions remained unanswered. The yield of 5,6,7,8-tetrahydro-product in the case of 6-methylquinoline (2) was somewhat lower, and the yield in the case of 8-methylquinoline (3) was considerably lower than for the parent compound (1).[2b] In consideration of the synthetic potential of the procedure it was interesting to determine the influence of other substituents at C-6 or C-8; *i.e.* if diminished yields of the 5,6,7,8-tetrahydro-product could be linked to the electron-donating properties of the substituents, and if the difference between 6- and 8-substitution was a general phenomenon with possibly steric reasons.

RESULTS

In addition to (1), (2), and (3), 8-isopropylquinoline (4), 6- and 8-t-butylquinoline (5) and (6), 8-phenylquinoline (7), 6- and 8-methoxyquinoline (8) and (9), 6- and 8-hydroxyquinoline (10) and (11), 6- and 8-trifluoromethylquinoline (12) and (13), and 8-fluoroquinoline (14) were investigated. Synthesis of (4) and (5) was accomplished by a modified Skraup synthesis as described for (3).[3] A synthetic procedure starting with substituted cyclohexanones to give 2,3,4,4a,5,6,7,8-octahydroquinolines [4] which were then oxidized to the fully aromatic compounds [5] was also used for (4) and (6). The remaining compounds were prepared as described in the literature (see Experimental section).

Hydrogenations in methanol proceeded extremely slowly at atmospheric pressure and were consequently carried out at elevated pressure in a Parr shaker-type apparatus. Hydrogen uptake stopped when the 1,2,3,4-tetrahydro-stage was reached, and yields of (15)—(28) were essentially quantitative with no hydrogenolysis being observed. Hydrogenations in trifluoroacetic acid were carried out at atmospheric pressure, and the hydrogen uptake was followed graphically by plotting the amounts of hydrogen absorbed against reduction time. A noticeable break in the curves indicated complete hydrogenation of the benzene rings in (1)—(6), and (less clearly) of the benzene rings in (7). The uptake curves for (8)—(14) showed no noticeable breaks because of simultaneously occurring hydrogenolysis of the hetero-substituents and because of the formation of considerable amounts of 1,2,3,4-tetrahydro-products which are then further reduced to more hydrogenated compounds. Hydrogenations were stopped when hydrogen 10% in excess of the amount to reach the tetrahydro-stage had been taken up. The reaction mixtures were worked up as described in the Experimental section, and the composition of the product mixtures was determined by g.l.c. Major products were isolated and identified by ^1H and ^{13}C n.m.r. spectroscopy, and by elemental analysis. The respective yields of products for the hydrogenations of (1)—(14) in CF_3CO_2H are collected in Table 1. The ^{13}C n.m.r. chemical-shift data of the 1,2,3,4- and of the 5,6,7,8-tetrahydroquinolines, together with the data of the starting quinolines not yet reported in the literature, are collected in Table 2. The hydroxy-substituted quinolines and 1,2,3,4-tetrahydroquinolines [(10), (11), (24), and (25)] were not soluble enough in $CDCl_3$ to record their spectra.

^{13}C *N.M.R. Spectra.*—Substituent effects for the *ortho*-carbons C-7 and C-8a, and for the *meta*-carbons C-6 and C-4a, are rather different for the quinolines substituted at C-8. This is not surprising because of the different substitution of these carbon atoms, and because of the additional interaction between R^2 and N.[6] In the case of the 6-substituted-quinolines, shift effects on the *meta*-positions C-8 and C-4a are nearly equal (and small). The effects on C-5 and C-7, on the other hand, are surprisingly different. This was observed previously for (2);[6] indeed, the two carbon atoms were wrongly assigned at first.[6a] In this work differences were found to be large for 6-t-butylquinoline (C-5, −5.0; C-7, −1.1 p.p.m.), but to be very large for the 6-methoxy-compound (8) (C-5, −22.6; C-7, −7.2 p.p.m.). Assignments were based on undecoupled spectra on the principles outlined previously.[6a,b] It is interesting that shift effects for C-5 and C-7 are nearly equal for the electron-withdrawing 6-trifluoromethyl substituent, but that the effects for the *meta*-carbons differ substantially in this case.

Assignment of the carbon atoms in (15) is based on comparison with the spectrum of tetralin [7] and substituent effects derived by comparison of aniline and toluene,[7] and on the effects of the substitution at C-6 and C-8. In contrast to the quinolines, substitution at C-6 leads to practically identical effects on C-5 and C-7 in all compounds investigated.

Assignment of signals in (29) is unambiguous except for the signals due to C-6 and C-7, which may be interchanged. The methyl groups of the 8-isopropyl-compound (32) and the carbon atoms C-2′ and C-6′ in the cyclohexane ring of (42) are diastereotopic and have different chemical shifts.

TABLE 1

Hydrogenation [a] of 6- and 8-substituted-quinolines in trifluoroacetic acid

Starting quinoline	Product reduced in benzene ring(s) [%]	Other products [%]
(1)	(29) [80]	(15) [6]
		Starting material [5]
		Higher hydrogenated [9]
(2)	(30) [59]	(16) [23]
		Starting material [12]
		Higher hydrogenated [6]
(3)	(31) [51]	(17) [31]
		Starting material [12]
		Higher hydrogenated [6]
(4)	(32) [70]	(18) [10]
		Octahydro-product [6]
		Higher hydrogenated [14]
(5)	(33) [86]	(19) [7]
		Starting material [3]
		Higher hydrogenated [4]
(6)	(34) [85]	Octahydro-product [12]
		Higher hydrogenated [3]
(7)	(35) [69]	(21) [23]
	(42) [6]	Higher hydrogenated [2]
b	(35) [64]	(21) [15]
	(42) [14]	Higher hydrogenated [6]
(8)	(29) [46]	(22) [19]
	(36) [9]	Starting material [29]
c	(29) [57]	(22) [16]
	(36) [11]	Starting material [13]
(9)	(29) [8]	(23) [33]
	(37) [43]	Starting material [4]
		Higher hydrogenated [10]
(10)	(29) [41]	*d*
	(38) [>5]	
(11)	(29) [13]	*d*
	(39) [38]	
(12)	(40) [25]	(26) [72]
		Starting material [3]
e	(40) [30]	(26) [68]
		Starting material [2]
(13)	(41) [44]	(27) [28]
		Starting material [11]
		Higher hydrogenated [17]
e	(41) [62]	(27) [28]
		Starting material [2]
		Higher hydrogenated [8]
(14)	(29) [43]	(28) [10]
		Starting material [26]
		(15) [8]
		(1) [13]
c	(29) [79]	(28) [10]
		(15) [9]
		(1) [2]

[a] At room temperature and at atmospheric pressure; 10 mmol starting quinoline in 30 ml CF_3CO_2H unless indicated. Hydrogenation to an uptake of 2.2 mol H_2 per mol quinoline unless indicated. [b] Uptake 3.3 mol H_2 per mol (7). [c] Deliberately over-hydrogenated. [d] Unchanged starting material and 1,2,3,4-tetrahydro product was not isolated in this case (see Experimental section). [e] Starting quinoline (10 mmol) in CF_3CO_2H (40 ml).

DISCUSSION

Only the two t-butyl compounds (5) and (6) of all the compounds investigated show an increase in hydrogenation selectivity compared to the parent compound (1). In the alkyl-substituted series the two methylquinolines lead to the highest proportion of pyridine-hydrogenated products; hydrogenation selectivity is (1) > (2) < (5) and (1) > (3) < (4) < (6). The influence of the alkyl substituents is thus not simply a question of increasing bulkiness. It is interesting that in early investigations [8] on quinoline hydrogenation in alkaline solution similar effects were observed: increasing methyl substitution led to a stabilization of the substituted (benzene or pyridine) part of the molecule against hydrogenation. Thus the selectivity of hydrogenation is reversed by the change from neutral to strongly acid medium, whereas the substituent effect of the methyl group is not.

Comparison of the 6- and 8-alkyl-substituted compounds shows that any molecular deformations caused by strain between the 8-substituent and NH^+ [which doubtlessly occurs in (5)] is of no consequence to the hydrogenation selectivity; the two t-butyl compounds give practically identical results. The difference between (2) and (3) (*cf.* ref. 2*b*) is more likely due to reasons of charge distribution than to steric causes. A still larger difference occurs between the 6- and 8-trifluoromethyl compounds (12) and (13). The strongly electron-withdrawing trifluoromethyl group in compounds (12) and (13) results in reduction of yield of 5,6,7,8-tetrahydro-products; the higher yield for the 8-trifluoromethyl derivative (13) compared to the 6-substituted compound (12) should also be noted.

Other substituents with electron-donating or -withdrawing properties, which are not changed by the conditions of hydrogenation, are unfortunately scarce. The results with the methoxy-, hydroxy-, and fluoro-substituted quinolines are difficult to interpret due to the extensive hydrogenolysis of substituents in trifluoro-

acetic acid (no hydrogenolysis occurred in methanol).* It is nevertheless evident that the electron-donating hydroxy- and methoxy-substituents, similar to the electron-withdrawing CF_3-group, lead to diminished selectivity of hydrogenation: the sum of 5,6,7,8-tetrahydro-products is always lower than the 80% obtained from (1). Any major change in electron density from the situation in (1) [or the t-butyl compounds (5) and (6), which show the highest selectivity] leads to a reduction of the stabilization of the pyridine, and of the activation of the benzene ring towards hydrogenation caused by the strong acid.

Hydrogenation of 8-phenylquinoline (7) shows a preferential saturation of the benzene ring fused to the pyridine compared to the phenyl substituent. This confirms a simultaneous activation of the benzene and passivation of the pyridine part of the quinoline by the strong acid, but the phenyl ring at C-8, totally stable against hydrogenation in methanol solution, is also activated by CF_3CO_2H to become eventually saturated; indeed, further hydrogenation after 3 mol H_2 per mol (7) had been consumed gave mainly (42), along with some perhydrogenated material.

First results of the hydrogenation of *N*-methylquinolinium salts [9] indicate that introduction of the positive charge at nitrogen is not the deciding factor for the selectivity of hydrogenation depending on the acidity of the solution: hydrogenation of *N*-methylquinolinium chloride in methanol gave *N*-methyl-1,2,3,4-tetrahydroquinoline in high yield; hydrogenation in CF_3CO_2H gave the *N*-methyl-5,6,7,8-tetrahydroquinolinium salts as the major product. Stabilization of the pyridine ring against hydrogenation at high concentration of acid has long been known,[10] and may be caused by strong solvation; the increase of the 6- and 8-trifluoromethyl-5,6,7,8-tetrahydroquinolines (40) and (41) upon further addition of CF_3CO_2H might have its cause in a still higher solvation. The activation of the benzene ring is difficult to understand. One possibility could be formation of π- or σ-complexes, changing the aromatic character and thus the ease of hydrogenation. Such interactions might be sensitive to changes in electron density caused by the different substituents. Since the activation by strong acid also takes place with the quinolinium salts,[9] this implies introduction of a second positive charge into the molecule. If such a species can occur in trifluoroacetic acid, the stationary concentration must certainly be low. Hydrogenation of (1) in CF_3CO_2D as solvent gave (29) with an average of three to four deuterium atoms in the hydrogenated ring (by mass spectrometry and n.m.r.),[9] giving support to this hypothesis, and additional experiments are presently being carried out to obtain further information.

* The synthetic possibilities are severely diminished by this hydrogenolysis. Platinum oxide, which gave excellent results with the alkyl-substituted compounds,[2b] was adhered to in order to have comparable results, but catalysts like rhodium or ruthenium will be tested to give a possible reduction in the amount of hydrogenolysis.

EXPERIMENTAL

^1H n.m.r. spectra were recorded on a Varian EM-360 spectrometer with internal-lock facility. Samples were dissolved in $CDCl_3$ with 5% $SiMe_4$ as internal reference and lock substance. ^{13}C N.m.r. spectra were recorded on a Varian XL-100-15 Fourier-transform spectrometer at 25.16 MHz in 12-mm o.d. tubes, solvent $CDCl_3$ with 2% $SiMe_4$ as reference. Digital resolution was 1.2 Hz (0.05 p.p.m.) at 8 000 data points and 5 KHz spectral width. G.l.c. determinations were carried out on a Carlo Erba 2300 AC gas chromatograph, on a glass capillary column (SE 30; length 50 m), and on a Varian Aerograph, Series 1400. Columns were aluminium, 0.125-in o.d., length 4 m. Phases were 20% Carbowax 20 M + 10% KOH, or 20% SE 30, on Chromosorb W, 80—100 mesh. Both instruments were equipped with flame-ionization detectors. T.l.c. was carried out on plastic sheets coated with aluminium oxide 60 F_{254} neutral (type E, Merck) or aluminium DC-cards SIF (Kieselgel + fluorescence indicator; Riedel-de Haen). Melting points were determined on a Kofler hot-stage except for hydrochlorides which were measured in sealed capillaries. Elemental analysis were carried out by Mr. H. Bieler, Institut für Organische Chemie, Universität Wien.

Starting Quinolines.—Quinoline (1) was obtained commercially and was purified prior to hydrogenation by heating with Raney nickel in ethanol, followed by distillation.[2,11] 6- and 8-Methylquinoline (2) and (3) were prepared from *p*- or *o*-toluidine by a modified Skraup synthesis.[3] Separation from unreacted toluidine and the by-products (16) or (17) was accomplished by acetylation [see below for (4)] rather than by diazotisation,[3] which gave diminished yields of coloured products.

8-*Isopropylquinoline* (4) *by Skraup synthesis.* 2-Isopropyl-nitrobenzene [12] (140 g) and hydrazine hydrate (106 g) in ethanol (1 l) were heated to 40 °C and Raney nickel [13] was added in small amounts. When the vigorous reaction had ceased, the mixture was refluxed for 2 h, the solution was decanted from the catalyst, the solvent was distilled off, and the residue was distilled to give 2-amino-isopropylbenzene (101.5 g), b.p. 95—97 °C at 10 mmHg. This was refluxed with anhydrous glycerol (234 g) and As_2O_5 (111 g), and concentrated H_2SO_4 (217 g) was slowly added. The reaction was carried out and the crude product isolated as described for (2) and (3).[3] Crude (4) was then heated with an excess of acetic anhydride on a boiling water bath for 2 h. The mixture was then poured onto ice–water–HCl, extracted with ether, the aqueous solution was basified with 50% NaOH solution and extracted repeatedly with light petroleum. The solvent was distilled off and the residue was distilled (b.p. 128 °C at 10 mmHg) to give (4) (71.6 g, 56%); the picrate had m.p. 199—200 °C (lit.,[14] 199—200 °C); δ 8.93 (1 H, H-2, dd), 8.0—7.0 (5 H), 4.5 (1 H, $CHPr^i$), and 1.39 (6 H, 2 Me, d, *J* 7 Hz).

6-*t-Butylquinoline* (5). 4-t-Butylnitrobenzene [15] was reduced to 4-amino-t-butylbenzene,[15] and this was reacted by Skraup synthesis as described above for (4), except that the crude (5) was extracted with benzene instead of steam-distillation. After purification *via* acetylation the *product* was distilled in a Kugelrohr apparatus, b.p. 85 °C at 0.05 mmHg, yield 30%; the *picrate* had m.p. 198—200 °C (Found: C, 54.95; H, 4.4. $C_{19}H_{18}N_4O_7$ requires C, 55.1; H, 4.4%); δ 8.87 (H-2, dd), 8.2—7.2 (5 H), and 1.40 (9 *H*, Bu^t, s).

8-*Isopropylquinoline* (4) *from* 2-*isopropylcyclohexanone.* 8-Isopropyl-2,3,4,4a,5,6,7,8-octahydroquinoline was pre-

TABLE 2

^{13}C N.m.r. chemical shifts [a] of quinolines, 1,2,3,4-tetrahydroquinolines, and 5,6,7,8-tetrahydroquinolines

Compound	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-8a	C-4a	C-α	Me
(4)	148.9$_1$	120.5$_4$	136.0$_3$	[125.5$_3$]	[125.0$_0$]	[126.4$_0$]	146.3$_3$	147.4$_1$	128.3$_8$	27.2$_8$	23.5$_5$
	(−1.4)	(−0.5)	(0.0)	(−2.2)	(−1.5)	(−3.0)	(+16.9)	(−0.9)	(+0.1)		
(5) [b]	149.6$_7$	120.9$_1$	135.8$_6$	122.6$_5$	149.2$_3$	128.3$_1$	129.1$_1$	146.9$_9$	128.0$_1$	34.8$_1$	31.1$_4$
	(−0.6)	(−0.1)	−(0.1)	(−5.1)	(+22.7)	(−1.1)	(−0.3)	(−1.3)	(−0.3)		
(6)	147.3$_1$	119.9$_8$	136.2$_8$	[125.9$_5$]	[125.9$_5$]	[126.6$_9$]	148.2$_4$	147.5$_6$	129.2$_7$	36.5$_6$	31.0$_5$
	(−3.0)	(−1.0)	(+0.3)	(−1.8)	(−0.6)	(−2.7)	(+18.8)	(−0.7)	(+1.0)		
(7) [c]	150.0$_9$	120.8$_6$	136.0$_3$	126.1$_5$	[127.2$_8$]	[130.1$_9$]	[139.5$_6$]	146.0$_2$	128.6$_7$		
	(−0.2)	(−0.1)	(0.0)	(−1.6)	(+0.8)	(+0.8)	(+10.2)	(−2.3)	(+0.4)		
(8) [b]	147.8$_1$	121.2$_3$	134.6$_2$	105.0$_8$	157.7$_0$	122.1$_8$	130.8$_2$	144.4$_8$	129.2$_8$		55.3$_0$
	(−2.5)	(+0.2)	(−1.4)	(−22.6)	(+31.2)	(−7.2)	(+1.4)	(−3.8)	(+1.0)		
(9)	149.0$_5$	121.5$_3$	135.6$_9$	119.4$_9$	126.6$_2$	107.5$_2$	155.3$_6$	140.2$_1$	129.2$_8$		55.7$_9$
	(−1.3)	(+0.5)	(−0.3)	(−8.2)	(+0.1)	(−21.9)	(+26.0)	(−8.1)	(+1.0)		
(12) [d]	152.6$_3$	122.3$_7$	136.7$_0$	[125.0$_5$]	128.8$_3$	[125.9$_3$]	131.0$_2$	149.3$_9$	127.3$_2$	124.4$_1$	
	(+2.3)	(+1.4)	(+0.7)	(−2.7)	(+2.3)	(−3.5)	(+1.6)	(+1.1)	(−1.0)		
(13) [e]	151.1$_9$	121.9$_8$	136.3$_1$	132.5$_9$	125.2$_0$	127.9$_9$	127.6$_7$	144.6$_7$		124.3$_8$	
	(+0.9)	(+1.0)	(+0.3)	(+4.9)	(−1.3)	(−1.4)	(−1.7)	(−3.6)			
(14) [f]	150.3$_8$	122.0$_0$	135.6$_6$	123.5$_1$	126.2$_5$	113.3$_6$	157.9$_1$	138.3$_3$	129.7$_7$		
	(+0.1)	(+1.0)	(−0.3)	(−4.2)	(−0.3)	(−16.0)	(+28.5)	(−10.0)			
(15)	41.9$_0$	22.1$_3$	26.9$_9$	129.3$_7$	116.7$_1$	126.6$_1$	114.0$_9$	144.7$_9$	121.1$_9$		
(16)	42.1$_4$	22.4$_8$	27.0$_2$	129.9$_8$	125.7$_9$	127.2$_3$	114.4$_0$	142.5$_3$	121.2$_7$		20.4$_0$
	(+0.2)	(+0.4)	(0.0)	(+0.6)	(+9.1)	(+0.6)	(+0.3)	(−2.3)	(+0.1)		
(17)	42.3$_8$	22.2$_0$	27.3$_2$	[127.3$_8$]	116.4$_0$	[127.8$_6$]	120.8$_3$	142.7$_3$	121.1$_1$		17.0$_9$
	(+0.5)	(+0.1)	(+0.3)	(−2.0)	(−0.3)	(+1.3)	(+6.7)	(−2.1)	(−0.1)		
(18)	42.3$_3$	22.1$_5$	27.6$_8$	127.1$_5$	116.6$_1$	122.6$_2$	131.3$_2$	141.4$_0$	121.0$_9$	26.9$_3$	22.3$_1$
	(+0.4)	(0.0)	(+0.7)	(−2.2)	(−0.1)	(−4.0)	(+17.2)	(−3.4)	(−0.1)		
(19)	42.0$_7$	22.4$_9$	27.2$_7$	126.1$_5$	139.4$_5$	123.5$_5$	114.0$_7$	142.4$_9$	120.6$_2$	33.7$_1$	31.6$_4$
	(+0.2)	(+0.4)	(+0.3)	(−3.2)	(+22.7)	(−3.1)	(0.0)	(−2.3)	(−0.6)		
(20)	42.1$_8$	22.0$_6$	28.0$_7$	127.8$_8$	116.2$_6$	124.0$_6$	132.3$_6$	143.0$_4$	122.0$_3$	33.9$_8$	29.9$_1$
	(+0.3)	(−0.1)	(+1.1)	(−1.5)	(−0.5)	(−2.6)	(+18.3)	(−1.8)	(+0.8)		
(21) [g]	41.9$_2$	22.0$_1$	27.5$_0$	128.8$_2$	116.2$_9$	126.9$_3$	126.5$_4$	141.6$_4$	121.0$_8$		
	(0.0)	(−0.1)	(+0.5)	(−0.6)	(−0.4)	(+0.3)	(+12.5)	(−3.2)	(−0.1)		
(22)	42.3$_2$	22.4$_9$	27.2$_3$	115.4$_7$	151.7$_3$	112.8$_9$	114.8$_4$	139.0$_6$	122.5$_7$		55.6$_0$
	(+0.4)	(+0.4)	(+0.2)	(−13.9)	(+35.0)	(−13.7)	(+0.8)	(−5.7)	(+1.4)		
(23)	41.4$_9$	22.2$_1$	26.7$_8$	121.7$_7$	115.6$_3$	107.4$_7$	146.2$_7$	134.5$_9$	121.1$_3$		55.2$_5$
	(−0.4)	(+0.1)	(−0.2)	(−7.6)	(−1.1)	(−19.1)	(+32.2)	(−10.2)	(−0.1)		
(26) [h]	41.6$_9$	21.4$_7$	27.0$_2$	126.4$_8$	117.9$_6$	124.0$_5$	113.0$_6$	147.5$_2$	120.6$_4$	125.3$_3$	
	(−0.2)	(−0.7)	(0.0)	(−2.9)	(+1.3)	(−2.6)	(−1.0)	(+1.7)	(−0.6)		
(27) [i]	41.9$_3$	21.2$_6$	27.7$_2$	133.1$_7$	115.2$_2$	124.6$_0$	112.4$_2$	142.7$_5$	122.9$_7$	125.7$_6$	
	(0.0)	(−0.9)	(+0.7)	(+3.8)	(−1.5)	(−2.0)	(−1.7)	(−2.0)	(+1.6)		
(28) [j]	41.2$_8$	21.8$_5$	26.6$_1$	124.5$_0$	115.4$_7$	112.1$_2$	150.9$_8$	133.2$_5$	123.5$_9$		
	(−0.6)	(−0.3)	(−0.4)	(−4.9)	(−1.3)	(−14.5)	(+36.9)	(−11.5)	(+2.4)		
(29)	146.7$_3$	120.8$_0$	136.5$_6$	28.7$_5$	[23.1$_2$]	[22.7$_4$]	32.5$_3$	157.2$_8$	132.0$_9$		
(30)	146.8$_0$	120.7$_7$	136.5$_2$	37.3$_0$	28.8$_5$	31.3$_0$	32.1$_8$	156.9$_9$	131.6$_4$		21.5$_9$
	(+0.1)	(0.0)	(0.0)	(+8.6)	(+5.7)	(+8.6)	(−0.4)	(−0.3)	(−0.5)		
(31)	146.8$_5$	120.4$_2$	136.5$_2$	29.3$_7$	20.1$_3$	31.3$_4$	35.6$_6$	161.2$_1$	131.7$_0$		21.2$_5$
	(+0.1)	(−0.4)	(0.0)	(+0.6)	(−3.0)	(+8.6)	(+3.1)	(+3.9)	(−0.4)		
(32)	146.7$_7$	120.4$_8$	136.3$_0$	29.6$_5$	[21.8$_1$]	[22.9$_0$]	46.2$_6$	160.0$_3$	133.1$_4$	30.4$_0$	20.9$_2$
	(0.0)	(−0.3)	(−0.3)	(+0.9)	(−1.3)	(+0.2)	(+13.7)	(+2.8)	(+1.1)		17.0$_4$
(33)	146.6$_2$	120.6$_9$	136.8$_2$	30.2$_6$	44.3$_7$	24.3$_9$	33.3$_9$	157.2$_2$	132.1$_6$	32.2$_9$	27.2$_3$
	(−0.1)	(−0.1)	(+0.3)	(+1.5)	(+21.3)	(+1.7)	(+0.9)	(−0.1)	(+0.1)		
(34)	145.7$_7$	120.5$_2$	135.8$_8$	29.7$_1$	22.0$_6$	26.1$_8$	49.2$_9$	159.7$_3$	134.3$_9$	35.8$_2$	28.8$_6$
	(−1.0)	(−0.3)	(−0.7)	(+1.0)	(−1.1)	(+3.4)	(+16.8)	(+2.5)	(+2.3)		
(35) [k]	147.4$_7$	121.2$_2$	136.7$_2$	29.0$_1$	19.5$_1$	32.8$_9$	47.7$_4$	158.4$_7$	132.9$_9$		
	(+0.7)	(+0.4)	(+0.2)	(+0.3)	(−3.6)	(+10.2)	(+15.2)	(+1.2)	(+0.9)		
(36) [l]	147.0$_2$	121.0$_4$	137.0$_2$	34.3$_4$	74.5$_8$	[29.3$_3$]	[27.1$_3$]	156.4$_6$			55.8$_0$
	(+0.3)	(+0.3)	(+0.5)	(+5.6)	(+51.5)	(+6.6)	(−5.4)	(−0.8)			
(37)	147.0$_4$	122.7$_6$	137.0$_4$	[28.3$_3$]	17.5$_6$	[27.7$_9$]	77.5$_1$	155.3$_7$	132.8$_2$		56.9$_5$
	(+0.3)	(+2.0)	(+0.5)	(−0.4)	(−5.6)	(+5.1)	(+45.0)	(−1.9)	(+0.7)		
(39)	146.6$_3$	122.2$_8$	137.0$_3$	28.5$_2$	19.0$_8$	31.0$_4$	68.2$_2$	158.1$_9$	131.9$_1$		
	(0.0)	(+1.5)	(+0.5)	(−0.1)	(−4.0)	(+8.0)	(+35.7)	(+0.9)	(−0.2)		
(40) [m]	147.7$_1$	121.4$_3$	136.9$_3$	27.6$_7$	38.8$_2$	22.0$_6$	31.1$_6$	155.7$_6$	128.8$_3$	127.6$_2$	
	(+1.0)	(+0.6)	(+0.4)	(−1.1)	(+15.7)	(−0.7)	(−1.4)	(−1.5)	(−3.3)		
(41) [n]	147.3$_1$	122.7$_9$	137.3$_3$	28.3$_2$	19.3$_3$	23.3$_0$	44.8$_2$	160.8$_8$	134.1$_1$	127.1$_9$	
	(+0.6)	(+2.0)	(+0.8)	(−0.4)	(−3.8)	(+0.6)	(+12.3)	(+3.6)	(+2.0)		
(42) [o]	146.8$_2$	120.4$_3$	136.3$_2$	29.6$_1$	21.8$_0$	24.2$_9$	46.0$_5$	159.9$_7$	133.2$_9$		
	(+0.1)	(−0.4)	(−0.2)	(+0.9)	(−1.3)	(+1.5)	(+13.5)	(+2.7)	(+1.2)		

[a] In p.p.m. from $SiMe_4$; solvent $CDCl_3$; shift difference from the respective parent compounds (1) (from ref. 6*c*), (15), and (29) are in parentheses. Chemical shifts of signals for which assignments are not unambiguous are in square parentheses. [b] Assignments confirmed by undecoupled spectrum (*cf.* ref. 6*a*). [c] Phenyl carbons: C-1′ (140.9$_0$); C-2′, -6′ 127.8$_9$; C-3′, -5′ 130.6$_5$; C-4′ (127.4$_3$). [d] Coupling with F (in Hz) : CF_3, J_{CF} 272.5; C-6, J_{CCF} 32.7; C-5, J_{CCCF} 2.6; C-7, J_{CCCF} 4. [e] Coupling with F (in Hz) : CF_3, J_{CF} 274; C-8, J_{CCF} 49; C-7, J_{CCCF} 5.8. Signal of C-4a not seen. [f] Coupling with F (in Hz) : C-8, J_{CF} 256.4; C-7, J_{CCF} 18.9; C-8a, J_{CCF} 11.7; C-6, J_{CCCF} 7.9; C-4a, J_{CCCF} 2.4; C-4, J_{CCCCF} 3.1; C-5, J_{CCCCF} 4.8. [g] Phenyl carbons: C-1′ 139.7$_1$; C-2′, -6′ 128.7$_9$; C-3′, -5′ 129.3$_2$; C-4′ 127.9$_8$. [h] Coupling with F (in Hz) : CF_3, J_{CF} 270.8; C-6, J_{CCF} 32.5; C-5, J_{CCCF} 3.7; C-7, J_{CCCF} 3.9. [i] Coupling with F (in Hz) : CF_3, J_{CF} 271.9; C-8, J_{CCF} 29.2; C-7, J_{CCCF} 5.6. [j] Coupling with F (in Hz): C-8, J_{CF} 237.5; C-7, J_{CCF} 17.9; C-8a, J_{CCF} 12.4; C-6, J_{CCCF} 7.3; C-4a, J_{CCCF} 3.8; C-4, J_{CCCCF} 3.2; C-5, J_{CCCCF} 2.5. [k] Phenyl carbons: C-1′ 146.4$_1$; C-2′, -6′ 128.1$_8$; C-3′, -5′ 128.6$_2$; C-4′ 125.8$_0$. [l] As minor component in mixture with mainly (29) and some (8). Signal of C-4a not seen. [m] Coupling with F (in Hz) : CF_3, J_{CF} 278.7; C-6, J_{CCF} 27.5; C-5, C-7, J_{CCCF} 2.6. [n] Coupling with F (in Hz) : CF_3, J_{CF} 282.2; C-8, J_{CCF} 25.4; C-7, J_{CCCF} 2.5. [o] Cyclohexyl carbons: C-1′ 41.4$_8$; C-2′ 31.7$_2$; C-3′, -5′ 26.8$_7$; C-4′ 27.1$_2$; C-6′ 27.8$_6$.

pared starting with 2-isopropylcyclohexanone in exactly the same way as the preparation of 8-t-butyl-2,3,4,4a,5,6,7,8-octahydroquinoline [4] from 2-t-butylcyclohexanone. 2-Isopropylcyclohexanone (40 g) was heated with pyrrolidine (35 g) and toluene-*p*-sulphonic acid (1 g) in toluene (500 ml) on a Dean–Stark trap to give (after distillation) *N*-(6-isopropylcyclohex-1-enyl)pyrrolidine (26 g, 47%), b.p. 120 °C at 9 mmHg; δ 4.62 (1 H, olefin, t, *J* 4 Hz), 3.15—2.55 (4 H, pyrrolidine-CH_2), 2.30—1.55 (12 H), 0.87 (Me, d, *J ca.* 7 Hz), and 0.80 (Me, d, *J ca.* 7 Hz). A solution of this and freshly distilled acrylonitrile (10 g) in anhydrous ethanol (50 ml) refluxed for 36 h gave, after distillation *N*-[2-(2-cyanoethyl)-6-isopropylcyclohex-1-enyl]pyrrolidine (26.5 g, 80%), b.p. 132—136 °C at 5 mmHg. It crystallized in the refrigerator, m.p. 43—45 °C; δ 3.3—2.7 (4 H, CH_2 of pyrrolidine), 2.5—1.3 (16 H), 1.00 (Me, d, *J ca.* 7.4 Hz), and 0.93 (Me, d, *J ca.* 7.4 Hz). A solution of this in anhydrous ether was added to a suspension of $LiAlH_4$ (4.5 g) in anhydrous ether. The resulting crude *N*-[2-(3-aminopropyl)-6-isopropylcyclohex-1-enyl]pyrrolidine was distilled on a small Vigreux column as described for the synthesis of 8-t-butyl-2,3,4,4a,5,6,7,8-octahydroquinoline [4] to give (after re-distillation, b.p. 105 °C at 9 mmHg) 8-*isopropyl*-2,3,4,4a,5,6,7,8-*octahydroquinoline* (14.8 g, 77%); δ 3.58 (2 H, 2 × H-2, s, $W_{\frac{1}{2}}$ 10 Hz), 2.26—1.13 (13 H), 1.00—0.75 (2 × Me, 4 d, overlapping; product is a mixture of α- and β-isomers); the *picrate* had m.p. 146—147 °C (Found: C, 53.0; H, 6.0. $C_{18}H_{24}N_4O_7$ requires C, 52.9; H, 5.9).

Aromatizations of (8R)-2,3,4,4a,5,6,7,8-*Octahydroquinolines*.—According to a literature procedure [5] the octahydroquinoline, nitrobenzene, and palladium (10% on C) were refluxed in *p*-xylene in a Dean–Stark trap. Light petroleum was used to extract the amines from the basified solution instead of ether.[5] The mixture of products was distilled on a Kugelrohr distillation unit and its composition was determined by g.l.c.

Aromatization of 8-*isopropyl*-2,3,4,4a,5,6,7,8-*octahydroquinoline*. By the above procedure a mixture of starting material (43%), (32) (26%), (4) (16%), and two other partially saturated compounds not further identified (9 and 6%) was obtained.

8-*t-Butylquinoline* (6).— 8-Butyl-2,3,4,4a,5,6,7,8-octahydroquinoline [4] (77.2 g, 0.4 mol) was treated by the above procedure. After distillation in a Kugelrohr apparatus 72 g of a mixture of equal amounts of (6) and (34), plus a small amount of (20), was obtained. The 1,2,3,4-tetrahydro-product was separated by acetylation. Distillation of the mixture of (6) and (34) on a spinning-band column gave nearly pure (6) (b.p. 122 °C at 10 mmHg), which could be recrystallized from ethanol to give pure *crystals* of (6), m.p. 34 °C (11 g) (Found: C, 84.0; H, 8.4. $C_{13}H_{15}N$ requires C, 84.3; H, 8.4); δ, 8.93 (H-2, dd), 8.1—7.15 (5 H), and 1.73 (9 H, Bu^t, s); the *picrate* had m.p. 162 °C (Found: C, 55.0; H, 4.3. $C_{19}H_{18}N_4O_7$ requires C, 55.1; H, 4.4).

8-*Phenylquinoline* (7).—This was prepared from 8-phenyl-2,3,4,4a,5,6,7,8-octahydroquinoline [5] by the above procedure as described.[5] In our hands the method did not yield pure (7) but a mixture of *ca.* equal amounts of (7), (21), and (35). A repeated treatment of this mixture for 10 days, followed by fractional distillation gave fairly pure (7) (b.p. 150 °C at 0.05 mmHg) which crystallized after several days at +5 °C. Recrystallization from ethanol gave pure (7), m.p. 48 °C (lit.,[16] 48—49 °C); δ 8.83 (1 H, H-2) and 8.0—6.3 (10 H).

6-*Methoxyquinoline* (8) [17] *and* 8-*Methoxyquinoline* (9).[18]—These were prepared from *p*- and *o*-anisidine by a Skraup synthesis as described for 6-methoxy-8-nitroquinoline.[19] 6-Hydroxyquinoline (10) [20] and 8-hydroxyquinoline (11) [18] were obtained by heating (8) or (9) with 48% HBr for 24 h. 6- and 8-Trifluoromethylquinolines (12) and (13) were prepared from the (commercial) *p*- and *o*-trifluoromethylanilines as described in the literature.[21] 8-Fluoroquinoline (14) [22] was synthesized from (commercial) *o*-fluoroaniline in a manner analogous to a procedure reported [23] for 6-fluoroquinoline, and separated from the by-product (1) by distillation on a spinning-band column.

Hydrogenations in Methanol.—The quinolines (1)—(14) (10 mmol) were dissolved in methanol (30 ml) in a 250-ml Parr bottle. Platinum oxide (400 mg) was added and the mixture was shaken with H_2 (3 bar pressure) until no further drop in pressure was observed. The catalyst was filtered off and washed with methanol, and the combined methanol solutions were concentrated and the residue was distilled in a Kugelrohr unit. The products were found pure by g.l.c. or [in the case of (24) and (25)] by t.l.c. Yields were 95—98% of distilled product.

The ^{13}C n.m.r. spectra of the compounds are reported in Table 2. ^1H n.m.r. spectra [in $CDCl_3$ except for (24) and (25) which were recorded in CF_3CO_2H] showed the aromatic protons at δ 7.5—6.1; the NH proton as a broad singlet at δ 3.5—4.5; the protons at C-2 as triplets (*J ca.* 5.5 Hz) at δ 3.1—3.28 p.p.m. [an exception was 8-trifluoromethyl-1,2,3,4-tetrahydroquinoline where the signal appeared at δ 3.35 as a triplet of doublets (*J* 5.5 and 3 Hz)]; the protons at C-3 were multiplets at δ 1.8—1.9; the protons at C-4 were triplets (*J ca.* 6 Hz) at δ 2.67—2.78. The spectra of the hydroxy-compounds (24) and (25) in CF_3CO_2H had the aromatic protons at δ 7.5—6.7, NH_2 at δ 8.8 and 8.5, respectively, H-2 at δ 3.73 (br s, $W_{\frac{1}{2}}$ 14 Hz), H-3 at δ 2.30 or 2.27, and H-4 at δ 2.97 (t, *J ca.* 6 Hz). In this way were prepared: 1,2,3,4-tetrahydroquinoline (15); the hydrochloride had m.p. 181 °C (lit.,[24] 181 °C): 6-methyl-1,2,3,4-tetrahydroquinoline (16), m.p. 35—36 °C (lit.,[25] m.p. 36—37 °C): 8-methyl-1,2,3,4-tetrahydroquinoline (17); the hydrochloride had m.p. 218 °C (lit.,[25] 216—219 °C): 8-*isopropyl*-1,2,3,4-*tetrahydroquinoline* (18); the *picrate* had m.p. 165 °C (Found: C, 53.5; H, 5.1. $C_{18}H_{20}N_4O_7$ requires C, 53.5; H, 5.0): 6-*t-butyl*-1,2,3,4-*tetrahydroquinoline* (19); the *picrate* had m.p. 154—155 °C (Found: C, 54.4; H, 5.2. $C_{19}H_{22}N_4O_7$ requires C, 54.5; H, 5.3): 8-*t-butyl*-1,2,3,4-*tetrahydroquinoline* (20); the *picrate* had m.p. 139—142 °C (Found: C, 54.4; H, 5.4. $C_{19}H_{22}N_4O_7$ requires C, 54.5; H, 5.3): 8-phenyl-1,2,3,4-tetrahydroquinoline (21); [26] the picrate had m.p. 185 °C (Found: C, 57.5; H, 4.1. $C_{21}H_{18}N_4O_7$ requires C, 57.5; H, 4.1): 6-methoxy-1,2,3,4-tetrahydroquinoline (22); the picrate had m.p. 160—162 °C (lit.,[27] 164—165 °C): 8-methoxy-1,2,3,4-tetrahydroquinoline (23); the picrate had m.p. 160—163 °C (lit.,[28] 156 °C): 6-hydroxy-1,2,3,4-tetrahydroquinoline (24), m.p. 156—158 °C (lit.,[29] 160 °C): 8-hydroxy-1,2,3,4-tetrahydroquinoline (25), m.p. 120 °C (lit.,[29] 119 °C): 6-*trifluoromethyl*-1,2,3,4-*tetrahydroquinoline* (26); the *hydrochloride* had m.p. 144—146 °C (decomp.) (Found: C, 50.6; H, 4.9. $C_{10}H_{11}F_3ClN$ requires C, 50.5; H, 4.7): 8-*trifluoromethyl*-1,2,3,4-*tetrahydroquinoline* (27); the *hydrochloride* had m.p. 176—178 °C (decomp.) (Found: C, 50.4; H, 4.8. $C_{10}H_{11}F_3ClN$ requires C, 50.5; H, 4.7): 8-*fluoro*-1,2,3,4-*tetrahydroquinoline* (28); the *picrate* had m.p. 135—136 °C (Found: C, 47.6; H, 3.4. $C_{15}H_{13}FN_4O_7$ requires C, 47.4; H, 3.45).

Hydrogenations in CF_3CO_2H.—Platinum oxide (400 mg)

in CF_3CO_2H (10 ml) was pre-hydrogenated at atmospheric pressure and the starting quinoline (1)—(14) (10 mmol) in trifluoroacetic acid (20 ml) was added from an addition flask with a male 14/20 joint on a 90° gooseneck. The mixture was stirred magnetically at constant speed. Hydrogenation was carried out until *ca.* 10% more than the theoretical amount of hydrogen [2 mol per mol quinoline, except for (7)] had been consumed. The solution was then purged with nitrogen, and the catalyst was filtered off and washed with acetic acid. The combined acid solutions were poured onto ice and were basified with *ca.* 50% NaOH solution. The amines were extracted with ether or light petroleum. The organic extract was washed with NaCl solution and dried over Na_2SO_4. The solvent was distilled off and the residue was distilled in a Kugelrohr distillation unit. Composition of the product mixture was determined by g.l.c. (see Table 1). Yields of recovered material were 90—95%, taking into consideration hydrogenolysis of the hetero-substituents. An exception were hydrogenations of (10) and (11) where the phenolic products (unreacted starting material and 1,2,3,4-tetrahydro-products) remained in the aqueous alkaline solution and were not isolated; composition of products in Table 1 relate to the amount of starting quinoline.

The 1,2,3,4-tetrahydro-compounds and other NH-impurities were separated by acetylation as described for the synthesis of (4). The 5,6,7,8-tetrahydro-compounds were purified from small amounts of starting material by repeated recrystallization of their picrates, or by column chromatography (aluminium oxide, eluant $CHCl_3$). Because of the small amounts of (36) formed this compound was not isolated in pure form, but only characterized by g.l.c.–mass spectrometry. The following compounds were prepared in this way.

5,6,7,8-Tetrahydroquinoline (29);[2] δ 8.29 (H-2, d, *J* 5 Hz), 7.25 (H-4, d, *J* 8 Hz), 6.91 (H-3, dd, *J* 8 and 5 Hz), 2.86 (H-8, t), 2.68 (H-5, t), and 2.10—1.65 (H-6, -7, m); the picrate had m.p. 159—160 °C (lit.,[30] 158—159 °C).

6-Methyl-5,6,7,8-tetrahydroquinoline (30);[2] δ 8.32 (H-2, d, *J* 5 Hz), 7.25 (H-4, d, *J* 8 Hz), 6.90 (H-3, dd, *J* 8 and 5 Hz), 2.92 (H-8), 2.50 (H-5), 2.10—1.20 (H-6 and H-7), and 1.03 (Me, d, *J* 5.6 Hz); the picrate had m.p. 161—162 °C (lit.,[31] 159.5—160.5 °C).

8-Methyl-5,6,7,8-tetrahydroquinoline (31);[2] δ 8.38 (H-2, d, 5 Hz), 7.29 (H-4, d, 8 Hz); 6.97 (H-3, dd, *J* 8 and 5 Hz), 2.98 (H-8; m), 2.72 (H-5, t), 2.20—1.50 (H-6, -7, m), and 1.35 (Me, d, *J* 7 Hz); the picrate had m.p. 126—127 °C (lit.,[31] 125—126 °C).

8-*Isopropyl*-5,6,7,8-*tetrahydroquinoline* (32); δ 8.15 (H-2, d, *J* 5 Hz), 7.30 (H-4, d, *J* 8 Hz); 6.95 (H-3, dd, *J* 8 and 5 Hz), 3.1—2.5 (H-8, H-5, and C*H*Me_2), 2.25—1.36 (H-6, -7), and 1.05 and 0.70 (Me, diastereotopic, d, *J* 7 Hz); the *picrate* had m.p. 125—127 °C (Found: C, 53.5; H, 5.15. $C_{18}H_{20}N_4O_7$ requires C, 53.5; H, 5.0).

6-*t-Butyl*-5,6,7,8-*tetrahydroquinoline* (33); δ 8.33 (H-2, d, *J* 5 Hz), 7.35 (H-4, d, *J* 8 Hz), 6.97 (H-3; dd, *J* 8 and 5 Hz), 3.15—2.50 (H-5, -8), 2.50—1.50 (H-6, -7), and 0.94 (Me, s); the *picrate* had m.p. 135—136 °C (Found: C, 54.6; H, 5.4. $C_{19}H_{22}N_4O_7$ requires C, 54.5; H, 5.3).

8-*t-Butyl*-5,6,7,8-*tetrahydroquinoline* (34); δ 8.40 (H-2; dd, *J* 5 and 1.6 Hz), 7.30 (H-4; dd, *J* 8 and 1.6 Hz), 6.94 (H-3, dd, *J* 8 and 5 Hz), 3.06—2.50 (H-5, -8), 2.2—1.3 (H-6, -7), and 1.06 (Me, s); the *picrate* had m.p. 169 °C (Found: C, 54.4; H, 5.3. $C_{19}H_{22}N_4O_7$ requires C, 54.5; H, 5.3).

8-Phenyl-5,6,7,8-tetrahydroquinoline (35);[32] δ 8.40 (H-2, dd, *J* 5 and 1.6 Hz), 7.56—6.86 (H-3, H-4 overlapping with phenyl protons), 4.33 (H-8, t, *J* 5 Hz), 2.90 (H-5, t), and 2.3—1.6 (H-6, -7); the picrate had m.p. 172—173 °C (Found: C, 57.3; H, 4.2. Calc. for $C_{21}H_{18}H_4O_7$: C, 57.5; H, 4.1).

8-*Cyclohexyl*-5,6,7,8-*tetrahydroquinoline* (42) [from deliberately over-hydrogenated (7)]; δ 8.55 (H-2, dd, *J* 5 and 1.5 Hz), 7.40 (H-4, dd, *J* 8 and 1.5 Hz), 7.00 (H-3, dd, *J* 8 and 5 Hz), and 3.10—0.95 (18 H; not resolved); the *picrate* had m.p. 148—149 °C (Found: C, 57.1; H, 5.25. $C_{21}H_{24}N_4O_7$ requires C, 56.75; H, 5.45).

6-Methoxy-5,6,7,8-tetrahydroquinoline (36) was only characterized by its ^{13}C n.m.r. spectrum [admixed with (29) and (8)] and by g.l.c.–mass spectrometry: *m/e* 163 (M^+, 62), 148 (100), 132 (52), 131 (22), 130 (74), 118 (30), and 117 (20).

8-*Methoxy*-5,6,7,8-*tetrahydroquinoline* (37); δ *J* 8.45 (H-2, d, *J* 5 Hz), 7.40 (H-4, d, *J* 8 Hz), 7.07 (H-3; dd, *J* 8 and 5 Hz), 4.33 (H-8, t), 3.53 (OMe, s), 2.77 (H-5, s), and 2.37—1.57 (H-6, -7, m); the *picrate* had m.p. 156—158 °C (Found: C, 48.90; H, 4.0. $C_{16}H_{16}N_4O_8$ requires C, 49.00; H, 4.1).

6-*Hydroxy*-5,6,7,8-*tetrahydroquinoline* (38); δ 8.36 (H-2, d, *J* 5 Hz), 7.40 (H-4, d, *J* 8 Hz), 7.06 (H-3, dd, *J* 8 and 5 Hz), 4.24 (H-6, m), 3.35—2.65 (H-5, -8), 2.40 (OH, br s), and 2.25—1.85 (H-7); m.p. 113—114 °C; the *picrate* had m.p. 182—184 °C (Found: C, 47.8; H, 3.8. $C_{15}H_{14}N_4O_8$ requires C, 47.65; H, 3.75).

8-Hydroxy-5,6,7,8-tetrahydroquinoline (39);[32] δ 8.38 (H-2, d, *J* 5 Hz), 7.40 (H-4, d, *J* 8 Hz), 7.07 (H-3; d, *J* 8 and 5 Hz), 5.10 (OH, br s), 4.77 (H-8, t), 2.77 (H-5), 2.3—1.6 (H-6, -7, m), m.p. 62—63 °C (lit.,[32] 64—65 °C); the picrate had m.p. 142—143 °C (Found: C, 47.75; H, 3.65. Calc. for $C_{15}H_{14}N_4O_8$ C, 47.65; H, 3.75).

6-*Trifluoromethyl*-5,6,7,8-*tetrahydroquinoline* (40); δ 8.38 (H-2, dd, *J* 5 and 2 Hz), 7.42 (H-4, d, *J* 8 Hz), 7.05 (H-3, dd, *J* 8 and 5 Hz), 2.98 (H-5, -8), and 2.8—1.45 (H-6, -7, m); the *picrate* had m.p. 131—132 °C (Found: C, 44.8; H, 3.0. $C_{16}H_{13}F_3N_4O_7$ requires C, 44.65; H, 3.05).

8-*Trifluoromethyl*-5,6,7,8-*tetrahydroquinoline* (41); δ 8.43 (H-2, d, *J* 5 Hz), 7.43 (H-4, d, *J* 8 Hz), 7.10 (H-3, dd, *J* 8 and 5 Hz), 4.0 (H-8, m), 2.78 (H-5, t), and 2.3—1.6 (H-6, -7, m); the *picrate* had m.p. 136 °C (Found: C, 44.7; H, 3.1. $C_{16}H_{13}F_3N_4O_7$ requires C, 44.65; H, 3.05).

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