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REDUCTION OF 3-SUBSTITUTED 2-METHYLQUINOLINES WITH SODIUM TETRAHYDROBORATE

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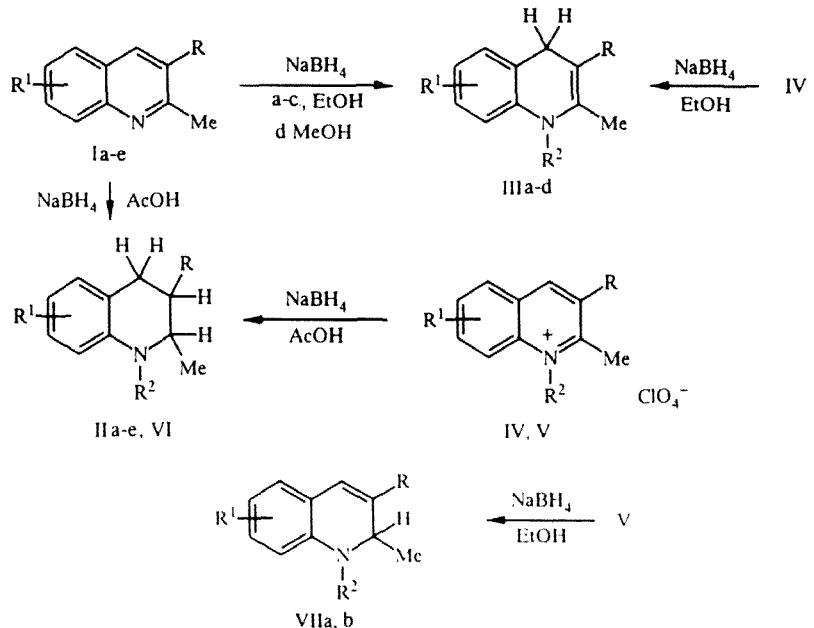
Reduction of esters of 2-methylquinoline-3-carboxylic acids and their perchlorates gave esters of 1,4-dihydro-2-methylquinoline-3-carboxylates, while derivatives of 1,2-dihydroquinoline were formed in the case of 1,2-dimethyl-3-ethoxycarbonyl-7-methoxyquinolinium perchlorate. Reduction of esters of 2-methylquinoline-3-carboxylic acid, 1,2-dimethyl-3-ethoxycarbonyl-7-methoxyquinolinium perchlorate and 3-acetyl-2-methylquinoline with sodium tetrahydroborate in acetic acid gave esters of 1,2-dimethyl- and 2-methyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid and 3-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline.

1,4-Dihydroquinolines have been studied very little [1-3] although they are close structural analogs of 1,4-dihydropyridines which have achieved practical use as (untranslated) media, radiation protectors and antioxidants. We have established previously [4] that 2-methyl-4-phenylquinolines with electron withdrawing groups in position 3 are reduced 1,2-dihydroquinolines and only the introduction of such very strong electron withdrawing groups as the nitro group into 2-methyl-4-phenylquinoline permitted reduction to 1,4-dihydroquinolines. The objective of the present work was the investigation of the reduction of 2-methylquinolines with electron withdrawing groups at position 3, but no substituents at position 4.



Ia-e

IIIa-d

IIa-e, VI

IV, V

VIIa, b

I—III a R = CO_2Et, R^1 = H, b R = CO_2Et, R^1 = 6-Cl, c R = CO_2Et, R^1 = 7-OMe, d R = CO_2Me, R^1 = 6-Cl, e R = COMe, R^1 = H; II, III R^2 = H; IV R = CO_2Et, R^1=7-OMe, R^2 = H; V, VI, VII R^1=7-OMe, R^2 = Me; V, VI R = CO_2Et; VII a R = CO_2Et, b R = CO_2H

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TABLE 1. Characteristics of the Synthesized Tetrahydroquinolines IIa-e and VI

Compound	Molecular formula	mp, °C	IR Spectrum, ν, cm^{-1}	Mass spectrum, m/z (M^+)	^1H NMR Spectrum (DMSO-D_6), δ, ppm							Yield, %
					2-CH_3 d, 3H (J = 7 Hz)	$CO_2CH_2\underline{CH_3}$ t, 3H (J = 7 Hz)	4-CH_2 and 3-CH, 3H	2-CH m, 1H	$CO_2\underline{CH_2}CH_3$ q, 2H (J = 8 Hz)	N—H d, 1H (J = 3 Hz)	aromatic protons	
IIa	$C_{13}H_{17}NO_2$	yellow oil	1510, 1610, 1740, 3400		0,96	1,18	2,78 br. s	3,67	4,06	5,76	6,2...6,5 (m, 2H), 6,6...6,9 (m, 2H)	33
IIb	$C_{13}H_{16}ClNO_2$	70...72	1510, 1610, 1720, 3400		0,98	1,16	2,78 br. s	3,64	4,06	5,95	6,40 (d, J = 9 Hz, 1H), 6,7...7,0 (m, 2H)	52
IIc*	$C_{14}H_{19}NO_3$	49	1630, 1720, 3380	249	0,98	1,15	2,73 br. s	3,64	4,06	5,78	5,9...6,1 (m, 2H), 6,6...6,8 (m, 1H)	32
IId†	$C_{12}H_{14}ClNO_2$	86...89	1500, 1610, 1730, 3400		1,02	–	2,80 br. s	3,71	–	6,02	6,44 (d, J = 8 Hz, 1H), 6,7...7,0 (m, 2H)	50
IIe‡	$C_{12}H_{15}NO$	93...94	1500, 1580, 1610, 1700, 3380	189	0,91	–	2,62...2,95 m	3,84	–	5,88	6,3...7,0 (m, 4H)	37
VI**	$C_{15}H_{21}NO_3$	yellow oil	1510, 1580, 1620, 1700, 1740	263	0,87	1,22	2,7...3,0 m	3,75	4,13	–	6,0...6,3 (m, 2H), 6,88 (d, J = 9 Hz, 1H)	91

*Resonance for the 7-OCH_3 group appears as singlets at 3.58 (IIc) and 3.66 ppm (VI).

†The resonance of the 3-$COOCH_3$ group is a singlet at 3.60 ppm.

‡The resonance of the 3-$COCH_3$ group is a singlet at 2.17 ppm.

**The resonance of the N–CH_3 group is a singlet at 2.84 ppm.

IIb NMR 13C: 13.9 (–$COOCH_2\underline{C}H_3$), 17.4 (–CH_3), 25.2 ($C_{(4)}$), 41.1 ($C_{(3)}$), 46.4 ($C_{(2)}$), 59.9 (–$COO\underline{C}H_2CH_3$), 115.0 ($C_{(5)}$), 119.0 ($C_{(4a)}$), 120.0 ($C_{(6)}$), 126.3 ($C_{(7)}$), 128.4 ($C_{(8)}$), 142.81 ($C_{(8a)}$), 172.2 (–$\underline{C}OOEt$). IIb PMR (360 MHz): 1.00 (3H, d, J = 6.5 Hz, 2-CH_3), 1.19 (3H, t, J = 7.0 Hz, –$COOCH_2\underline{CH_3}$), 2.7-2.9 (3H, m, 4-CH_2 + 3-CH), 3.69 (1H, m, 2-CH), 4.10 (2H, m, –$COO\underline{CH_2}CH_3$), 6.02 (1H, m, NH), 6.47 (1H, d, J = 8.5 Hz, 8-CH), 6.87 (H, dd, J = 8.5, 2.8 Hz, 7-CH), 6.95 (1H, d, J = 2.8 Hz, 5-CH).

The principal methods for preparing 1,4-dihydroquinolines is the reduction of quinolines with mildly nucleophilic reagents, like sodium tetrahydroborate [1, 4, 5] or reduction of the corresponding quinolinium salts [1]. A decisive condition for the reduction of quinolines to their 1,4-dihydro derivatives using complex hydrides is the presence of an electron withdrawing group in position 3 [1], while the presence of a substituent at position 2 or 4 precludes reduction of the quinoline in ethanol, but in aliphatic carboxylic acids it changes the direction of reduction to give the 1,2-dihydro isomers [4].

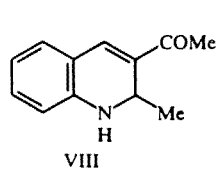
To determine the effects of substituents in positions 3, 4, 5 and 6 and the solvent on the reduction of 2-methylquinolines we carried out the reduction of quinolines Ia-e in alcohols and in acetic acid.

We have established that esters of 2-methylquinoline-3-carboxylic acid Ia-d and 3-acetyl-2-methylquinoline Ie were reduced by sodium tetrahydroborate in acetic acid to the 1,2,3,4-tetrahydroquinolines IIa-e. The unstable intermediate 1,2-dihydroquinolines VIII were observed in the reaction mixture by TLC and HPLC, but they could not be isolated. It is possible that, in addition to further reduction of the 1,2-dihydroquinolines to 1,2,3,4-tetrahydroquinolines [1], the unstable 1,2-dihydro compounds may disproportionate to quinolines and tetrahydroquinolines [8]. For example, on reduction of quinoline Ie with an equimolar amount of sodium tetrahydroborate under the given conditions the principal reduction product is the 1,2,3,4-tetrahydroquinoline IIe (quinoline Ie, 39%, 1,2,3,4-tetrahydroquinoline IIe 45%, 1,2-dihydroquinoline VIII (10%) according to HPLC).

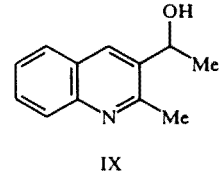
The structure of the unstable intermediate 1,2-dihydroquinolines was confirmed by their visible electronic spectra (405 and 450 nm from the reduction of quinolines Ic and Ie respectively) which agree with the visible electronic absorptions of ethyl 1,2-dihydro-2-methyl-4-phenylquinoline-3-carboxylate [4].

1,2,3,4-Tetrahydroquinolines IIa-e are formed from quinolines Ia-e in average yield. The electronic absorpton spectra of the tetrahydroquinolines IIa-e have three characteristic absorption bands in the ranges ~205-210 nm, ~250-260 nm, and ~300-310 nm, which are in excellent agreement with the long wavelength absorptions of 1,2,3,4-tetrahydropyridines [9]. In comparison with 1,4-dihydroquinolines and 1,2-dihydroquinolines, which absorb at λ_{max} 335 and 400 nm [2, 4], the long wavelength bands of the 1,2,3,4-tetrahydroquinolines IIa-e show strong hypsochromic shifts, as expected, because of the lack of conjugation. The band at 1740 cm^{-1} (C=O) in the IR spectra of the synthesized 1,2,3,4-tetrahydroquinolines IIa-e shows the absence of conjugation with the C=C bond. There is also a band at 3440 cm^{-1} (NH). The structures of the synthesized 1,2,3,4-tetrahydroquinolines IIa-e were confirmed by their ^1H and ^{13}C NMR spectra (Table 1).

In contrast to the reduction of quinolines Ia-e in acetic acid, reduction of the ethyl 2-methylquinoline-3-carboxylates Ia-c in ethanol and of methyl 2-methylquinoline-3-carboxylate Id in methanol gave the 1,4-dihydroquinolines IIIa-d. Reduction of quinolines Ia, Ic and Id was incomplete, which made isolation difficult (yields did not exceed 40%). (All operations for the isolation of the 1,4-dihydroquinolines IIIa-d were carried out in a single day to avoid oxidation.) The 4-phenyl derivative of compound Ia was not reduced by sodium tetrahydroborate even on prolonged boiling in ethanol [4]. Reduction of 3-acetyl-2-methylquinoline Ie under these conditions did not give the 1,4-dihydro derivative. Only the acetyl group was reduced to give the corresponding alcohol IX in 71% yield.



VIII



IX

The electronic absorption spectra of the 1,4-dihydroquinolines IIIa-d have two characteristic absorption bands: ~205-210 and ~340-345 nm, which agree with the absorption bands of 2-unsubstituted ethyl 1,4-dihydroquinoline-3-carboxylate (λ_{max} 338 nm) [2] and ethyl 1,4-dihydro-2-methyl-4-phenylquinoline-3-carboxylate (λ_{max} 334 nm) [10]. An analogous bathochromic shift has been observed in dihydropyridines on going from 4-phenyl to 4-unsubstituted 1,4-dihydropyridines [11].

^1H PMR and IR spectra for compounds IIIa-d and the mass spectrum of compound IIIb confirm the suggested structures (Table 2).

We have established that reduction of quinolinium (IV) and N-methylquinolinium (V) perchlorates with sodium tetrahydroborate in acetic acid gives the tetrahydroquinolines IIc and VI. Reduction of perchlorate IV occurred more readily and with greater yield than that of the corresponding quinoline Ic, while reduction of the N-methyl quinolinium perchlorate V was almost quantitative because quaternization of the nitrogen atom increased the electron density in the pyridine ring.

TABLE 2. Characteristics of the Synthesized 1,4-Dihydroquinolines IIIa-d and the 1,2-Dihydroquinolines VIIa and VIIb

Compound	Molecular formula	mp, °C	IR spectrum, ν, cm^{-1}	Mass spectrum, m/z (M^+)	^1H NMR Spectrum, (DMSO-D_6), δ, ppm						Yield, %
					$CO_2CH_2\underline{CH_3}$ t, 3H (J = 7 Hz)	2-CH_3, 3H	4-CH_2, s, 2H	$CO_2\underline{CH_2}CH_3$ q, 2H (J = 8 Hz)	aromatic protons	N—H, br.s, 1H (N—CH_3, s, 3H)	
IIIa	$C_{13}H_{15}NO_2$	116...118	1500, 1530, 1600, 1620, 1640, 3340	–	1,20	2,20 (s)	3,62	4,04	6,6...7,2 (m, 4H)	8,69	20
IIIb	$C_{13}H_{14}ClNO_2$	168...170	1500, 1520, 1600, 1620, 1640, 3330	251	1,20	2,20 (s)	3,60	4,00	6,6...6,8 (m, 1H), 6,9...7,1 (m, 2H)	8,76	87
IIIc†	$C_{14}H_{17}NO_3$	132...134	1530, 1620, 1640, 3340	–	1,20	2,20 (s)	3,53	4,02	6,2...6,5 (m, 2H), 6,87 (d, J = 9 Hz, 1H)	8,62	33
IIId†	$C_{12}H_{12}ClNO_2$	156...158	–	–	–	2,20 (s)	3,64	–	6,6...6,8 (m, 1H), 6,9...7,1 (m, 2H)	8,80	37
VIIa†	$C_{15}H_{19}NO_3$	yellow oil	1510, 1560, 1610, 1640, 1700	261	1,24	1,00 (d, J = 6 Hz)		4,18	6,06...6,3(m, 2H), 7,11 (d, J = 8 Hz, 1H)	(2,88)	46
VIIb†	$C_{13}H_{15}NO_3$	150...152	–	233	–	1,00 (d, J = 6 Hz)		–	6,0...6,3 (m, 2H), 7,06 (d, J = 9 Hz, 1H)	(2,88)	19

*The resonance of the 3-COOH proton (VIIb) is a broad singlet at 12.18 ppm, that of 2-H at 4.40 (q, J = 6 Hz) (VIIa) and 4.34 (q, J = 6 Hz) (VIIb), and that of 4-H as singlets at 7.31 ppm (VIIa) and 7.29 ppm (VIIb).

†Resonances of the 7-OCH_3 protons occur as singlets at 3.64 ppm (IIIc), 3.76 (VIIa) and 3.76 (VIIb).

‡The resonance of the 3-$COOCH_3$ group is a singlet at 3.60 ppm.

UV spectrum of IIIb, λ_{max}, nm (lg ε): 205.4 (4.643), 228 sh (4.23), 342 (4.24).

Reduction of quinolinium IV and N-methylquinolinium perchlorates with sodium tetrahydroborate in ethanol differs from that in acetic acid. We had found previously that reduction of 3-substituted-2-methyl-4-phenylquinolinium salts in an acetonitrile and methanol mixture gave 1,2-dihydroquinolines while 2-methyl-3-nitro-4-phenylquinolinium salts with sodium tetrahydroborate in pyridine gave the 1,4-dihydroquinolines in almost quantitative yield [12]. Perchlorates containing weaker electron withdrawing groups were not reduced under these conditions [4].

Reduction of the perchlorate IV in ethanol parallels that of the corresponding quinoline Ic to give the 1,4-dihydroquinoline IIIc, and it occurs more readily. This contrasts with the behavior of 2-methyl-4-phenylquinolinium perchlorates containing electron withdrawing groups in position 3 which are not reduced in analogous conditions (in ethanol) [4].

Unlike compound IV, the N-methylquinolinium perchlorate V is reduced to the 1,2-dihydro derivative VIIa like the 3-substituted 1,2-dimethyl-4-phenylquinolinium perchlorates [4]. Partial hydrolysis of the ethoxycarbonyl group to the carboxyl group in the basic medium to give the acid VIIc was also observed. Preparative TLC was used to separate the reduction products. It was shown in a separate experiment that compound VIIa hydrolyzes readily, which agrees with the properties of 1,2,6-trimethyl-3,5-diethoxycarbonyl-4-phenyl-1,2-dihydropyridine [13].

It has thus been shown that esters of 2-methylquinoline-3-carboxylic acids are reduced by sodium tetrahydroborate in ethanol with more difficulty than quinolines without substituents in positions 2 and 4 [1] to give 1,4-dihydroquinolines as a result of the electronic and steric effects of the methyl group. These 1,4-dihydroquinolines are less stable than 1,4-dihydroquinolines without 2 substituents for the reasons cited. Introduction of a phenyl substituent in position 4 in 2-methylquinolines with an electron withdrawing substituent in position 3 gives compounds which are not reduced by sodium tetrahydroborate in ethanol [4].

2-Methylquinoline-3-carboxylate esters and 3-acetyl-2-methylquinoline are reduced by sodium tetrahydroborate in acetic acid to give the 1,2,3,4-tetrahydro derivatives. As a result of protonation of the quinolines by acetic acid, the initial reduction products are the unstable 1,2-dihydroquinolines which are either reduced further or disproportionate to the 1,2,3,4-tetrahydroquinolines. This is an important difference from the reduction of the 4-phenyl-3-substituted 2-methylquinolines, where the principal reduction products are the N-ethyl-1,2-dihydroquinolines [4]. The phenyl group at position 4 stabilizes the 1,2-dihydroquinolines and sterically hinders further reduction of the initially formed 1,2-dihydroquinolines to 1,2,3,4-tetrahydroquinolines.

The N-methylquinolinium quaternary salts are reduced in ethanol predominantly to the 1,2-dihydroquinolines as expected because the quaternized nitrogen atom increases the electrophilicity of the pyridine at position 2.

EXPERIMENTAL

IR spectra of Nujol mulls were recorded with a Perkin-Elmer 580B spectrometer, ^{1}H NMR spectra of DMSO-D_6 solutions with TMS as internal standard were obtained with Bruker WH-90 (90 MHz) or Bruker WM-360 (360 MHz) machines. UV spectra of ethanol solutions were recorded with a Carl Zeiss/Jena Specord M-40 and mass spectra were obtained with an AEI MS-50 machine. Reactions were monitored and the purity of products determined by TLC on Silufol UV-254 strips with chloroform–hexane–acetone 9:7:1 solvent system. HPLC used an Exsil OH column (5 μm, 150 × 4.6 mm) (SGE, Australia) with a hexane–chloroform–isopropanol 10:4:1 solvent system and a Uv-254 detector. Preparative chromatography was carried out on 220 × 260 mm plates with a 2-3 mm layer of Silpearl UV-254 silica gel without binder. The quinoline starting materials Ia-d were obtained by condensation of the corresponding substituted anilines with derivatives of β-ketocarboxylic acids under Vilsmeier-Haack conditions [14, 15] and quinoline Ie was prepared by condensation of 2-aminobenzaldehyde with acetylacetone under Friedlander synthesis conditions [16].

C, H, N and Cl elemental analyses of the synthesized compounds agreed with calculated values.

Reduction of 3-Substituted 2-Methylquinolines (Ia-e) in Acetic Acid. The corresponding quinoline Ia-e (2.5 mmol) was dissolved in glacial acetic acid (25 cm^3) and argon was passed through the solution for 30 min. Sodium tetrahydroborate (0.57 g, 15 mmol) was added in portions over 10 min and the solution was kept at room temperature under argon for 3 h. The reaction mixture was poured into water (50 cm^3), extracted with chloroform (3 × 50 cm^3) and the extract was dried over anhydrous magnesium sulfate. The solvent was removed in vacuum, the residue was dissolved in chloroform (5 cm^3) and subjected to preparative thin layer chromatography using chloroform–hexane–acetone 9:7:1 as solvent. The products were located with UV light, the upper band of the tetrahydroquinoline (IIa-e) was removed, and the product eluted with chloroform.

The solvent was removed in vacuum and the yellow oil (with the exception of IIa) was recrystallized from a mixture of hexane and chloroform.

Reduction of 3-Substituted 2-Methylquinolines (Ia-e) in Alcohols. The quinoline (Ia-e) (2.5 mmol) was dissolved in ethanol (30 cm^3) (compound Id was dissolved in methanol (30 cm^3)) and argon was passed through the solution for 30 min. Sodium tetrahydroborate (0.57 g, 15 mmol) was added in portions over 10 min and the solution was boiled for about 4 h. The reaction was monitored by TLC. The reaction mixture was poured into water (50 cm^3), extracted with chloroform (3 × 50 cm^3) and the extract was dried with anhydrous magnesium sulfate. The solvent was removed in vacuum, the residue dissolved in chloroform (5 cm^3) and subjected to preparative thin layer chromatography using chloroform–hexane–acetone 9:7:1 as solvent. The solvent system chloroform–hexane–isopropanol 10:1:1 was used for compound IIIc. The products were located with UV light, the lower band of the 1,4-dihydroquinoline (IIa-d) was removed and the product eluted with chloroform. The solvent was removed in vacuum and the residue was recrystallized from a mixture of hexane and chloroform. In the case of quinoline Ie, the lower band consisted of 2-methyl-3-(1-hydroxyethyl)quinoline IX, yield 0.33 g (71%), m.p. 83-84°C. ^1H PMR spectrum ($CDCl_3$): 1.57 (3H, d, J = 7Hz, $-CH(OH)C\underline{H}_3$), 2.60 (1H, br.s, OH), 2.71 (3H, s, 2-CH_3), 5.17 (1H, q, J = 6Hz, 3-$C\underline{H}(OH)CH_3$), 7.3-8.1 (4H, m, aromatic protons), 8.18 ppm (1H, br.s, 4-CH).

2-Methyl-7-methoxy-3-ethoxycarbonylquinolinium Perchlorate (IV). 57% Perchloric acid (0.6 cm^3, 5 mmol) was added to a solution of quinoline Ic (1.23 g, 5 mmol) in ethanol (30 cm^3), the mixture was boiled for 3 h, the solvent was removed in vacuum, then cooled and treated with ether. The white crystals were filtered off and recrystallized from isopropanol to give the perchlorate IV (1.25 g, 72%), m.p. 213-215°C. ^1H PMR spectrum (DMSO-D_6): 1.40 (3H, t, J = 7 Hz, 3-$CH_2\underline{CH}_3$), 3.04 (3H, s, 2-CH_3), 4.02 (3H, s, OCH_3), 4.42 (2H, q, J = 7 Hz, 3-$\underline{CH}_2CH_3$), 7.4-7.7 (2H, m, aromatic protons), 8.31 (1H, d, J = 9 Hz, aromatic proton), 9.33 ppm (1H, s, 4-CH).

1,2-Dimethyl-7-methoxy-3-ethoxycarbonylquinolinium Perchlorate (V). Quinoline Ic (1.23 g, 5 mmol) and freshly distilled dimethyl sulfate (1.42 cm^3, 16 mmol) were boiled for 6 h. The mixture was cooled, washed with ether (3 × 10 cm^3), the residue was dissolved in water (20 cm^3) and a saturated solution was added of sodium perchlorate until separation of a white precipitate stopped. The solid was filtered off, washed with water and recrystallized from isopropanol to give the perchlorate V (1.20 g, 67%), m.p. 205-207°C. ^1H PMR spectrum (DMSO-D_6): 1.40 (3H, t, J = 7 Hz, 3-$CH_2\underline{CH}_3$), 3.18 (3H, s, 2-CH_3), 4.15 (3H, s, OCH_3), 4.42 (3H, s, N-CH_3), 4.49 (2H, q, J = 7 Hz, 3-$\underline{CH}_2CH_3$), 7.6-7.8 (2H, m, aromatic protons), 8.42 (1H, d, J = 9 Hz, aromatic proton), 9.40 ppm (1H, s, 4-CH).

Ethyl 1,2-Dimethyl-7-methoxy-1,2,3,4-tetrahydroquinolin-3-carboxylate (V) and Ethyl 2-Methyl-7-methoxy-1,2,3,4-tetrahydroquinolin-3-carboxylate (IIc). The method of reducing the perchlorates IV and V was analogous to that used to reduce quinolines Ia-e in acetic acid. Tetrahydroquinoline VI was isolated by preparative TLC using 10:1 hexane–isopropanol. The upper band was collected and compound VI was eluted with acetone. The solvent was evaporated in vacuum to give a yellow oil (0.61 g, 91%). The yield of tetrahydroquinoline IIc was 0.40 g (64.3%).

Reduction of 2-methyl-7-methoxy-3-ethoxycarbonylquinolinium perchlorate (IV) in ethanol was analogous to that used for the reduction of quinolines Ia-e in ethanol. Yield of the 1,4-dihydroquinoline IIIc was 0.35 g (57%).

Reduction of 1,2-Dimethyl-7-methoxy-3-ethoxycarbonylquinolinium Perchlorate (V) in Ethanol. The method of reduction of perchlorate V was analogous to that for the reduction of quinolines Ia-e in ethanol. The reaction time was 2 h. Preparative TLC with chloroform–heptane–acetone 9:9:1 as solvent gave an upper band of ethyl 1,2-dihydro-1,2-dimethyl-7-methoxyquinolin-3-carboxylate (VIIa) and a lower yellow band of 1,2-dihydro-1,2-dimethyl-7-methoxyquinolin-3-carboxylic acid (VIIb). Compounds VIIa and VIIb were eluted from the silica gel with acetone and the solvent was evaporated in vacuum. Compound VIIb crystallized from a hexane–ethyl acetate mixture as green crystals, while compound VIIa was a yellow fluorescent oil which slowly oxidized.

Hydrolysis of Ethyl 1,2-Dihydro-1,2-dimethyl-7-methoxyquinolin-3-carboxylate (VIIa). Potassium hydroxide (0.02 g, 3 mmol) was added to a solution of compound VIIa (0.26 g, 1 mmol) in ethanol (10 cm^3) and the mixture was boiled for 2 h. The solution was poured into water, neutralized with dilute hydrochloric acid, extracted with chloroform (3 × 50 cm^3), the extract was dried with anhydrous magnesium sulfate, the solvent was evaporated in vacuum and the residue was crystallized from hexane-ethyl acetate to give the acid VIIb (0.11 g, 40%).

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