REDUCTION OF 2-, 3- AND 4-METHYLQUINOLINES, 2-, 3- AND 4-QUINOLYLMETHANOLS AND CORRESPONDING QUINOLINECARBOXALDEHYDES WITH TRIETHYLAMMONIUM FORMATE*

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Reduction of the compounds mentioned in the title with triethylammonium formate gave 1-formyl-C-methyl-1,2,3,4-tetrahydroquinolines *IIa—IIc*. On reduction of derivatives substituted in the position 3 and 4 (*Ib*, *Ic*, *Ie*, *If*, *Ih*, *Ii*) the products of 1,2-addition are also formed *i.e. IIIa*, *IIIb*, and on reduction of 3-quinolylmethanol (*Ie*) and 3-quinolinecarboxaldehyde (*Ih*) the products of 1,4-addition, *i.e. IVa*, *IVb* also result. Alcohol *If* and aldehyde *Ii* also give the product of the reduction of the functional groups, *i.e.* 4-methylquinoline (*Ic*). When 3-quinolylmethanol (*Ie*) was prepared by reduction of aldehyde *Ih* with sodium borohydride 1,2,3,4-tetrahydro-3-quinolylmethanol (*IIe*) was also isolated.

In preceding papers we have described reductions of quinolinecarboxylic acids[1], acetylquinolines[2], quinolinecarbonitriles[3] and some other 3-substituted derivatives of quinoline[4] with triethylammonium formate. In order to complete our knowledge we decided also to reduce in this manner methylquinolines *Ia—Ic*, alcohols *Id—If* and aldehydes *Ig—Ii*. In doing this we isolated in all instances corresponding 1-formyl-C-methyl-1,2,3,4-tetrahydroquinolines *IIa—IIc*, see Table I. On reduction of 3-methylquinoline (*Ib*) and 4-methylquinoline (*Ic*) 1,2-dihydro derivatives *IIIa* and *IIIb* are also formed. Their stability could be demonstrated by the fact that their ratio to tetrahydro derivatives did not change even after a prolonged effect of the reducing agent. In spite of this these dihydro derivatives can be converted to tetrahydro derivatives by means of catalytic hydrogenation.

After reduction of derivatives substituted in the position 2, alcohol *Id* and aldehyde *Ig*, we also identified in the reaction mixture 1-formyl-1,2,3,4-tetrahydroquinoline (*IId*) in addition to tetrahydroderivative *IIa*. This could be also formed by decomposition of the product of primary reduction, *i.e.* 1-formyl-1,2-dihydro-2-quinolylmethanol (*V*), to formaldehyde and 1-formyl-1,4-dihydroquinoline (*IVc*), which is transformed to *IId* on reduction of the enamine grouping. A similar reaction

* Part X in the series Quinoline and Isoquinoline Derivatives; Part IX: This Journal *46*, 503 (1981).

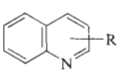
TABLE I

Reduction of Quinoline Derivatives *Ia—Ii* with Triethylammonium Formate

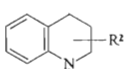
Starting compound	Products, %				Yield[a], %
Ia	*IIa* (100)[b]	—	—	—	71
Ib (ref.[9])	*IIb* (60)[c]	*IIIa* (40)[d,e]	—	—	75
Ic	*IIc* (68)[f]	*IIIb* (32)[e,g]	—	—	79
Id (ref.[10])	*IIa* (79)[h] *IId* (12)[h]	—	—	9[i]	30
Ie	*IIb* (80)[h]	*IIIa* (5)[h]	*IVa* (15)[j]	—	23
If (ref.[11])	*IIc* (77)[h]	*IIIb* (12)[h]	—	11[k]	27
Ig (ref.[12])	*IIa* (71)[h] *IId* (19)[h]	—	—	10[l]	23
Ih (ref.[8])	*IIb* (65)[h]	*IIIa* (26)[h]	*IVa* (9)[h]	*IVb* (47)[h]	74[l]
Ih (ref.[8])	*IIb* (69)[h]	*IIIa* (31)[h]	—	*IVb* (35)[h,n]	74[m]
Ii (ref.[13])	*IIc* (73)[h]	*IIIb* (5)[h]	—	22[h,k]	24

[a] The values (with the exception of *IVb*) are referred to corresponding tetrahydroquinolines *IIa—IIc*. [b] B.p. 93—94°C/13·3 Pa. Lit.[14] gives b.p. 129—130°C/1—2 Torr. For $C_{11}H_{13}NO$ (175·2) calculated: 75·40% C, 7·48% H, 7·99% N; found: 75·56% C, 7·53% H, 7·94% N. ^{1}H-NMR spectrum ($CDCl_3$), ppm: 1·22 (d, 3 H, $J = 6·5$) CH_3; 1·49—2·35 (m, 2 H) CH_2(3); 2·49—3·05 (m, 2 H) CH_2(4); 4·80 (m, 1 H) CH(2); 7·15 (bs, 4 H) benzene ring; 8·68 (s, 1 H) CHO. [c] B.p. 108°C/13·3 Pa (after hydrogenation of *IIb* + *IIIa* on PtO_2). For $C_{11}H_{13}NO$ (175·2) calculated: 75·40% C, 7·48% H, 7·94% N; found: 75·70% C, 7·72% H, 8·06% N. ^{1}H-NMR spectrum ($CDCl_3$) ppm: 1·10 (d, 3 H, $J = 6·5$) CH_3; 1·81—2·24 (m, 1 H) 3-Ha; 2·31—2·63 (m, 1 H, $^2J = 16$, $^3J_{Ha,3a} = 9·5$) 4-Ha; 2·78—3·01 (m, 1 H, $^3J_{He,3a} = 5$) 4-He; 3·01—3·26 (m, 1 H, $^2J = 13$, $^3J_{2a,3a} = 10$) 2-Ha; 4·07—4·30 (dd, 1 H, $^3J_{2e,3a} = 4$, $^4J_{2e,4e} = 2$) 2-He; 7·12 (bs, 4 H) benzene ring; 8·81 (s, 1 H) CHO. [d] ^{1}H-NMR spectrum of *IIIa* ($CDCl_3$), ppm: 1·93 (s, 3 H), CH_3; 4·33 (s) CH_2(2); 6·20 (s) CH(4); 8·61 (s) CHO. [e] The ratio of the products does not change with the prolongation of the reaction time. [f] B.p. 99—100°C/13·3 Pa (after hydrogenation of *IIc* + *IIIb* on PtO_2). For $C_{11}H_{13}NO$ (175·2) calculated: 75·40% C, 7·48% H, 7·94% N; found: 75·49% C, 7·54% H, 8·05% N. ^{1}H-NMR spectrum ($CDCl_3$), ppm: 1·33 (d, 3 H, $J = 6$ Hz) CH_3; 1·48—2·24 (m, 2 H) CH_2(3); 2·90 (m, 1 H) CH(4); 3·81 (m, 2 H) CH_2(2); 7·16 (bs, 2 H) benzene ring; 8·78 (s, 1 H) CHO. [g] ^{1}H-NMR spectrum of *IIIb* ($CDCl_3$), ppm: 2·08 (s) CH_3; 4·39 (m) CH_2(2); 5·78 (m) CH(3); 8·54 (s) CHO. [h] Identical according to GLC and ^{1}H-NMR with the standard. [i] Unidentified component. [j] ^{1}H-NMR spectrum of *IVa* ($CDCl_3$), ppm: 1·91 (s) CH_3; 3·48 (s) CH_2(4); 5·04 (s) CH(2); 8·68 (s) CHO. [k] 4-Methylquinoline. [l] Composition of the mixture after 3 h of reduction. [m] Composition of the mixture after 13 h of reduction. [n] M.p. 171—172°C (ethanol–ethyl acetate). For $C_{10}H_9NO$ (159·2) calculated: 75·45% C, 5·70% H, 8·80% N; found: 75·72% C, 5·75% H, 9·03% N. IR spectrum ($CHCl_3$; cm^{-1}): 3 640, 3 300 ν(NH); 1 637, 1 607 ν(N—C=C—CHO). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide), ppm: 3·49 (s, 2 H) CH_2(4); 6·66—7·08 (m, 4 H) benzene ring; 7·20 (d, 1 H, $J_{NH,CH(2)} = 5$) CH(2); 9·02 (s, 1 H) CHO; 9·45 (bs, 1 H) NH.

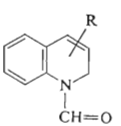
is also described in the series of monoterpenic unsaturated alcohols[5]. Reduction of 3-substituted derivatives, alcohol *Ie* and aldehyde *Ih*, gave 1,4-dihydro derivative *IVa* in addition to 1,2-dihydro derivative *IIIa*. By reduction of aldehyde *Ih* the 1,4-dihydro derivative *IVb* was also isolated. The formed derivative *IVa* disappeared on prolongation of the reaction time of the reduction of aldehyde *Ih*. This course of the reduction of aldehyde *Ih* resembles a similar reduction of 3-acetylquinoline, when we also isolated 1,4-dihydro derivative[2]. Reduction of 4-substituted derivatives, alcohol *If* and aldehyde *Ii*, affords in addition to 1,2-dihydro derivative *IIIb* a product of mere reduction of the functional group, without the nucleus being attacked, *i.e.* 4-methylquinoline (*Ic*). In these cases the effect of the substituents in the position 4 evidently plays a role, since they partially hinder the access of the reducing agent.



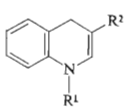
Ia, R = 2-CH_3
Ib, R = 3-CH_3
Ic, R = 4-CH_3
Id, R = 2-CH_2OH
Ie, R = 3-CH_2OH
If, R = 4-CH_2OH
Ig, R = 2-CHO
Ih, R = 3-CHO
Ii, R = 4-CHO



IIa, R^1 = CHO, R^2 = 2-CH_3
IIb, R^1 = CHO, R^2 = 3-CH_3
IIc, R^1 = CHO, R^2 = 4-CH_3
IId, R^1 = CHO, R^2 = H
IIe, R^1 = H, R^2 = 3-CH_2OH



IIIa, R = 3-CH_3
IIIb, R = 4-CH_3



IVa, R^1 = CHO, R^2 = CH_3
IVb, R^1 = H, R^2 = CHO
IVc, R^1 = CHO, R^2 = H

From the results obtained it follows that the reduction of the mentioned 2-substituted derivatives of quinoline with triethylammonium formate gives rise to 1,2,3,4-tetrahydro derivatives, the reduction of corresponding 3-substituted derivatives gives a mixture of 1,2-dihydro and 1,4-dihydro derivatives in addition, and the reduction of 4-substituted derivatives gives simultaneously 1,2-dihydro derivatives. Hence, it may be assumed that the reduction of aldehydes takes place *via* the stage of alcohols.

When preparing 3-quinolylmethanol (*Ie*) on reduction of 3-quinolinecarboxaldehyde (*Ih*) with sodium borohydride we observed a side-reaction, *i.e.* partial reduction of the ring under formation of 1,2,3,4-tetrahydro-3-quinolylmethanol (*IIe*). Quinoline behaves in a similar manner in that it gives a mixture of 1,2-dihydro derivatives and 1,2,3,4-tetrahydro derivatives under the effect of sodium borohydride. In contrast to this the 3-substituted derivatives of quinoline, with substituents that are not reduced with sodium borohydride, afford 1,4-dihydro derivatives[6].

EXPERIMENTAL

Gas chromatography was carried out on a Chrom II instrument (column length 170 cm, diameter 0·6 cm, 15% poly(1,4-butanediol succinate) on Chromaton N-AW) with FID. Nitrogen was used as carrier gas. The infrared spectra were measured on a Perkin–Elmer Model 325 spectrophotometer. The ^{1}H-NMR spectra were measured on a Varian XL-100-15 (100·1 MHz) instrument at 37°C, using tetramethylsilane as internal standard. The ultraviolet spectra were measured on a UV Specord (Zeiss, Jena) apparatus, in ethanol. The temperature data are not corrected. The amount of the triethylammonium formate[7] used for the reductions is expressed in mol, which are referred to the amount of formic acid.

Reduction of 3-Quinolinecarboxaldehyde with $NaBH_4$

A solution of $NaBH_4$ (1·9 g; 0·05 mol) in water (20 ml) was added to a stirred and cooled suspension (0°C) of *Ih* (8 g; 0·051 mol) in ethanol (20 ml) and the mixture was stirred at room temperature for 2 h. After decomposition with hydrochloric acid it was concentrated in a vacuum, alkalized and extracted with dichloromethane. The extract was dried over magnesium sulfate and evaporated to yield 8·3 g of a crude product which was crystallized to give 3·5 g (43%) of *Ie*, m.p. 87°C. Lit.[8] gives 89°C.

From the mother liquors *IIe* was isolated by chromatography on silica gel (with ethyl acetate) b.p. 128°C/13·3 Pa, 1·2 g (14%). For $C_{10}H_{13}NO$ (163·2) calculated: 73·59% C, 8·03% H, 8·58% N; found: 73·44% C, 7·94% H, 8·57% N. IR spectrum ($CHCl_3$), cm^{-1}: 3640, 3440 OH. ^{1}H-NMR spectrum ($CDCl_3$), ppm: 1·90—2·30 (m, 1 H,) CH(3); 2·30—3·72 (m, 8 H) CH_2OH, CH_2(4), CH_2(2), NH; 2·95 (s) OH and NH; 6·35—7·05 (m, 4 H,) benzene ring.

Reduction of *Ia*—*Ii* with Triethylammonium Formate

A mixture of compound *I* (0·042 mol) and 54·4 g (0·63 mol) of triethylammonium formate was heated at 160°C under stirring until the escape of CO_2 ceased. Triethylammonium formate was distilled off in a vacuum, the distillate diluted with water, extracted with benzene and the extract washed with water and dried over $MgSO_4$. The distillation residue was alkalized with a saturated K_2CO_3 solution, extracted with ether and the extract washed with water and dried over $MgSO_4$. The benzene and the ether extracts were combined, the solvents evaporated under reduced pressure and the product distilled and identified by means of GLC and ^{1}H-NMR spectrometry (Table I).

The elemental analyses were carried out in the analytical laboratory of our Department (head Dr L. Heleš ic), the NMR *measurements were conducted by Dr P. Trška, and the measurements of the* IR *spectra were done by Dr E. Janečková and Dr A. Kohoutová.*

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