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INVESTIGATIONS ON 2,3'-BIQUINOLYL.
16*. THE REGIOSELECTIVITY OF REDUCTION OF 1-ALKYL-3-(2-QUINOLYL)QUINOLINIUM AND 1,1'-DIALKYL-3,3'-DI(2-QUINOLYL)-1,1',4,4'-BIQUINOLYL IODIDES USING METALLIC ZINC, LITHIUM AND POTASSIUM

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The reaction of 1-alkyl-3-(2-quinolyl)quinolinium iodides with excess zinc in THF gives a diastereomeric mixture of 1,1'-dialkyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyls. An excess of lithium in THF gives a mixture of 1',2'-dihydro-2,3'-biquinolyl and 1'-alkyl-1',4'-dihydro-2,3'-biquinolyl with the former predominating. The reduction by lithium in THF of 1,1'-dialkyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyls leads to analogous products. Reduction of 1-alkyl-3-(2-quinolyl)quinolinium iodides by metallic potassium gives 1-alkyl-1',4'-dihydro-2,3'-biquinolyls.

Keywords: 1'-alkyl-1',4'-dihydro-2,3'-biquinolyls, 1,1'-dialkyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyls, 1',2'-dihydro-2,3'-biquinolyl, 1-alkyl-3-(2-quinolyl)quinolinium iodides, potassium, lithium, zinc, reduction.

We have previously [2] studied the reduction of 2,3'-biquinolyls and have shown that it occurs *via* two reversible one-electron stages to form an anion radical and a dianion. It was of interest of study the reduction of quaternary 2,3'-biquinolyls **1** and compare this with the reduction of 2,3'-biquinolyls.

We have found that, in contrast to 2,3'-biquinolyl, the electrochemical reduction of 1'-methyl-3'-(2-quinolyl)quinolinium chloride (**1a**) occurs through a single irreversible stage, probably via the formation of the radicals **2**, recombination of which gives the stable dimer species **3** or **4** (see Scheme 1).

As shown by calculations for the radical **2a** (see Fig. 1) the position with the greatest spin density is position 4'. Hence the formation of the "dimers" **3** and **4** can be expected.

The chemical reductions were carried out using metallic zinc, lithium, and potassium.

In fact, the reduction of the salts **1a,b** with zinc in THF leads to the formation of a mixture of the diastereomer compounds **3a,b**, the ratio of which as determined by an NMR spectroscopic method is 4.1:1 (for **3a**) or 4.2:1 (for **3b**). Unfortunately, the configuration of the diastereomers and the separation of the minor diastereomer have not been achieved yet.

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* For Communication 15 see [1].

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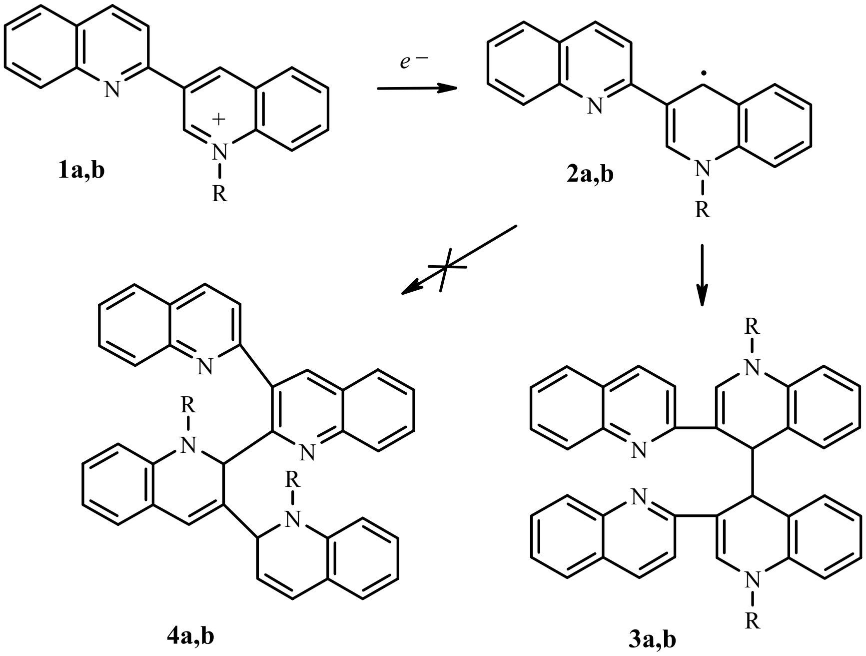
Scheme 1



1-4 **a** R = Me; **b** R = Et

The ^{1}H NMR spectra of the mixture of diastereomers show signals for both the main and for the minor diastereomers (for **3a**: 2.73 and 2.85 (6H, s, CH_3), 6.65 and 5.04 (2H, s, H-4,4'): for **3b**: 0.89 and 1.04 (6H, t, $CH_aCH_bC\underline{H}_3$), 3.16 and 3.19 (2H, dq, $C\underline{H}_aH_bCH_3$), 3.26 and 3.32 (2H, dq, $CH_a\underline{H}_bCH_3$), 4.75 and 5.08 (2H, s, H-4,4')). When using the salt **1** which contained a deuterium in position 4' the intensity of the proton signals for 4 and 4' in the reaction products is lowered.

Reduction of the salt **2a** with metallic potassium in THF leads after protonation of the reaction mixture to 1'-methyl-1',4'-dihydro-2,3'-biquinolyl **5** in 84% yield.

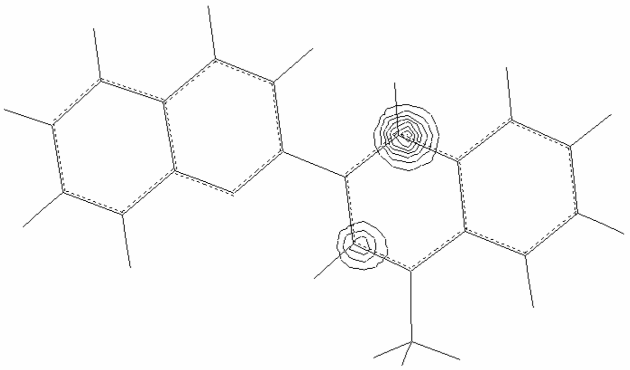
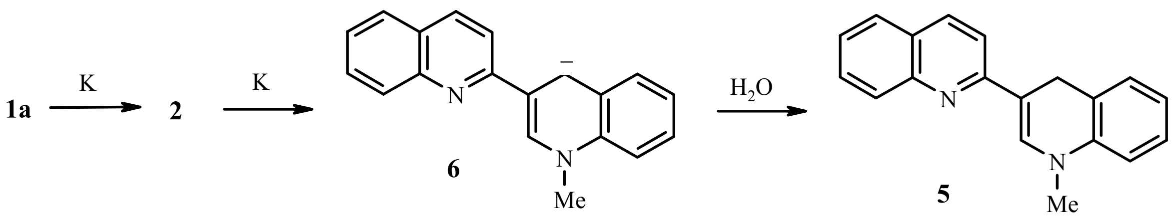
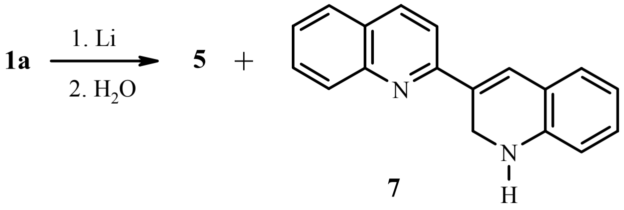


Fig. 1. Distribution of spin density in the radical **2a** using an *ab initio* calculation method.



Such a change in regioselectivity on going from zinc to potassium can be explained in the following way. Potassium has a lower ionization potential than zinc and can reduce the radical **2** to the anion **6**. Protonation of the latter gives the dihydro derivative **5**.

It might be expected that metallic lithium would reduce the salt **2a** similarly to potassium. Unexpectedly, we found that the reaction of compound **2a** with an excess of metallic lithium in THF gave a mixture of 1'-methyl-1',4'-dihydro-2,3'-biquinolyl (**5**) and 1',2'-dihydro-2,3'-biquinolyl (**7**) in 38 and 51% yield respectively.



It is likely that the radical **2** formed in the course of the reaction is partially reduced to the anion **6**, protonation of which gives the dihydro derivative and partly via a recombination to give the dimer **3a**. Subsequent reduction of the latter gives compound **7**.

$$\begin{tikzcd}
\mathbf{1} \arrow[r, "\text{Li}"] & \mathbf{2} \arrow[r, "\mathbf{2}"] \arrow[d, "\text{Li}"'] & \mathbf{3a} \arrow[r, "\text{1. Li}", "\text{2. } H_2O"'] & \mathbf{7} \\
 & \mathbf{6} \arrow[r, "H_2O"] & \mathbf{5} &
\end{tikzcd}$$

This scheme shows that the reduction of compound **3a** at room temperature by excess lithium in absolute THF over 1 h gives the dihydro derivative **7** in 68% yield after protonation of the reaction mixture.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WP-200 instrument (200 MHz) using TMS as internal standard. Monitoring of the reaction course and the purity of the synthesized compounds was carried out on Silufol UV-254 plates using the solvent system ethyl acetate–hexane (1:1). Flash chromatography was performed using method [3] (column: *d* = 60 mm, *l* = 50 mm) with benzene as low polarity and ethyl acetate as polar solvent.

Reduction of 1-Alkyl-3-(2-quinolyl)quinolinium Iodides (1) by Metallic Zinc (General Method). A mixture of compound **1** (2.5 mmol) and zinc dust (0.32 g, 5 mmol) in absolute THF (10 ml) was stirred at ~20°C to the disappearance of the starting salt (~3 h). Water (50 ml) was added and the product was extracted with benzene (3 × 30 ml). The benzene extracts were combined, dried over sodium sulphate, and evaporated to give the mixture of diastereomers of compound **3a** as dark red crystals. The yield was close to quantitative.

For separation of the main diastereomer the mixture of diastereomers was separated by flash chromatography. The first colored fraction contains the main diastereomer.

1,1'-Dimethyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyl (3a) (General Method) was obtained from 1-methyl-3-(2-quinolyl)quinolinium iodide. Yield 0.434 g (64%); mp 172-174°C (alcohol), R_f 0.56 (Silufol UV-254, ethyl acetate). ^{1}H NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 2.73 (6H, s, CH_3); 4.65 (2H, s, H-4,4'); 6.53 (2H, d, $J_{7'8'}$ = 8.25, H-8,8'); 6.82 (2H, dd, $J_{5'6'}$ = 7.57, $J_{6'7'}$ = 7.32. H-6,6'); 7.00 (2H, dd, $J_{5'6'}$ = 7.57, $J_{57'}$ =1.71, H-5,5'); 7.08 (2H, ddd, $J_{78'}$ = 8.25, $J_{6'7'}$ = 7.32, $J_{5'7'}$ = 1.71, H-7,7'); 7.47 (2H, s, H-2,2'); 7.48 (2H, dd, J_{56} = 8.05, J_{67} = 7.32, 6-Ar); 7.75 (2H, ddd, J_{78} = 8.30, J_{67} = 7.32, J_{57} = 1.71, 7-Ar); 7.91 (2H, dd, J_{56} = 8.05, J_{57} =1.71, 5-Ar); 8.06 (2H, d, J_{78} = 8.30, 8-Ar); 8.30 (2H, d, J_{34} = 8.79, 4-Ar); 8.35 (2H, d, J_{34} = 8.79, 3-Ar). Found, %: C 84.18; H 5.53; N 10.29. $C_{38}H_{30}N_4$. Calculated, %: C 84.10; H 5.57; N 10.33.

1,1'-Diethyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyl (3b) (General Method) was obtained from 1-ethyl-3-(2-quinolyl)quinolinium iodide. Yield 0.499 g (70%), mp 151-153°C (alcohol), R_f 0.63 (Silufol, UV-254, ethyl acetate). ^{1}H NMR spectrum (CD_3CN), δ, ppm (*J*, Hz): 0.89 (6H, t, *J* = 7.15, $CH_aH_bC\underline{H}_3$); 3.16 (2H, dq, J_{gem} = 14.30, $J_{CH\text{-}CH_3}$ = 7.15, $C\underline{H}_aH_bCH_3$); 3.26 (2H, dq, J_{gem} = 14.30, J_{CH-CH_3} = 7.15, $CH_aC\underline{H}_bCH_3$); 4.75 (2H, s, H-4,4;); 6.56 (2H, d, $J_{7'8'}$ = 8.25, H-8,8'); 6.78 (2H, dd, $J_{5'6'}$ = 7.57, $J_{6'7'}$ = 7.32, H-6,6'); 7.92 (2H, dd, $J_{5'6'}$ = 7.57; $H_{5'7'}$ = 1.71, H-5,5'); 7.07 (2H, ddd, $J_{7'8'}$ = 8.25, $J_{6'7'}$ = 7.32, $J_{5'7'}$ = 1.71, H-7,7'); 7.46 (2H, dd, J_{56} = 8.05, J_{67} = 7.32, 6-Ar); 7.55 (2H, s, H-2,2'); 7.75 (2H, ddd, J_{78} = 8.30, J_{67} = 7.32; J_{57} = 1.71, 7-Ar); 7.88 (2H, dd, J_{56} = 8.05, J_{57} = 1.71, Ar-5); 8.06 (2H, d, J_{78} = 8.30, 8-Ar); 8.30 (2H, d, J_{34} = 8.79, 4-Ar); 8.37 (2H, d, J_{34} = 8.79, 3-Ar). Found, %: C 84.22; H 5.96; N 9.82. $C_{40}H_{34}N_4$. Calculated, %: C 84.18; H 6.00; N 9.82.

Method for the Reduction of 1-Methyl-3-(2-quinolyl)quinolinium Iodide (1a) by Metallic Potassium (M1 = Method 1). A mixture of 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and metallic potassium (0.21 g, 5.4 mmol) in THF (10 ml) was stirred at reflux to the disappearance of the starting salt (2-2.5 h). The reaction mixture was quenched with tert-butanol. Water (50 ml) was added and the product was extracted with benzene (3 × 30 ml). The benzene extracts were combined, dried over sodium sulphate and evaporated to give orange crystals.

Method for the Reduction of 1-Methyl-3-(2-quinolyl)quinolinium Iodide (1a) by Metallic Potassium (M2). A mixture of 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and metallic potassium (0.21 g, 5.4 mmol) in THF (10 ml) was stirred at reflux until the disappearance of the starting salt (~2 h). Water (50 ml) was added carefully and the product was extracted with benzene (3 × 30 ml). The benzene extracts were combined, dried over sodium sulphate, and evaporated. The residue was separated chromatographically.

Method for the Reduction of 1,1'-Dimethyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyl (3a) by Metallic Lithium (M3). A mixture of the 1,1'-dimethyl-3,3'-di(2-quinolyl)-1,1',4,4'-tetrahydro-4,4'-biquinolyl diastereomers (0.678 g, 1.25 mmol) and metallic lithium (0.036 g, 5.12 mmol) in absolute THF (10 ml) was stirred at room temperature for 3 h. Water (50 ml) was carefully added and the product was extracted with ethyl acetate (3 × 30 ml). The combined extracts were dried over sodium sulphate and evaporated to give yellow crystals.

1'-Methyl-1',4'-dihydro-2,3'-biquinolyl (5). M1: yield 0.571 g (84%). **M2**: yield 0.258 g (38%); mp 146-147°C (alcohol). According to data in [4], mp 146-147°C. A mixed sample with an authentic material did not give a depression of melting point. The ^{1}H NMR spectra are identical.

1',2'-Dihydro-2,3'-biquinolyl (7) M2: yield 0.329 g (51%). **M3**: yield 0.439 g (68%); mp 271-272°C (benzene). ^{1}H NMR spectrum (DMF-d_7), δ, ppm (*J*, Hz): 3.10(2H, d, $J_{2'\text{-NH}}$ = 4.4, H-2'); 5.89 (1H, br. d, $J_{2'\text{-NH}}$ = 4.4, NH); 6.48 (1H, ddd, $J_{5'6'}$ = 7.63, $J_{6'7'}$ = 7.93, $J_{6'8'}$ = 0.91, H-6'); 6.76 (1H, dd, $J_{7'8'}$ = 7.95, $J_{6'8'}$ = 0.91, H-8'); 7.03 (1H, ddd, $J_{6'7'}$ = 7.93, $J_{7'8'}$ = 7.95, $J_{5'7'}$ = 1.52, H-7'); 7.29 (1H, dd, $J_{5'6'}$ = 7.63, $J_{5'7'}$ = 1.52, H-5'); 7.49 (1H, ddd, J_{56} = 7.99; H_{67} = 7.95, J_{68} = 1.45, H-6); 7.69 (1H, ddd, J_{67} = 7.95, J_{78} = 8.01, J_{57} = 1.51, H-7); 7.85 (2H, m, H-5,8); 7.93 (1H, d, J_{34} =8.85, H-3); 7.98 (1H, s, H-4'); 8.23 (1H, d, J_{34} = 8.85, H-4). Found, %: C 84.00; H 5.30; N 10.70. $C_{18}H_{14}N_2$. Calculated, %: C 83.69; H 5.46; N 10.85.

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