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SYNTHESIS AND PROTONATION OF 2,3′-BIQUINOLYL DIANIONS

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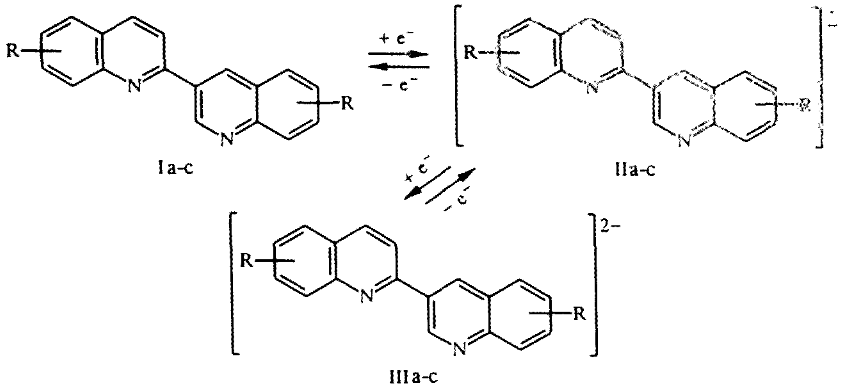
It has been shown that the reaction of 2,3′-biquinolyls with an excess of lithium in tetrahydrofuran leads to the formation of dianions, treatment of which with water or D_2O gives 1′,4′-dihydro-2,3′-biquinolyls or their 4′-D derivatives in good yield. Oxidation of the latter leads to 4′-D-2,3′-biquinolyl. The polarographic reduction of 2,3′-biquinolyl has been studied.

We have recently developed a convenient method for obtaining the 2,3′-biquinolyls (Ia-c) [1], previously available with extreme difficulty. This has permitted investigation of their reactivity. The generation and subsequent protonation of their dianions is reported in the present work.

Similar molecules are well known in the arene and heteroarene series [1-3]. Quinoline forms a dianion on reaction with metallic sodium, which is converted into 3′,4′-dihydro-2,3′-biquinolyl [1]. We suggested that 2,3′-biquinolyl (Ia) must also react with alkali metals. Its dianion (IIIa) proved to be more stable both as a result of steric factors and also due to the high delocalization of the negative charge (Scheme 1).

Scheme 1



I-III a R = H, b R = 6(6′)-Me, c R = 7(7′)-Me

Reduction of 2,3′-biquinolyl (Ia) on a platinum electrode in dry DMF occurs in two one-electron stages (Scheme 1) (determined by comparison of the values of the one-electron oxidation currents of ferrocene under the same conditions) more readily than quinoline by 0.2 V [4] ($E_{1/2} = -2.1$ and -2.6), which is explained by the lower energy of its lowest unoccupied molecular orbital.

Anodic peaks corresponding to both cathodic peaks were observed, which points to the stability of the reaction products formed under the experimental conditions and to the formation of stable particles, viz. an anion-radical and a dianion (Fig. 1).

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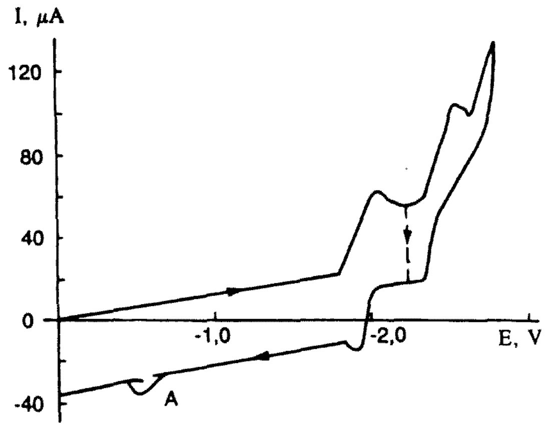


Fig. 1. Cyclic volt–amperogram of 0.005 M biquinolyl in 0.05 M $LiBF_4$ in dimethylformamide.

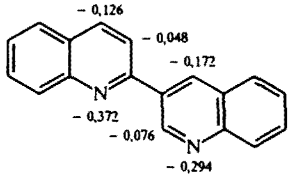
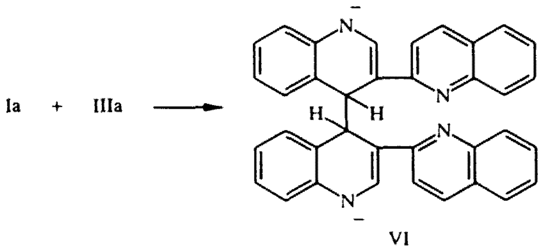


Fig. 2. Charge distribution in the dianion (IIIa) (by MNDO).

Peak A on the anodic branch of the volt–amperogram is displayed only after the second reduction stage. Judging by the size of the potentials it may correspond to the oxidation of an unstable dimerization product (VI) formed on reacting the dianion (IIIa) with the initial biquinolyl (Ia) (Scheme 2).

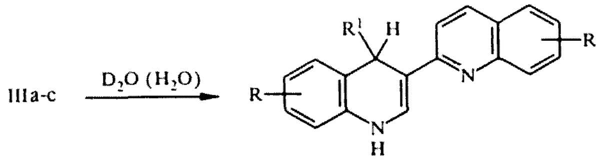
Scheme 2



VI

Calculations on the dianion (IIIa) by the MNDO method showed that apart from the nitrogen atoms the greatest negative charge was localized at position 4′ (Fig. 2). Consequently it is logical to expect that its protonation will lead to the formation of 1′,4′-dihydro-2,3′-biquinolyl (IVd).

Scheme 3



IV a-d

IV a R = H, R^1 = D; b R = 6-Me, R^1 = D; c R = 7-Me, R^1 = D; d R = R^1 = H

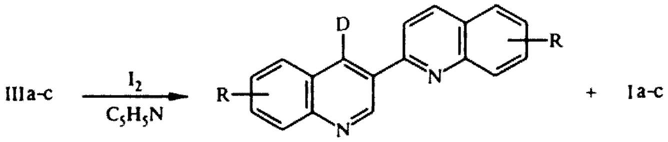
The reaction of biquinolyls (Ia-c) with lithium was carried out at room temperature in absolute THF at a molar ratio of (Ia-c) to metal of 1:3. The process was accompanied by the rapid development of a red color, deepening to a reddish violet. Compound (IVd) was isolated in practically quantitative yield on subsequent treatment of the reaction mixture with water (Scheme 3) [5]. In our opinion, this points in favor of the formation of dianion (IIIa), since it is known that under these conditions anion-radicals form a mixture of the starting material and the dihydro derivative in a 1:1 ratio [2, 3]. The use of heavy water leads to the formation of 4'-D-1',4'-dihydro-2,3'-biquinolyl (IVa).

The ^1H NMR spectra of compounds (IVd) [5] and (IVa) were identical except for the signals of the protons at position 4' [(IVd), 4.19 ppm (2H, s); (IVa), 4.16 ppm (1H, s)].

Compounds (IVb, c) were not successfully isolated in the pure state, since they gradually oxidized to form biquinolyls. Signals were present in the ^1H NMR spectra of the mixture of substances obtained for both deuterodihydrobiquinolyls (IVb, c) [(IVb), 2.28 (3H, s, 6'-CH_3); 2.50 (3H, s, 6-CH_3); 4.12 (1H, s, 4'-H); 5.84 (1H, d, J = 5.5, NH); 6.53 (1H, d, J = 7.94, 8'-H) etc., (IVc), 2.26 (3H, s, 7'-CH_3); 2.53 (3H, s, 7-CH_3); 4.10 (1H, s, 4'-H); 5.84 (1H, d, J = 5.6, NH); 6.41 (1H, s, 8'-H) etc.] and for the corresponding deuterobiquinolyls (see below).

The 4'-D-2,3'-biquinolyls (Va-c) were readily obtained on oxidation of compounds (IV) (Scheme 4).

Scheme 4



Va-c

Va R = H, b R = 6-Me, c R = 7-Me

The ^1H NMR spectra of the given compounds and of (Ia-c) were identical except for the signal of the proton at position 4' (8.93, 8.99, 8.86 respectively). It was absent from the spectra of compounds (Va-c).

The extent of deuterium exchange was determined by ^1H NMR spectroscopy from the reduction in intensity of the signals of the 4' protons and also by mass spectrometry. The extent of deuterium exchange in the dihydrobiquinolyls (IVa-c) was 92%, in the 2,3'-biquinolyls 67%. The sequence of operations given above was repeated three times and it was possible to achieve a degree of deuterium exchange greater than 95%.

EXPERIMENTAL

The mass spectra were drawn on a Varian MAT 331A instrument and the NMR spectra on a Bruker WP 200 instrument. Volt-amperograms were taken on a PI 50-1 potentiostat at a potential scanning rate of 0.5 V/sec. The operating electrode was a platinum disk of diameter 2 mm and the auxiliary electrode a platinum wire. The reference electrode was saturated calomel electrode. Base electrolyte was 0.05 M $LiBF_4$ (for lithium current sources) in DMF (purified by the standard procedure). The THF was purified by distillation over $LiAlH_4$, and 2,3'-biquinolyl was recrystallized from benzene with subsequent sublimation.

1',4'-Dihydro-2,3'-biquinolyl (IVd) $C_{18}H_{14}N_2$. A mixture of 2,3'-biquinolyl (0.64 g: 2.5 mmole) and powdered metallic lithium (0.05 g: 7 mmole) in THF (10 ml) was stirred for 3 h at room temperature in an atmosphere of argon. Water (4 ml) was then added dropwise. The lower aqueous salt layer was separated off and the organic layer evaporated. Yellow crystals were obtained. Yield was 0.58 g (90%) of mp 209-211°C (from benzene). According to [5] mp 209-211°C. ^1H NMR spectrum ($CDCl_3$): 4.19 (2H, s, 4'-H); 5.92 (1H, d, $J_{NH\text{-}2'H}$ = 6.0 Hz, NH); 6.62 (1H, d d, $J_{7'8'}$ = 7.68, $J_{6'8'}$ = 1.1 Hz, 8'-H); 6.91 (1H, d t, $J_{5'6'}$ = 7.67, $J_{6'7'}$ = 7.31, $J_{6'8'}$ = 1.1 Hz, 6'-H); 7.07 (1H, d t, $J_{6'7'}$ = 7.31, $J_{7'8'}$ = 7.68, $J_{5'7'}$ = 1.46 Hz, 7'-H); 7.2 (1H, d d, $J_{5'6'}$ = 7.67, $J_{5'7'}$ = 1.46 Hz, 5'-H); 7.37 (1H, d t, J_{56} = 8.04, J_{67} = 7.31, J_{68} = 1.1 Hz, 6-H); 7.41 (1H, d, $J_{NH\text{-}2'H}$ = 6.0 Hz, 2'-H); 7.47 (1H, d, J_{34} = 8.8 Hz, 3-H); 7.63 (1H, d t, J_{78} = 8.55, J_{67} = 7.31, J_{57} = 1.46 Hz, 7-H); 7.71 (1H, d d, J_{56} = 8.04, J_{57} = 1.46 Hz, 5-H); 7.98 (1H, d, J_{34} = 8.8 Hz, 4-H); 7.99 ppm (1H, d d, J_{78} = 8.55, J_{68} = 1.1 Hz, 8-H). Mass spectrum: (m/z 70 eV) 258 (M^+, 72%).

4'-D-1',4'-Dihydro-2,3'-biquinolyl (IVa) $C_{18}H_{13}DN_2$ was obtained similarly to 1',4'-dihydro-2,3'-biquinolyl, but in place of the usual water the reaction mixture was treated initially with D_2O (0.5 ml) and stirred for 30 min and then with water (4 ml). Yield was 0.58 g (90%) of mp 209-211°C (from benzene). The extent of deuteration was 98%. ^1H NMR spectrum ($CDCl_3$): 4.16 (1H, s, 4'-H); 5.92 (1H, d, $J_{NH\text{-}2'H}$ = 6.0 Hz, NH); 6.62 (1H, d d, $J_{7'8'}$ = 7.68, $J_{6'8'}$ = 1.1 Hz, 8'-H); 6.91 (1H, d t, $J_{5'6'}$ = 7.67, $J_{6'7'}$ = 7.31, $J_{6'8'}$ = 1.1 Hz, 6'-H); 7.07 (1H, d t, $J_{6'7'}$ = 7.31, $J_{7'8'}$ = 7.68, $J_{5'7'}$ = 1.46 Hz, 7'-H); 7.2 (1H, d d, $J_{5'6'}$ = 7.67, $J_{5'7'}$ = 1.46 Hz, 5'-H); 7.37 (1H, d t, J_{56} = 8.04, J_{67} = 7.31, J_{68} = 1.1 Hz, 6-H); 7.41 (1H, d, $J_{NH\text{-}2'H}$ = 6.0 Hz, 2'-H); 7.47 (1H, d, J_{34} = 8.8 Hz, 3-H); 7.63 (1H, d t, J_{78} = 8.55, J_{67} = 7.31, J_{57} = 1.46 Hz, 7-H); 7.71 (1H, d d, J_{56} 8.04, J_{57} = 1.46 Hz, 5-H); 7.98 (1H, d, J_{34} = 8.8 Hz, 4-H); 7.99 (1H, d d, J_{78} = 8.55, J_{68} = 1.1 Hz, 8-H). Mass spectrum: (m/z 70 eV) 259 (M^+, 74%).

4'-D-2,3'-Biquinolyl (Va) $C_{18}H_{11}DN_2$. A mixture of 4'-D-1',4'-dihydro-2,3'-biquinolyl (0.33 g: 1.25 mmole) and iodine (0.33 g: 1.3 mmole) in pyridine (5 ml) was boiled under reflux for 10 min. The reaction mixture was then poured into water (100 ml) containing sodium thiosulfate (1 g) and sodium hydroxide (0.5 g). The white solid which precipitated was filtered off and washed with water (3 × 30 ml). Yield was 0.29 g (90%) of mp 175-176°C (from benzene). Extent of deuterium exchange was 67%. According to the data of [1] mp 175-176°C. Mass spectrum: (m/z 70 eV) 257 (M^+, 100%).

4'-D-6,6'-Dimethyl-2,3'-biquinolyl (Vb) $C_{20}H_{15}DN_2$. A mixture of 6,6'-dimethyl-2,3'-biquinolyl (0.71 g: 2.5 mmole) and powdered metallic lithium (0.05 g: 7 mmole) in THF (10 ml) was stirred for 3 h at room temperature in an atmosphere of argon. Heavy water (0.5 ml) was added dropwise, the mixture stirred for 30 min, and then water (4 ml) was added. The lower aqueous salt layer was separated off, and the organic layer evaporated. Yellow crystals were obtained, which were stirred with iodine (0.65 g: 2.6 mmole) in pyridine (5 ml), and the mixture boiled for 10 min. The reaction mixture was then poured into water (100 ml) containing sodium thiosulfate (1 g) and sodium hydroxide (0.5 g). The precipitated white solid was filtered off and washed with water (3 × 30 ml). Yield was 0.61 g (86%) of mp 206-207°C (from benzene). The extent of deuterium exchange was 65%. According to the data of [1] mp 206-207°C. Mass spectrum: (m/z 70 eV) 285 (M^+, 100%).

4'-D-7,7'-Dimethyl-2,3'-biquinolyl (Vc) $C_{20}H_{15}DN_2$ was obtained similarly to 4'-D-6,6'-dimethyl-2,3'-biquinolyl from 7,7'-dimethyl-2,3'-biquinolyl (0.71 g: 2.5 mmole), metallic lithium (0.05 g: 7 mmole), and iodine (0.65 g: 2.6 mmole). Yield was 0.62 g (88%) of mp 215-217°C (from benzene). The extent of deuterium exchange was 68%. According to the data of [1] mp 215-217°C. Mass spectrum: (m/z 70 eV) 285 (M^+, 100%).

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