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INVESTIGATIONS OF 2,3'-BIQUINOLYL. 8.* REDUCTION OF 1-ALKYL-3-(2-QUINOLYL)-QUINOLINIUM HALIDES WITH SODIUM BOROHYDRIDE

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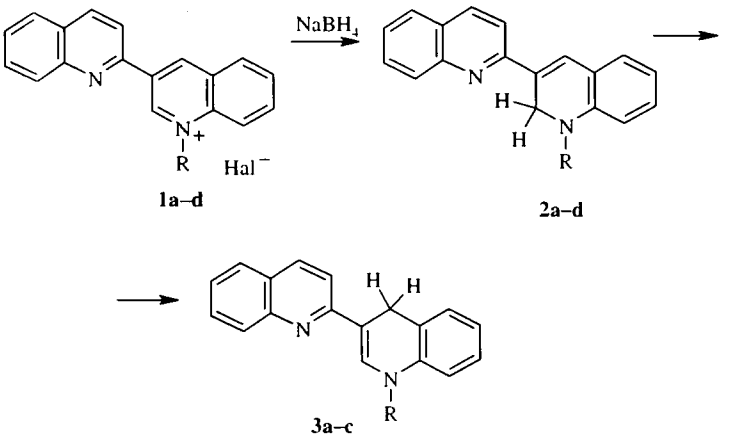
Reduction of 1-alkyl-3-(2-quinolyl)quinolinium halides with sodium borohydride leads to 1'-alkyl-1',2'-dihydro-2,3'-biquinolyls which, except for the ethoxycarbonyl derivative, undergo rearrangement to 1'-alkyl-1',4'-dihydro-2,3'-biquinolyls. The last can be synthesized by the alkylation of the corresponding 1',4'-dihydro-2,3'-biquinolyls under conditions of interphase catalysis and in the system KOH–DMSO.

Keywords: 1-alkyl-3-(quinolyl)quinolinium halides, 2,3-biquinolyl, 1,4-dihydro-2,3-biquinolyls, 1,2-dihydro-2,3-biquinolyls, sodium borohydride, nucleophilic addition, regioselectivity.

In the continuation of work [1] to investigate electrophilic properties of compounds of the 2,3'-biquinolyl series, we studied the reduction of 1'-alkyl-3'-(2-quinolyl)quinolinium halides **1** by sodium borohydride. We reported previously [2] that "strict" nucleophilic reagents such as $NaBH_4$ [3], reacting with salts **1**, form addition products at the position 2', corresponding to the maximal positive charge. It could be proposed that the reaction of the compounds **1** with sodium borohydride will lead to 1'-alkyl-1',2'-dihydro-2,3'-biquinolyls **2**. In fact, the reaction of **1a-d** with $NaBH_4$ in alcohol at 0°C results in the formation of the compounds **2a-d** exclusively.



1, 2, 3 a R = Me; **b** R = CH_2CHCH_2; **c** R = $PhCH_2$; **d** R = COOEt

* For Communication 7, see [1].

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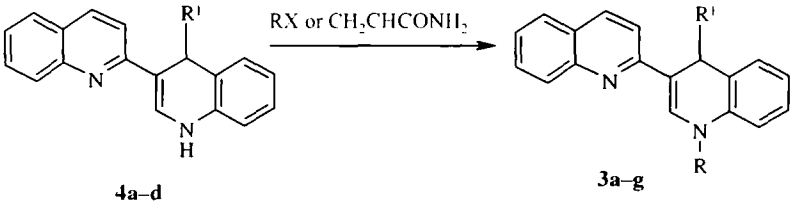
The products **2a-c** were not identified in the pure form since they undergo rapid rearrangement to the thermodynamically more stable 1'-alkyl-1',4'-dihydro-2,3'-biquinolyls **3a-c**. The rearrangement even proceeds in the crystals at room temperature. The ^{1}H NMR spectrum of the mixture of substances contains signals for both **2a** and **3a**, whereby **2a** is characterized at 3.11 ppm (3H, s, Me), 8.05 ppm (1H, d, J_{78} = 8.44 Hz, 8-H), and 8.10 ppm (1H, d, J_{34} = 8.94 Hz, 4-H) etc., and **3a** is characterized at 3.37 ppm (3H, s, Me), 7.91 ppm (1H, dd, 8-H, J_{78} = 8.55 Hz, J_{68} = 1.22 Hz), and 8.07 ppm (1H, d, 4-H, J = 8.85 Hz). The stability of **2d** under the given conditions is explained by the electron-acceptor properties of the ethoxycarbonyl group hampering the rearrangement by both the 1,3-shift of the hydride ion, and the protonation–deprotonation.

The boiling of the corresponding salts with sodium borohydride in alcohol was found to be the most expedient for the synthesis of the dihydro derivatives **3a-c**. Under these conditions, the reduction is combined with the rearrangement, which leads to the compounds **3a-c** with the yield of 55-95%.

The 1'-ethoxycarbonyl-1',2'-dihydro-2,3'-biquinolyl **2d** is synthesized with the yield of 90% by the reaction of salt **1d**, produced in situ from ethyl chloroformate and 2,3'-biquinolyl, with $NaBH_4$ in aqueous dioxane.

The 1'-R-1',4'-dihydro-2,3'-biquinolyls were also synthesized by alkylation of the 1',4'-dihydro-2,3'-biquinolyls **4** by alkyl halides, dimethyl sulfate, and acrylamide under conditions of interphase catalysis and in the system KOH–DMSO with the yield close to quantitative (the 1',2'-dihydro-2,3'-biquinolyls are not alkylated under the given conditions).



4a–d **3a–g**

3d R = $CH_2CH_2CONH_2$, R^1 = H; **e** R = R^1 = Me; **f** R = Me, R^1 = Ph; **g** R = Me, R^1 = 1-$C_{10}H_7$; **4 a** R^1 = Me; **b** R^1 = Ph; **c** R^1 = 1-$C_{10}H_7$

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on the Bruker WP-200 instrument with the utilization of TMS as the internal standard. The mass spectra were recorded on the Varian MAT-331A instrument (70 eV). The monitoring of the course of reactions and the purity of the compounds synthesized was accomplished on plates of Silufol UV-254 in the 1:1 solvent system of ethyl acetate–hexane or in ethyl acetate.

1'-Ethoxycarbonyl-1',2'-dihydro-2,3'-biquinolyl (2d). The mixture of 2,3'-biquinolyl (1.28 g, 5 mmol) and ethyl chloroformate (1.09 g, 10 mmol) in dioxane (10 ml) is stirred at room temperature for 5 min, whereby the residue of the salt separates out. Sodium borohydride (0.2 g, 5.5 mmol) and water (1 ml) are then added and the mixture is stirred for 5 h more. The mixture is treated with water (40 ml) and extracted with benzene (3×30 ml), and the benzene extract is washed with water and dried over sodium sulfate. The benzene is evaporated prior to the isolation of yellow crystals or yellow oil, crystallized by the addition of alcohol. Yield 1.49 g (90%); mp 106-107°C (alcohol). ^{1}H NMR spectrum (acetone-d_6): 1.31 (3H, t, J = 7.25 Hz, 1'-$CO_2CH_2\underline{CH_3}$); 4.26 (2H, q, J = 7.25 Hz, 1'-$CO_2\underline{CH_2}CH_3$); 5.20 (2H, d, $J_{2'4'}$ = 1.28 Hz, 2'-H); 7.16 (1H, dd, $J_{5'6'}$ = 7.68 Hz, $J_{6'7'}$ = 7.47 Hz, 6'-H); 7.32 (1H, dd, $J_{6'7'}$ = 7.47 Hz, $J_{7'8'}$ = 8.15 Hz, 7'-H); 7.40 (1H, d, $J_{5'6'}$ = 7.68 Hz, 5'-H); 7.58 (1H, dd, J_{56} = 8.10 Hz, J_{67} = 7.16 Hz, 6-H); 7.66 (1H, d, $J_{2'4'}$ = 1.28 Hz, 4'-H); 7.75 (1H, d, $J_{7'8'}$ = 8.15 Hz, 8'-H); 7.76 (1H, dd, J_{67} = 7.16 Hz, J_{78} = 8.45 Hz, 7-H); 7.94 (1H, d, J_{56} = 8.10 Hz, 5-H); 8.07 (1H, d, J_{78} = 8.45 Hz, 8-H); 8.08 (1H, d, J_{34} = 8.97 Hz, 3-H); 8.34 ppm (1H, d, J_{34} = 8.97 Hz, 4-H). Found, %: C 76.14; H 5.54; N 8.56. $C_{21}H_{18}N_2O_2$. Calculated, %: C 76.34; H 5.49; N 8.48.

General Method for the Reduction of 1-Alkyl-3-(2-quinolyl)quinolinium Halides 1a-c with Sodium Borohydride. A. The mixture of 1-methyl-3-(2-quinolyl)quinolinium halide (2.5 mmol) and sodium borohydride (0.145 g, 4 mmol) in isopropyl alcohol (30 ml) is boiled with vigorous stirring for 20 min. The resulting solution is filtered and cooled, and is then poured into water (100 ml) prior to the extraction with benzene (3×20 ml). The benzene extracts are combined, dried over sodium sulfate, and concentrated. Yellow crystals or a yellow oil are obtained.

General Method for the Alkylation of 1',4'-Dihydro-2,3'-biquinolyls 4a-c under Conditions of Interphase Catalysis. B. The mixture of the corresponding 1',4'-dihydro-2,3'-biquinolyl (2.5 mmol), the alkylating reagent (dimethyl sulfate, benzyl chloride, allyl bromide, acrylamide) (2.75 mmol), tetrabutylammonium bromide (0.1 g, 0.31 mmol), 50% NaOH (1 ml), and benzene (5 ml) is boiled with vigorous stirring for 4 h. Water (50 ml) is added and the mixture is extracted with benzene (3×30 ml). The benzene extracts are combined, dried over sodium sulfate, and concentrated. Yellow crystals or a yellow oil are obtained.

General Method for the Alkylation of 1',4'-Dihydro-2,3'-biquinolyls (4a-c) in DMSO. C. The mixture of the corresponding 1',4'-dihydro-2,3'-biquinolyl (2.5 mmol), the alkylating reagent (methyl iodide, benzyl chloride, acrylamide) (2.75 mmol), and ground KOH (0.05 g) in DMSO (5 ml) is stirred at room temperature for 4 h. The reaction mixture is poured into water (50 ml), and the resulting yellow residue is filtered.

1'-Methyl-1',4'-dihydro-2,3'-biquinolyl (3a). Yields: 0.65 g (95%) for the method A, 0.65 g (95%) for the method B, and 0.62 g (91%) for the method C; mp 146-147°C (alcohol). ^{1}H NMR spectrum ($CDCl_3$): 3.32 (3H, s, 1'-CH_3); 4.18 (2H, s, 4'-H); 6.77 (1H, d, $J_{5'6'}$ = 7.93 Hz, 5'-H); 6.95 (1H, dd, $J_{6'7'}$ = 7.53 Hz, $J_{7'8'}$ = 7.81 Hz, 7'-H); 7.17 (1H, dd, $J_{5'6'}$ = 7.93 Hz, $J_{6'7'}$ = 7.53 Hz, 6'-H); 7.21 (1H, d, $J_{7'8'}$ = 7.81 Hz, 8'-H); 7.34 (1H, s, 2'-H); 7.37 (1H, dd, J_{56} = 7.61 Hz, J_{67} = 7.47 Hz, 6-H); 7.45 (1H, d, J_{34} = 8.79 Hz, 3-H); 7.63 (1H, dd, J_{67} = 7.47 Hz, J_{78} = 8.52 Hz, 7-H); 7.70 (1H, d, J_{56} = 7.61 Hz, 5-H); 7.98 (1H, d, J_{78} = 8.52 Hz, 8-H); 7.99 ppm (1H, d, J_{34} = 8.79 Hz, 4-H). Found, %: C 83.91; H 5.84; N 10.25. $C_{19}H_{16}N_2$. Calculated, %: C 83.79; H 5.92; N 10.29.

1'-Allyl-1',4'-dihydro-2,3'-biquinolyl (3b). Yields: 0.41 g (55%) for the method A and 0.65 g (87%) for the method B. A yellow oil is obtained. ^{1}H NMR spectrum ($CDCl_3$): 4.21 (2H, s, 4'-H); 4.63 (2H, m, J_{vic} = 5.13 Hz, J_{gem} = 1.71 Hz, 1'-$\underline{CH_2}CH{=}CH_2$); 5.28 (1H, dd, J_{trans} = 15.37 Hz, J_{gem} = 3.84 Hz, 1'-$CH_2CH{=}C\underline{H^A}H^B$); 5.33 (1H, dd, J_{cis} = 10.24 Hz, J_{gem} = 3.84 Hz, 1'-$CH_2CH{=}CH^A\underline{H^B}$); 5.97 (1H, m, 1'-$CH_2\underline{CH}{=}CH_2$); 6.76 (1H, d, $J_{7'8'}$ = 8.10 Hz, 8'-H); 7.07 (1H, dd, $J_{5'6'}$ = 7.52 Hz, $J_{6'7'}$ = 7.37 Hz, 6'-H); 7.12 (1H, dd, $J_{6'7'}$ = 7.37 Hz, $J_{7'8'}$ = 8.16 Hz, 7'-H); 7.29 (1H, d, $J_{5'6'}$ = 7.61 Hz, 5'-H); 7.46 (1H, dd, J_{56} = 8.09 Hz, J_{67} = 7.14 Hz, 6-H); 7.54 (1H, s, 2'-H); 7.58 (1H, d, J_{56} = 8.09 Hz, 5-H); 7.61 (1H, d, J_{34} = 8.97 Hz, 3-H); 7.78 (1H, dd, J_{67} = 7.14 Hz, J_{78} = 8.41 Hz, 7-H); 7.98 (1H, d, J_{78} = 8.41 Hz, 8-H); 8.07 ppm (1H, d, J_{34} = 8.97 Hz, 4-H). Found, %: C 84.62; H 6.02; N 9.36. $C_{21}H_{18}N_2$. Calculated, %: C 84.53; H 6.08; N 9.39.

1'-Benzyl-1',4'-dihydro-2,3'-biquinolyl (3c). Yields: 0.7 g (81%) for the method A, 0.81 g (93%) for the method B, and 0.79 g (91%) for the method C; mp 158-159°C (alcohol). ^{1}H NMR spectrum (acetone-d_6): 5.04 (2H, s, 1'-$\underline{CH_2}$Ph); 4.22 (2H, s, 4'-H); 6.77 (1H, d, $J_{5'6'}$ = 7.65 Hz, 5'-H); 6.88 (1H, dd, $J_{6'7'}$ = 7.59 Hz, $J_{7'8'}$ = 7.81 Hz, 7'-H); 7.16 (1H, dd, $J_{5'6'}$ = 7.65 Hz, $J_{6'7'}$ = 7.59 Hz, 6'-H); 7.21 (1H, d, $J_{7'8'}$ = 7.81 Hz, 8'-H); 7.37-7.42 (5H, m, 1'-$CH_2\underline{Ph}$); 7.43 (1H, dd, J_{56} = 8.22 Hz, J_{67} = 7.50 Hz, 6-H); 7.64 (1H, dd, J_{67} = 7.50 Hz, J_{78} = 8.27 Hz, 7-H); 7.71 (1H, s, 2'-H); 7.77 (1H, d, J_{56} = 8.22 Hz, 5-H); 7.81 (1H, d, J_{34} = 8.85 Hz, 3-H); 7.93 (1H, d, J_{78} = 8.27 Hz, 8-H); 8.07 ppm (1H, d, J_{34} = 8.85 Hz, 4-H). Found, %: C 86.31; H 5.71; N 7.98. $C_{25}H_{20}N_2$. Calculated, %: C 86.18; H 5.79; N 8.04.

1'-(2-Carbamoylethyl)-1',4'-dihydro-2,3'-biquinolyl (3d). Yields: 0.69 g (84%) for the method B and 0.76 g (92%) for the method C; mp 217-219°C (dioxane). ^{1}H NMR spectrum (DMSO-d_6): 2.51 (2H, d, J = 6.43 Hz, 1'-$CH_2\underline{CH_2}CONH_2$); 5.47 (2H, d, J = 6.43 Hz, 1'-$\underline{CH_2}CH_2CONH_2$); 4.18 (2H, s, 4'-H); 6.77 (1H, d, $J_{5'6'}$ = 7.93 Hz, 5'-H); 6.95 (1H, dd, $J_{6'7'}$ = 7.53 Hz, $J_{7'8'}$ = 7.81 Hz, 7'-H); 7.17 (1H, dd, $J_{5'6'}$ = 7.93 Hz, $J_{6'7'}$ = 7.53 Hz, 6'-H); 7.21 (1H, d, $J_{7'8'}$ = 7.81 Hz, 8'-H); 7.34 (1H, s, 2'-H); 7.37 (1H, dd, J_{56} = 7.61 Hz, J_{67} = 7.47 Hz, 6-H); 7.45 (1H, d, J_{34} = 8.79 Hz, 3-H); 7.63 (1H, dd, J_{67} = 7.47 Hz, J_{78} = 8.52 Hz, 7-H); 7.70 (1H, d, J_{56} = 7.61 Hz, 5-H); 7.98 (1H, d, J_{78} = 8.52 Hz, 8-H); 7.99 ppm (1H, d, J_{34} = 8.79 Hz, 4-H). Mass spectrum (m/z): 329 (M^+, 19%). Found, %: C 76.69; H 5.66; N 12.72. $C_{21}H_{19}N_3O$. Calculated, %: C 76.57; H 5.81; N 12.76.

1',4'-Dimethyl-1',4'-dihydro-2,3'-biquinolyl (3e). Yield 0.665 g (93%, method B); mp 126-127°C (benzene–hexane). According to the data of [2], mp 126-127°C. The mixed test with a known sample does not give a depression of the melting temperature, and the ^{1}H NMR spectra are identical.

1'-Methyl-4'-phenyl-1',4'-dihydro-2,3'-biquinolyl (3f). Yields: 0.84 g (96%) for the method B and 0.77 g (88%) for the method C; mp 173-174°C (alcohol). According to the data of [4], mp 173-174°C. The mixed test with the known sample does not give a depression of the melting temperature, and the ^{1}H NMR spectra are identical.

1'-Methyl-4'-(1-naphthyl)-1',4'-dihydro-2,3'-biquinolyl (3g). Yields: 0.97 g (97%) for the method B and 0.91 g (91%) for the method C; mp 151-153°C (benzene–hexane). According to the data of [4], mp 151-153°C. The mixed test with the known sample does not give a depression of the melting temperature, and the ^{1}H NMR spectra are identical.

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