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INVESTIGATIONS IN THE REGION OF 2,3′-BIQUINOLYL

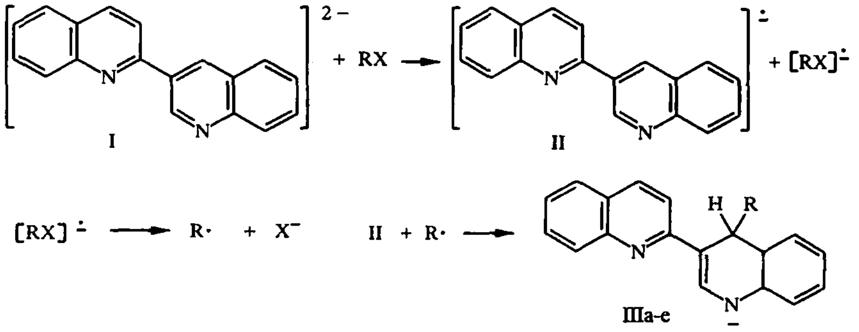
4.* ALKYLATION OF THE DIANION OF 2,3′-BIQUINOLYL

A. V. Aksenov, I. V. Aksenova, I. V. Borovlev,
and Yu. I. Smushkevich

With alkyl chlorides and alkyl phenyl ethers the dianion of 2,3′-biquinolyl forms the products from alkylation at position 4′. Their treatment with alkyl halides or water gives 1′,4′-dialkyl-1′,4′-dihydro-2,3′-biquinolyls or 4′-alkyl-1′,4′-dihydro-2,3′-biquinolyls respectively.

While continuing investigations into the properties of the dianion of 2,3′-biquinolyl (I), a convenient method for the generation of which was proposed earlier [2], we studied its alkylation by halogen derivatives and by the ethers of phenol.

As we reported in [3], the dianion (I) can act as electron donor toward aryl halides. As the result of a series of successive transformations this leads to the formation of the products from arylation at position 4′, which corresponds to maximum spin density in the radical-anion (II). We supposed that the dianion (I) could act as electron donor not only toward aryl halides but also toward alkyl halides and phenyl ethers, which would subsequently lead to the formation of the anion (III).



III a R = Pr; b R = Me; c R = Bu; d R = CH_2Ph; e R = $CH_2CH{=}CH_2$;
X = Cl, Br, OPh

In fact, the gradual addition of alkyl chlorides to the dianion (I), obtained by the reaction of 2,3′-biquinolyl with metallic lithium or potassium, and treatment of the reaction mixture with water led to the formation of 4′-alkyl-1′,4′-dihydro-2,3′-biquinolyls (IVa-e) with yields of 78-86%.

Analogous results were obtained when allyl phenyl and benzyl phenyl ethers were used instead of the respective halogen derivatives. However, the alkylation products were not formed with anisole.

The use of alkyl bromides instead of alkyl chlorides reduces the yield of compounds (IVa-e) by 5-7%, and in the case of alkyl iodides, such as methyl iodide, a complex mixture of substances is formed. A similar effect of the nature of the halogen derivative on the alkylation of dianions (radical-anions) was reported in [4].

It could be expected that alkylation, unlike arylation, would not be limited to the monoalkylation stage. In fact, the dialkylation product (IVg) was formed with a yield of 78% when the dianion (I), obtained from metallic lithium and an equi-

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*For communication 3, see [1].

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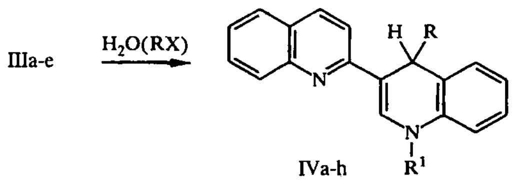

IV a R = Pr, R^1 = H; b R = Me, R^1 = H; c R = Bu, R^1 = H;
d R = CH_2Ph, R^1 = H; e R = $CH_2CH{=}CH_2$, R^1 = H;
f R = CH_2Ph, R^1 = Me; g R = CH_2Ph, R^1 = CH_2Ph; h R = Pr, R^1 = Pr

molar amount (to the latter) of benzyl chloride, was boiled for 1.5 h. With other alkyl chlorides, however, the dialkylation stage takes place very slowly. Thus, when (I) was boiled with a fivefold excess of propyl chloride for 6 h the yield of compound (IVh) was not higher than 15%.

It was possible to solve the problem by using the dianion generated with metallic potassium [in this case compound (IVh) was formed with an 81% yield after 3 h] or by using alkyl iodides at the final stage. This makes it possible to obtain the dialkylation products with various R and R^1 groups. For instance, the successive treatment of the dianion (I) with benzyl chloride led to the formation of the dialkylation product (IVf).

EXPERIMENTAL

The PMR spectra were recorded on a Bruker WP-200 instrument for solutions in deuterochloroform with TMS as internal standard. The reactions and the individuality of the compounds were monitored on Silufol UV-254 plates in a 1:1 mixture of ethyl acetate and hexane. Column chromatography was conducted on silica gel L 40/100. The THF was purified by distillation over lithium aluminum hydride and then over benzophenone ketyl. The 2,3′-biquinolyl was purified by crystallization from benzene followed by sublimation. The halogen derivatives were distilled and were then dried over molecular sieves with a pore diameter of 3 Å.

4′-Propyl-1′,4′-dihydro-2,3′-biquinolyl (IVa). A mixture of 0.64 g (2.5 mmole) of 2,3′-biquinolyl and 0.05 g (7 mmole) of finely divided metallic lithium in 10 ml of THF was stirred in an atmosphere of argon for 3 h at room temperature. A solution of 0.35 g (4.5 mmole) of 1-chloropropane in 4 ml of THF was then added drop by drop. The reaction mixture was stirred for 1 h at room temperature and was then stirred for a further hour, after which 40 ml of water was added, and the product was extracted with 3 × 30 ml of benzene. The organic layer was evaporated. The obtained yellow oil crystallized when hexane was added. The yield was 0.61 g (81%); mp 127-129°C (from benzene with hexane). Published data [5]: 127-129°C. A mixed melting test with an authentic sample did not give a melting point depression. The PMR spectrum was identical with the spectrum given in [5].

The following compounds were obtained by similar methods.

4′-Methyl-1′,4′-dihydro-2,3′-biquinolyl (IVb). The compound was obtained from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.05 g (7 mmole) of lithium, and 0.36 g (7 mmole) of methyl chloride. The yield was 0.57 g (84%); mp 148-149°C (from benzene). Published data [5]: mp 148-149°C. A mixed melting test with an authentic sample did not give a melting point depression. The PMR spectrum was identical with the spectrum in [5].

4′-Butyl-1′,4′-dihydro-2,3′-biquinolyl (IVc). The compound was obtained from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.05 g (7 mmole) of lithium, and 0.42 g (4.5 mmole) of butyl chloride, except that the product was purified by column chromatography in a 1:1 mixture of benzene and ethyl acetate. The fraction with R_f 0.62 was collected (Silufol UV-254, 1:1 ethyl acetate–hexane). The solvent was evaporated, and a yellow oil was obtained. The yield was 0.61 g (78%). According to data in [1], the compound is a yellow oil. The PMR spectrum was identical with that given in [1].

4′-Benzyl-1′,4′-dihydro-2,3′-biquinolyl (IVd). The compound was obtained from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.05 g (7 mmole) of lithium, and 0.57 g (4.5 mmole) of benzyl chloride or 0.83 g (4.5 mmole) of benzyl phenyl ether. The yield was 0.75 g (86%) with benzyl chloride and 0.72 g (83%) with benzyl phenyl ether; mp 161-163°C (from benzene). Published data [5]: mp 161-163°C. A mixed melting test with an authentic sample did not give a melting point depression. The PMR spectra were identical.

4′-Allyl-1′,4′-dihydro-2,3′-biquinolyl (IVe). The compound was obtained from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.05 g (7 mmole) of lithium, and 0.34 g (4.5 mmole) of allyl chloride or 0.6 g (4.5 mmole) of allyl phenyl ether. The yield was 0.6 g (81%) with allyl chloride and 0.57 g (77%) with allyl phenyl ether; mp 107-109°C (from benzene with hexane). ^1H NMR spectrum (deuterochloroform), ppm: 2.46 (2H, m, $\underline{CH_2}CH{=}CH_2$); 4.7 (2H, m, 4′-H, $CH_2CH{=}C\underline{H}^AH^B$); 4.86 (1H, dd, J_{AB} = 2.13, $J_{B\text{-}CH}$ = 10.24 Hz, $CH_2CH{=}CH^A\underline{H}^B$); 5.80 (1H, m, $CH_2\underline{CH}{=}CH_2$); 6.17 (1H, d, $J_{NH\text{-}2'H}$ = 5.97 Hz, NH); 6.69 (1H, d, $J_{7'8'}$ = 7.92 Hz, 8′-H); 6.95 (1H, dd, $J_{5'6'}$ = 7.61, $J_{6'7'}$ = 7.32 Hz, 6′-H); 7.09 (1H, dd, $J_{6'7'}$ = 7.32, $J_{7'8'}$ = 7.92 Hz, 7′-H); 7.22 (1H, d, $J_{5'6'}$ = 7.61 Hz, 5′-H); 7.38 (1H, dd, J_{56} = 8.15, J_{67} = 7.44 Hz, 6-H); 7.48 (1H, d, $J_{NH\text{-}2'H}$ = 5.97 Hz, 2′-H); 7.52 (1H, d, J_{34} = 8.54 Hz, 3-H); 7.64 (1H, dd, J_{67} = 7.44, J_{78} = 8.42 Hz, 7-H); 7.70 (1H, d, J_{56} = 8.15 Hz, 5-H); 7.96 (1H, d, J_{34} = 8.54 Hz, 4-H); 7.98 (1H, d, J_{78} = 8.42 Hz, 8-H). Found %: C 84.81; H 5.91; N 9.28. $C_{21}H_{18}N_2$. Calculated %: C 84.53; H 6.08; N 9.39.

1′-Methyl-4′-benzyl-1′,4′-dihydro-2,3′-biquinolyl (IVf). A mixture of 0.64 g (2.5 mmole) of 2,3′-biquinolyl and 0.05 g (7 mmole) of finely divided metallic lithium in 10 ml of THF was stirred in an atmosphere of argon for 3 h at room temperature. A solution of 0.38 g (3 mmole) of benzyl chloride in 4 ml of THF was then added drop by drop. The reaction mixture was stirred for 1 h at room temperature and was then boiled for a further hour. It was cooled to room temperature, and 0.71 g (5 mmole) of methyl iodide in 2 ml of THF was added. The mixture was stirred for 1 h, poured into 50 ml of water, and extracted with 3 × 30 ml of benzene. The extracts were combined, dried over sodium sulfate, and evaporated. The residue was dissolved in 10 ml of benzene and chromatographed on a column in the 1:2 benzene−ethyl acetate system, and the fraction with R_f 0.68 (Silufol UV-254, 1:2 ethyl acetate−hexane) was collected. The yield was 0.7 g (77%); mp 136-137°C (from ethanol). PMR spectrum (deuterochloroform, δ, ppm): 2.83 (1H, dd, J_{AB} = 12.82, $J_{A4'}$ = 7.63 Hz, 4′-$C\underline{H}^{\underline{A}}H^BPh$); 3.00 (1H, dd, J_{BA} = 12.82, $J_{B4'}$ = 4.28 Hz, 4′-$CH^A\underline{H}^{\underline{B}}Ph$); 3.16 (3H, s, 1′-$CH_3$); 4.79 (1H, dd, $J_{4'A}$ = 7.63, $J_{4'B}$ = 4.28 Hz, 4′-H); 6.74 (1H, d, $J_{8'7'}$ = 7.74 Hz, 8′-H); 6.81 (1H, dd, $J_{6'5'}$ = 7.61, $J_{6'7'}$ = 7.53 Hz, 6′-H); 6.86 (3H, m, 5′-H, 2″-H, 6″-H); 7.10 (3H, m, 3″-H, 4″-H, 5″-H); 7.16 (1H, dd, $J_{7'6'}$ = 7.53, $J_{7'8'}$ = 7.74 Hz, 7′-H); 7.28 (1H, s, 2′-H); 7.38 (1H, dd, J_{65} = 8.18, J_{67} = 7.52 Hz, 6-H); 7.54 (1H, d, J_{34} = 8.85 Hz, 3-H); 7.65 (1H, dd, J_{76} = 7.52, J_{78} = 8.24 Hz, 7-H); 7.71 (1H, d, J_{56} = 8.18 Hz, 5-H); 7.96 (1H, d, J_{43} = 8.85 Hz, 4-H); 8.03 (1H, d, J_{87} = 8.24 Hz, 8-H). Found %: C 86.41; H 6.01; N 7.58. $C_{26}H_{22}N_2$. Calculated %: C 86.20; H 6.07; N 7.73.

1′,4′-Dibenzyl-1′,4′-dihydro-2,3′-biquinolyl (IVg). A mixture of 0.64 g (2.5 mmole) of 2,3′-biquinolyl and 0.27 g (7 mmole) of metallic potassium in 12 ml of THF was stirred in an atmosphere of argon for 1 h at room temperature and then for 4 h at boiling point. A solution of 0.9 g (7.1 mmole) of benzyl chloride in 5 ml of THF was then added drop by drop. The reaction mixture was stirred for 1 h at room temperature and was then boiled for a further hour. It was then cooled to room temperature, and 5 ml of *tert*-butyl alcohol was added. The mixture was poured into 50 ml of water and extracted with 3 × 30 ml of benzene. The benzene extracts were combined, dried over sodium sulfate, and evaporated. The residue was dissolved in 10 ml of benzene and chromatographed on a column in the 1:2 benzene−ethyl acetate solvent system. The fraction with R_f 0.5 (Silufol UV-254, 1:4 ethyl acetate−hexane) was collected. The solvent was evaporated, and yellow crystals were obtained. The yield was 0.9 g (82%); mp 133-134°C (from hexane). PMR spectrum (δ, ppm): 3.00 (1H, dd, J_{AB} = 12.38, $J_{A4'}$ = 7.48 Hz, 4′-$C\underline{H}^{\underline{A}}H^BPh$); 3.06 (1H, dd, J_{BA} = 12.82, $J_{B4'}$ = 4.27 Hz, 4′-$CH^A\underline{H}^{\underline{B}}Ph$); 4.68 (1H, d, J_{AB} = 17.07 Hz, 1′-$C\underline{H}^{\underline{A}}H^BPh$); 4.76 (1H, d, J_{BA} = 17.07 Hz, 1′-$CH^A\underline{H}^{\underline{B}}Ph$); 4.96 (1H, dd, $J_{4'A}$ = 7.48, $J_{4'B}$ = 4.27 Hz, 4′-H); 6.57 (1H, d, $J_{8'7'}$ = 7.84 Hz, 8′-H); 6.85 (3H, m, 5′-H, 4′-$CH_2\underline{Ph}$ (2″-H, 6″-H)); 6.91 (1H, dd, $J_{6'5'}$ = 7.71, $J_{6'7'}$ = 7.54 Hz, 6′-H); 7.01 (1H, dd, $J_{7'6'}$ = 7.54, $J_{7'8'}$ = 7.84 Hz, 7′-H); 7.05 [2H, d, J = 7.12 Hz, 1′-$CH_2\underline{Ph}$ (2‴-H, 6‴-H)]; 7.12 [3H, m, 4′-$CH_2\underline{Ph}$ (3″-H, 4″-H, 5″-H)]; 7.28 [3H, m, 1′-$CH_2\underline{Ph}$ (3‴-H, 4‴-H, 5‴-H)]; 7.34 (1H, s, 2′-H); 7.40 (1H, dd, J_{65} = 8.15, J_{67} = 7.49 Hz, 6-H); 7.54 (1H, d, J_{34} = 8.96 Hz, 3-H); 7.66 (1H, dd, J_{76} = 7.49, J_{78} = 8.29 Hz, 7-H); 7.77 (1H, d, J_{56} = 8.15 Hz, 5-H); 7.98 (1H, d, J_{43} = 8.96 Hz, 4-H); 8.05 (1H, d, J_{87} = 8.29 Hz, 8-H). Found %: C 87.82; H 5.86; N 6.32. $C_{32}H_{26}N_2$. Calculated %: C 87.68; H 5.93; N 6.39.

1′,4′-Dipropyl-1′,4′-dihydro-2,3′-biquinolyl (IVh). Method A. The compound was obtained like 1′-methyl-4′-benzyl-1′,4′-dihydro-2,3′-biquinolyl from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.05 g (7 mmole) of lithium, 0.35 g (4.5 mmole) of 1-chloropropane, and 0.68 g (4 mmole) of 1-iodopropane. The yield was 0.74 g (87%).

Method B. The compound was obtained like 1′,4′-dibenzyl-1′,4′-dihydro-2,3′-biquinolyl from 0.64 g (2.5 mmole) of 2,3′-biquinolyl, 0.27 g (7 mmole) of potassium, and 0.7 g (9 mmole) of 1-chloropropane except that after the addition of the halogen derivative the reaction mixture was boiled for 3 h. The yield was 0.69 g (81%). The product formed a yellow oil; R_f 0.6 (Silufol UV-254, 1:1 ether−hexane). ^1H PMR spectrum (deuterochloroform, δ, ppm): 0.8 (3H, t, J = 7.08 Hz, 4′-$\underline{CH_3}CH_2CH_2$); 1.01 (3H, t, J = 6.88 Hz, 4′-$\underline{CH_3}CH_2CH_2$); 1.25 (2H, m, 4′-$CH_3\underline{CH_2}CH_2$); 1.61 (2H, m, 1′-$CH_3\underline{CH_2}CH_2$); 1.82 (2H, m, 4′-$CH_3CH_2\underline{CH}^A\underline{H}^B$); 3.5 (2H, m, 1′-$CH_3CH_2\underline{CH_2}$); 4.47 (1H, dd, $J_{4'H\text{-}B}$ = 4.78, $J_{4'\text{-}A}$ = 6.39 Hz, 4′-H);

6.84 (1H, d, $J_{7'8'}$ = 7.84 Hz, 8'-H); 6.98 (1H, dd, $J_{5'6'}$ = 7.58, $J_{6'7'}$ = 7.36 Hz, 6'-H); 7.14 (1H, dd, $J_{6'7'}$ = 7.36, $J_{7'8'}$ = 7.84 Hz, 7'-H); 7.21 (1H, d, $J_{5'6'}$ = 7.58 Hz, 5'-H); 7.35 (1H, dd, J_{56} = 7.88, J_{67} = 7.12 Hz, 6-H); 7.45 (1H, s, 2'-H); 7.53 (1H, d, J_{34} = 8.91 Hz, 3-H); 7.60 (1H, dd, J_{67} = 7.12, J_{78} = 8.51 Hz, 7-H); 7.67 (1H, d, J_{56} = 7.88 Hz, 5-H); 7.94 (1H, d, J_{78} = 8.51 Hz, 8-H); 7.95 (1H, d, J_{34} = 8.91 Hz, 4-H). Found %: C 84.32; H 7.51; N 8.17. $C_{24}H_{26}N_2$. Calculated %: C 84.22; H 7.60; N 8.18.

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