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INVESTIGATIONS ON 2,3'-BIQUINOLYLS. 15*. REGIOSELECTIVITY OF THE ADDITION OF NITROMETHANE ANION TO 1'-ALKYL-3'-(2-QUINOLYL)QUINOLINIUM HALIDES

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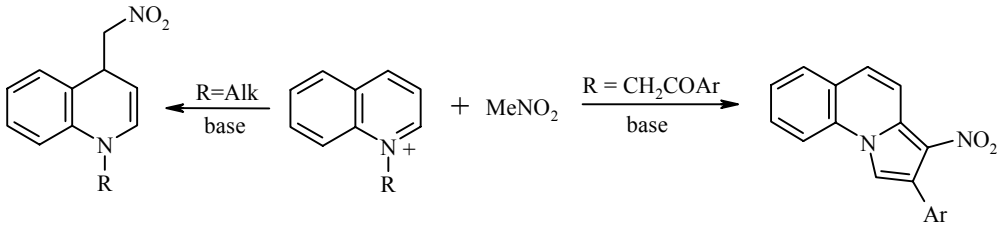
1'-R-3'-(2-Quinolyl)quinolinium halides react with nitromethane forming products of addition at the position 4', the 1'-R-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyls. A method has been developed for the synthesis of 1'-phenacyl-1',4'-dihydro-2,3'-biquinolyls based on the alkylation of 1',4'-dihydro-2,3'-biquinolyl with halogen derivatives in DMF.

Keywords: 1'-R-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyls, 1'-phenacyl-1',4'-dihydro-2,3'-biquinolyls, 1'-R-3'-(2-quinolyl)quinolinium halides, alkylation, nucleophilic addition.

While continuing the investigation of the regioselectivity of nucleophilic addition to 2,3'-biquinolyls we have studied the reaction of 1'-R-3'-(2-quinolyl)-quinolinium halides **1a-e** with nitromethane anion.

It is known [2] that alkylquinolinium salts form products of addition at position 4 with nitroalkane anions. 1-Phenacylquinolinium salts form cyclization products with nitromethane, *viz*. 2-aryl-3-nitropyrrolo-[1,2-*a*]quinolines [3] (Scheme 1), the formation of which probably comprises first the addition of nitromethane anion at position 2 or condensation at the carbonyl group, to which complexation of a metal cation or the formation of an intermolecular hydrogen bond with the oxygen atom of the carbonyl group may assist.

Scheme 1



An analogous result might also be expected for the quaternized 2,3'-biquinolyls **1a-e**. However in the case of the phenacyl salts **1d,e** complexation is possible both with the oxygen atom of the carbonyl group and with the nitrogen atom at position 1, which will assist attack of the nucleophilic reagent both at position 2' and

* For Part 14 see [1].

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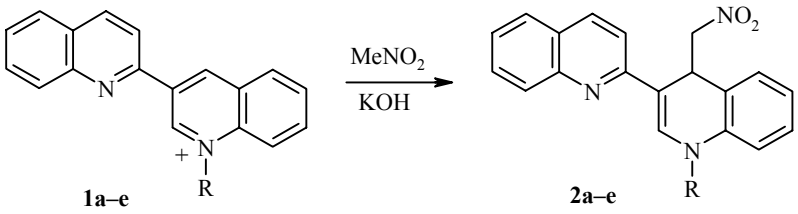
at position 4'. Taking this circumstance into account and the fact that nitromethane anion is a "soft" nucleophile, it might have been supposed that, unlike quinolinium salts **1**, irrespective of the structure of the residue on the nitrogen atom, addition products at position 4' will be formed (Scheme 2).

Scheme 2

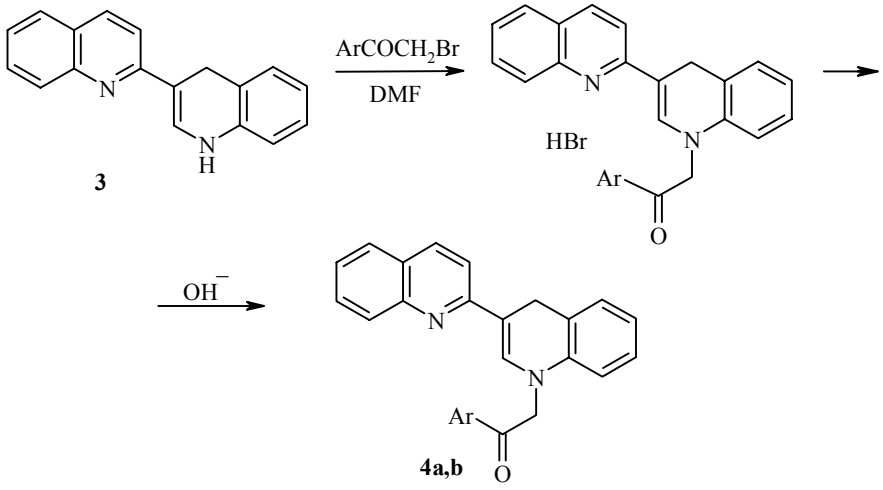


1, **2 a** R = Me; **b** R = Et; **c** R = Bu; **d** R = $PhCOCH_2$; **e** R = 4-$BrC_6H_4COCH_2$

In reality the reaction of biquinolyls **1a-e** with nitromethane in the presence of alkali or triethylamine, both in aqueous dioxane and in aqueous alcohol, leads to the formation of 1'-R-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyls **2a-e** in yields close to quantitative. The use of triethylamine proved to be less effective than using alkali and in the present case the reaction time significantly increased.

A method was then developed to synthesize the previously unknown 1'-phenacyl-1',4'-dihydro-2,3'-biquinolyls **4a,b** by the alkylation of 1',4'-dihydro-2,3'-biquinolyl (**3**) with phenacyl bromides in DMF (Scheme 3). The yield was 87-91%.

Scheme 3



4 a Ar = Ph; **b** Ar = 4-BrC_6H_4

However we failed to convert compounds **4a,b** into pyrrolo[1,2-*a*]quinoline derivatives by condensation with nitromethane in alkaline medium.

EXPERIMENTAL

The NMR spectra were recorded on a Bruker WP-200 (200 MHz) instrument in $CDCl_3$ (compounds **2a-c, 4a,b**) and acetonitrile-d_3 (compounds **2d,e**), internal standard was TMS. A check on the progress of reactions and the homogeneity of the compounds synthesized was carried out on Silufol UV-254 plates, solvent system was ethyl acetate–hexane, 1:1.

Synthesis of 1'-R-4'-Nitromethyl-1',4'-dihydro-2,3'-biquinolyls (2a-e) (General Method). A solution of KOH (0.2 g, 5 mmol) in water (20 ml) was added gradually with stirring to a solution of nitromethane (0.6 g, 10 mmol) in 1,4-dioxane (20 ml) or isopropyl alcohol and the mixture was stirred for 5 min. The 1-R-3-(2-quinolyl)quinolinium halide (**1a-e**) (2.5 mmol) was added and the mixture stirred for 15 min at room temperature, then for 30 min at 60°C (a homogeneous solution was formed). The solution was poured into water (200 ml) and extracted with benzene (3 × 30 ml). The organic layer was separated, dried over Na_2SO_4, and evaporated.

1'-Methyl-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyl (2a). Yield 0.75 g (91%); mp 148-149°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.39 (3H, s, Me); 4.53 (1H, dd, $J_{CHa-CHb}$ = 10.87, $J_{CHa-4'}$ = 8.32, CHaHb); 4.77 (1H, dd, $J_{CHa-CHb}$ = 10.87, $J_{CHb-4'}$ = 4.05, CHaHb); 5.49 (1H, dd, $J_{CHa-4'}$ = 8.32, $J_{CHb-4'}$ = 4.05, 4'-H); 6.92 (1H, dd, $J_{7'8'}$ = 8.11, $J_{6'8'}$ = 1.28, 8'-H); 7.04 (1H, dt, $J_{5'6'}$ = 7.31, $J_{6'7'}$ = 6.85, $J_{6'8'}$ = 1.28, 6'-H); 7.28 (2H, m, 5'-, 7'-H); 7.34 (1H, s, 2'-H); 7.40 (1H, dt, J_{56} = 8.11, J_{67} = 7.26, J_{68} = 1.28, 6-H); 7.54 (1H, d, J_{34} = 8.54, 3-H); 7.65 (1H, dt, J_{67} = 7.26, J_{78} = 8.54, J_{57} = 1.28, 7-H); 7.71 (1H, dd, J_{56} = 8.11, J_{57} = 1.28, 5-H); 7.98 (1H, d, J_{34} = 8.54, 4-H); 8.00 (1H, dd, J_{78} = 8.54, J_{68} = 1.28, 8-H). Found, %: C 72.58; H 5.04; N 12.76. $C_{20}H_{17}N_3O_2$. Calculated, %: C 72.49; H 5.17; N 12.76.

1'-Ethyl-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyl (2b). Yield 0.77 g (89%); mp 136-137°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.38 (3H, dd, J_{CHa-Me} = 7.26, J_{CHb-Me} = 6.83, Me); 3.75 (1H, dq, J_{CHa-Me} = 7.26, $J_{CHa-CHb}$ = 14.94, CHaHbMe); 3.88 (1H, dq, J_{CHb-Me} = 6.83, $J_{CHa-CHb}$ = 14.94, CHaHbMe); 4.55 (1H, dd, $J_{CHa-CHb}$ = 10.68, $J_{CHa-4'}$ = 7.89, CHaHbNO$_2$); 4.75 (1H, dd, $J_{CHa-CHb}$ = 10.68, $J_{CHb-4'}$ = 4.06, CHaHbNO$_2$); 5.46 (1H, dd, $J_{CHa-4'}$ = 7.89, $J_{CHb-4'}$ = 4.06, 4'-H); 6.95 (1H, dd, $J_{7'8'}$ = 8.11, $J_{6'8'}$ = 1.28, 8'-H); 7.02 (1H, dt, $J_{5'6'}$ = 7.28, $J_{6'7'}$ = 6.83, $J_{6'8'}$ = 1.28, 6'-H); 7.27 (2H, m, 5'-, 7'-H); 7.37 (1H, s, 2'-H); 7.40 (1H, dt, J_{56} = 8.11, J_{67} = 6.83, J_{68} = 1.28, 6-H); 7.56 (1H, d, J_{34} = 8.53, 3-H); 7.64 (1H, dt, J_{67} = 6.83, J_{78} = 8.11, J_{57} = 1.28, 7-H); 7.70 (1H, dd, J_{56} = 8.11, J_{57} = 1.28, 5-H); 7.98 (1H, d, J_{34} = 8.53, 4-H); 7.99 (1H, dd, J_{78} = 8.11, J_{68} = 1.28, 8-H). Found, %: C 73.12; H 5.40; N 12.25. $C_{21}H_{19}N_3O_2$. Calculated, %: C 73.03; H 5.54; N 12.17.

1'-Butyl-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyl (2c). Yield 0.81 g (87%); mp 112-113°C (alcohol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.26, Me); 1.47 (2H, m, *J* = 7.26, $CH_2CH_2CH_2$Me); 1.78 (2H, m, $CH_2CH_2CH_2$Me); 3.59 (1H, dt, $J_{CHa-CH2}$ = 7.26, $J_{CHa-CHb}$ = 14.52, CHaHbPr); 3.85 (1H, dt, $J_{CHb-CH2}$ = 7.26, $J_{CHa-CHb}$ = 14.52, CHaCHbPr); 4.54 (1H, dd, $J_{CHa-CHb}$ = 10.67, $J_{CHa-4'}$ = 8.11, CHaHbNO$_2$); 4.77 (1H, dd, $J_{CHa-CHb}$ = 10.67, $J_{CHb-4'}$ = 4.27, CHaHbNO$_2$); 5.46 (1H, dd, $J_{CHa-4'}$ = 8.11, $J_{CHb-4'}$ = 4.27, 4'-H); 6.94 (1H, dd, $J_{7'8'}$ = 8.11, $J_{6'8'}$ = 1.26, 8'-H); 7.02 (1H, dt, $J_{5'6'}$ = 7.68, $J_{6'7'}$ = 7.26, $J_{6'8'}$ = 1.26, 6'-H); 7.27 (2H, m, 5'-, 7'-H); 7.35 (1H, s, 2'-H); 7.40 (1H, dt, J_{56} = 7.68, J_{67} = 7.26, J_{68} = 0.85, 6-H); 7.55 (1H, d, J_{34} = 8.54, 3-H); 7.64 (1H, dt, J_{67} = 7.26, J_{78} = 8.54, J_{57} = 1.28, 7-H); 7.71 (1H, dd, J_{56} = 7.68, J_{57} = 1.28, 5-H); 7.99 (1H, d, J_{34} = 8.54, 4-H); 8.00 (1H, dd, J_{78} = 8.54, J_{68} = 0.85, 8-H). Found, %: C 74.06; H 6.05; N 11.32. $C_{23}H_{23}N_3O_2$. Calculated, %: C 73.97; H 6.21; N 11.25.

4'-Nitromethyl-1'-phenacyl-1',4'-dihydro-2,3'-biquinolyl (2d). Yield 1 g (92%); mp 178-179°C (benzene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.65 (1H, dd, $J_{CHa-CHb}$ = 10.99, $J_{CHa-4'}$ = 8.80, CHaHbNO$_2$); 4.85 (1H, dd, $J_{CHa-CHb}$ = 10.99, $J_{CHb-4'}$ = 4.40, CHaHbNO$_2$); 5.37 (1H, d, $J_{CHa-CHb}$ = 19.25, CHaCHbCO); 5.43 (1H, d, $J_{CHa-CHb}$ = 19.25, CHaHbCO); 5.50 (1H, dd, $J_{CHa-4'}$ = 8.80, $J_{CHb-4'}$ = 4.40, 4'-H); 6.83 (1H, dd, $J_{7'8'}$ = 7.70, $J_{6'8'}$ = 0.98, 8'-H); 7.05 (1H, dt, $J_{5'6'}$ = 7.70, $J_{6'7'}$ = 7.33, $J_{6'8'}$ = 0.98, 6'-H); 7.22 (1H, dt, $J_{7'8'}$ = 7.70, $J_{6'7'}$ = 7.33, $J_{5'7'}$ = 1.65, 7'-H); 7.31 (1H, dd, $J_{5'6'}$ = 7.70, $J_{5'7'}$ = 1.65, 5'-H); 7.49 (1H, dt, J_{56} = 8.05, J_{67} = 7.08, J_{68} = 1.22, 6-H); 7.58 (1H, s, 2'-H); 7.63-7.75 (5H, m, 3-, 7-H, 3-, 4-, 5-H$_{Ph}$); 7.64 (1H, dt, J_{67} = 6.83, J_{78} = 8.11, J_{57} = 1.28, 7-H);

7.84 (1H, dd, J_{56} = 8.80, J_{57} = 0.97, 5-H); 7.98 (1H, dd, J_{78} = 8.25, J_{68} = 1.22, 8-H); 8.11 (1H, d, J_{34} = 8.97, 4-H); 8.12 (2H, d, J = 8.54, 2-, 6-H_{Ph}). Found, %: C 74.54; H 4.12; N 9.62. $C_{27}H_{21}N_3O_3$. Calculated, %: C 74.47; H 4.86; N 9.65.

1'-(*p*-Bromophenacyl)-4'-nitromethyl-1',4'-dihydro-2,3'-biquinolyl (2e). Yield 1.21 g (94%); mp 143-145°C (benzene). ^{1}H NMR spectrum, δ, ppm (J, Hz): 4.64 (1H, dd, $J_{CHa-CHb}$ = 10.99, $J_{CHa-4'}$ = 8.55, C<u>Ha</u>HbNO$_2$); 4.83 (1H, dd, $J_{CHa-CHb}$ = 10.99, $J_{CHb-4'}$ = 4.40, CHa<u>Hb</u>NO$_2$); 5.39 (1H, d, $J_{CHa-CHb}$ = 18.8, C<u>Ha</u>HbCO); 5.42 (1H, d, $J_{CHa-CHb}$ = 18.8, CHa<u>Hb</u>CO); 5.52 (1H, dd, $J_{CHa-4'}$ = 8.55, $J_{CHb-4'}$ = 4.40, 4'-H); 6.85 (1H, dd, $J_{7'8'}$ = 8.04, $J_{6'8'}$ = 0.98, 8'-H); 7.08 (1H, dt, $J_{5'6'}$ = 7.33, $J_{6'7'}$ = 7.57, $J_{6'8'}$ = 0.98, 6'-H); 7.24 (1H, dt, $J_{7'8'}$ = 8.04, $J_{6'7'}$ = 7.57, $J_{5'7'}$ = 1.47, 7'-H); 7.32 (1H, dd, $J_{5'6'}$ = 7.33, $J_{5'7'}$ = 1.47, 5'-H); 7.40 (1H, s, 2'-H); 7.52 (1H, dt, J_{56} = 8.05, J_{67} = 7.08, J_{68} = 1.22, 6-H); 7.72 (1H, d, J_{34} = 8.79, 3-H); 7.76 (1H, dt, J_{78} = 8.79, J_{67} = 7.08, J_{57} = 0.97, 7-H); 7.80 (2H, d, J = 8.54, 3-, 5-H_{Ph}); 7.87 (1H, dd, J_{56} = 8.05, J_{57} = 0.97, 5-H); 8.01 (2H, d, J = 8.54, 2-, 6-H_{Ph}); 8.12 (1H, dd, J_{78} = 8.79, J_{68} = 1.22, 8-H); 8.20 (1H, d, J_{34} = 8.79, 4-H). Found, %: C 63.14; H 3.86; N 8.12. $C_{27}H_{20}BrN_3O_3$. Calculated, %: C 63.05; H 3.92; N 8.17.

Alkylation of 1',4'-Dihydro-2,3'-biquinolyl (3) in DMF (General Method). A mixture of biquinolyl **3** (0.52 g, 2 mmol) and the appropriate phenacyl bromide (2.2 mmol) in DMF (5 ml) was boiled for 1 h. After cooling, the precipitate of the corresponding biquinolyl hydrobromide was filtered off, washed with a little 2-propanol, and with 20% ammonia solution. Yellow crystals of the free bases of compounds **4a,b** were obtained.

1'-Phenacyl-1',4'-dihydro-2,3'-biquinolyl (4a). Yield 0.66 g (87%); mp 188-189°C (benzene). ^{1}H NMR spectrum, δ, ppm (J, Hz): 4.24 (2H, s, 4'-H); 5.07 (2H, s, CH_2CO); 6.44 (1H, dd, $J_{7'8'}$ = 8.25, $J_{6'8'}$ = 1.1, 8'-H); 6.92 (1H, dt, $J_{5'6'}$ = 7.69, $J_{6'7'}$ = 7.14, $J_{6'8'}$ = 1.1, 6'-H); 7.04 (1H, dt, $J_{7'8'}$ = 8.25, $J_{6'7'}$ = 7.14, $J_{5'7'}$ = 1.52, 7'-H); 7.23 (1H, dd, $J_{5'6'}$ = 7.69, $J_{5'7'}$ = 1.52, 5'-H); 7.32 (1H, s, 2'-H); 7.39 (1H, dt, J_{56} = 7.69, J_{67} = 6.83, J_{68} = 1.1, 6-H); 7.46 (1H, d, J_{34} = 8.80, 3-H); 7.55 (3H, m, 3-, 4-, 5-H_{Ph}); 7.63 (1H, dt, J_{67} = 6.83, J_{78} = 8.25, J_{57} = 1.28, 7-H); 7.71 (1H, dd, J_{56} = 7.69, J_{57} = 1.28, 5-H); 7.98 (1H, dd, J_{78} = 8.25, J_{68} = 1.22, 8-H); 7.99 (1H, d, J_{34} = 8.8, 4-H); 8.05 (2H, d, J = 7.14, 2-, 6-H_{Ph}). Found, %: C 83.04; H 5.27; N 17.41. $C_{26}H_{20}N_2O$. Calculated, %: C 82.95; H 5.35; N 7.44.

1'-(*p*-Bromophenacyl)-1',4'-dihydro-2,3'-biquinolyl (4b). Yield 0.83 g (91%); mp 211-212°C (alcohol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 4.23 (2H, s, 4'-H); 5.09 (2H, s, CH_2CO); 6.43 (1H, dd, $J_{7'8'}$ = 8.25, $J_{6'8'}$ = 1.1, 8'-H); 6.94 (1H, dt, $J_{5'6'}$ = 7.69, $J_{6'7'}$ = 7.14, $J_{6'8'}$ = 1.1, 6'-H); 7.05 (1H, dt, $J_{7'8'}$ = 8.25, $J_{6'7'}$ = 7.14, $J_{5'7'}$ = 1.52, 7'-H); 7.24 (1H, dd, $J_{5'6'}$ = 7.69, $J_{5'7'}$ = 1.52, 5'-H); 7.32 (1H, s, 2'-H); 7.41 (1H, dt, J_{56} = 7.69, J_{67} = 6.83, J_{68} = 1.1, 6-H); 7.46 (1H, d, J_{34} = 8.81, 3-H); 7.63 (1H, dt, J_{67} = 6.83, J_{78} = 8.25, J_{57} = 1.28, 7-H); 7.71 (1H, dd, J_{56} = 7.69, J_{57} = 1.28, 5-H); 7.81 (2H, d, J = 8.54, 3-, 5-H_{Ph}); 7.98 (1H, dd, J_{78} = 8.25, J_{68} = 1.22, 8-H); 7.99 (1H, d, J_{34} = 8.81, 4-H); 8.05 (2H, d, J = 8.54, 2-, 6-H_{Ph}). Found, %: C 68.74; H 4.16; N 6.05. $C_{26}H_{19}BrN_2O$. Calculated, %: C 68.58; H 4.21; N 6.15.

REFERENCES

1. A. V. Aksenov and N. V. Demidova, *Khim. Geterotsikl. Soedin.*, 1051 (2002).
2. I. S. Poddubnyi, *Khim. Geterotsikl. Soedin.*, 774 (1995).
3. W. Kiel and F. Krohnke, *Chem. Ber.*, **105**, 3709 (1972).