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INVESTIGATIONS ON 2,3'-BIQUINOLYL SERIES. 20*. NOVEL METHOD FOR THE SYNTHESIS OF 2,3'-BIQUINOLINES BY CYCLIZATION OF β-(2-QUINOLYL)-2-AMINOSTYRENES

A. S. Lyakhovnenko[1], V. V. Trifonov[1], V. I. Goncharov[2], and A. V. Aksenov[1]

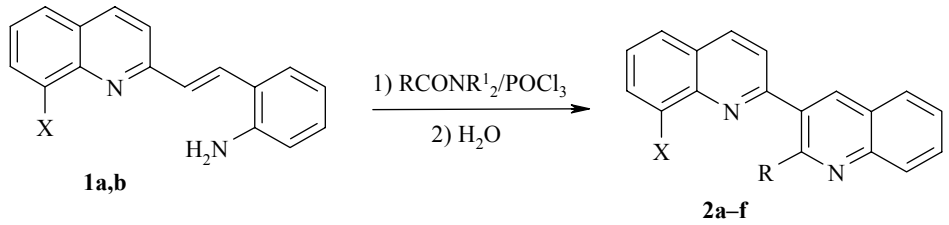
A method has been developed for the synthesis of 2,3'-biquinolines based on the reaction of β-(2-quinolyl)-2-aminostyrenes with acid amides under Vilsmeier reaction conditions.

Keywords: acid amides, 2,3'-biquinoline, β-(2-quinolyl)-2-aminostyrene, cyclization.

A series of methods for the synthesis of 2,3'-biquinolines **2** has been developed which includes either formation of quinoline rings (e.g. in [2-5]) or of a bond between them [6, 7]. These methods have a number of drawbacks which include the low availability of starting compounds or the possibility of synthesizing only symmetrically substituted 2,3'-biquinoline derivatives.

In this work we report a method for the synthesis of 2,3'-biquinolines which allows one to synthesize, from one starting compound, 2,3'-biquinolines with different substituents in the 2'-position.

We have shown that the reaction of the amines **1a,b** with DMF or the diethylamides of other carboxylic acids in the presence of $POCl_3$ gives high yields (82-88%) of the 2,3'-biquinolines **2a-f**.



1a,b **2a–f**

1 a X = H, **b** X = NO_2; **2 a** R = H, **b** R = Me, **c** R = Pr, **d** R = Bu, **e** R = Ph; **a-e** X = H, **f** R = H, X = NO_2

The reaction of the amine **1** with acid chlorides in the presence of Et_3N and subsequent treatment with $POCl_3$ occurs similarly. In this case the yields of the reaction products are lower.

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* For Communication 19 see [1].

[1] Stavropol State University, Stavropol 355009, Russia; e-mail: nauka@stavsu.ru, k-biochem-org@stavsu.ru. [2] Stavropol State Medicinal Academy, Stavropol 335000, Russia; e-mail: sgma@stavropol.ru.
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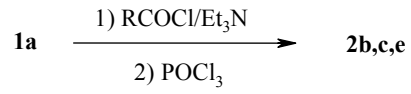

EXPERIMENTAL

NMR spectra were recorded on a Bruker WP-200 (200 MHz) instrument using TMS as internal standard. Monitoring of the reaction course and purity of the synthesized compounds was performed on Silufol UV-254 plates in the solvent system ethyl acetate–hexane (1:1). Flash chromatography was carried out by the method in [8] (column: d = 60 mm, l = 50 mm) with benzene as the low polarity solvent and ethyl acetate as the polar solvent.

Synthesis of 2'-R-2,3'-Biquinolines 2a-f Using Acid Amides (General Method). A. Phosphorus oxychloride (1.83 g, 12 mmol) was added dropwise with vigorous stirring to the corresponding acid dialkylamide (12 mmol) at 0°C over 30 min. The reaction mixture was stirred for a further 30 min at room temperature after which the corresponding β-(2-quinolyl)-2-aminostyrene (4 mmol) in chloroform (10 ml) was added in small portions and then refluxed for 3 h. The reaction mixture was then cooled and poured into crushed ice (50 g), neutralized with a solution of ammonia, and extracted with benzene (3 × 30 ml). Solvent was evaporated and compounds **2a,e,f** were purified by recrystallization (compounds **2b-d** by flash chromatography).

Synthesis of 2'-R-2,3'-Biquinolyls 2b,c,e Using Acid Anhydrides (General Method). B. The appropriate acid anhydride (2.5 mmol) was added carefully over 30 min to a mixture of β-(2-quinolyl)-2-aminostyrene (0.49 g, 2 mmol) and triethylamine (0.5 g, 5 mmol) in chloroform (5 ml) at room temperature. The reaction mixture was refluxed for 1 h, cooled, and phosphorus oxychloride (2.14 g, 14 mmol) was added. The product was refluxed for 1 h, poured into crushed ice (50 g), neutralized with ammonia solution, and extracted with benzene (3 × 30 ml). The solvent was evaporated and compound **2e** was purified by recrystallization (compounds **2b,c** by flash chromatography).

2-3'-Biquinolyl (2a). From DMF and β-(2-quinolyl)-2-aminostyrene in 0.9 g (88%) yield; mp 175-176°C (benzene) (mp 175-176°C [6, 7]). When mixed with a known sample no depression of melting point was produced. The ^{1}H NMR spectrum was identical to that given in [7].

2'-Methyl-2,3'-biquinoline (2b). A. From N,N-diethylacetamide and β-(2-quinolyl)-2-aminostyrene in 0.91 g (84%) yield. B. From acetyl chloride in 0.41 g (76%) yield; mp 57-58°C (benzene–hexane) (mp 57-58°C [9]). When mixed with a known sample no depression of melting point was produced. The ^{1}H NMR spectrum was identical to that given in [9].

2'-Propyl-2,3'-biquinoline (2c). A. From butyric acid N,N-diethylamide and β-(2-quinolyl)-2-aminostyrene in 1.04 g (87%) yield. B. From butyryl chloride in 0.44 g (72%) yield. White oil. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (J, Hz): 0.95 (3H, t, J = 7.2, 2'-$CH_2CH_2C\underline{H}_3$); 1.70 (2H, m, 2'-$CH_2C\underline{H}_2CH_3$); 3.20 (2H, m, 2'-$C\underline{H}_2CH_2CH_3$); 7.60 (1H, dd, $J_{5',6'}$ = 8.38, $J_{6',7'}$ = 6.96, H-6'); 7.67 (1H, dd, $J_{5,6}$ = 8.05, $J_{6,7}$ = 7.02, H-6); 7.79 (1H, dd, $J_{6',7'}$ = 6.96, $J_{7',8'}$ = 8.35, H-7'); 7.85 (1H, dd, $J_{6,7}$ = 7.02, $J_{7,8}$ = 8.31, H-7); 7.87 (1H, d, $J_{3,4}$ = 8.54, H-3); 8.02 (1H, d, $J_{5',6'}$ = 8.38, H-5'); 8.07 (1H, d, $J_{8',7'}$ = 8.35, H-8'); 8.06 (1H, d, $J_{5,6}$ = 8.05, H-5); 8.12 (1H, d, $J_{7,8}$ = 8.31, H-8); 8.43 (1H, s, H-4'); 8.52 (1H, d, $J_{3,4}$ = 8.5, H-4). Found, %: C 84.81; H 6.02; N 9.17. $C_{21}H_{18}N_2$. Calculated, %: C 84.52; H 6.08; N 9.39.

2'-Butyl-2,3'-biquinoline (2d). A. From valeric acid N,N-diethylamide and β-(2-quinolyl)-2-aminostyrene. Yield 1.04 g (83%). White oil (white oil [8]). When mixed with a known sample no depression of melting point was produced. The ^{1}H NMR spectrum was identical to that given in [9].

2'-Phenyl-2,3'-biquinoline (2e). A. From benzoic acid N,N-diethylamide and β-(2-quinolyl)-2-aminostyrene in 1.13 g (85%) yield. B. From benzoyl chloride in 0.52 g (79%) yield; mp 76-77°C (benzene–hexane) (mp 76-77°C [9]). When mixed with a known sample no depression of melting point was produced. The ^{1}H NMR spectrum was identical to that given in [9].

8-Nitro-2,3'-biquinoline (2f). A. From DMF and β-(8-nitroquinolin-2-yl)-2-aminostyrene in 0.99 g (82%) yield; mp 227-229°C (DMF) (mp 227-229°C [10]). When mixed with a known sample no depression of melting point was produced. The ^{1}H NMR spectrum was identical to that given in [10].

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