Chemistry of Heterocyclic Compounds, Vol. 36, No. 11, 2000

INVESTIGATION OF 2,3'-BIQUINOLYL. 10*. THE REGIOSELECTIVITY OF THE REACTION OF 2,3'-BIQUINOLYL AND 1'-ALKYL-3-(2-QUINOLYL)QUINOLINIUM HALIDES WITH HALO DERIVATIVES IN THE PRESENCE OF METALLIC LITHIUM AND MAGNESIUM

A. V. Aksenov and O. N. Nadein

2,3'-Biquinolyl reacts with halo derivatives in the presence of metallic lithium to give addition products at position 4', treatment of which with water gives 4'-R-1',4'-dihydro-2,3'-biquinolyls and with halo derivatives gives 1'-alkyl-4'-R-1',4'-dihydro-2,3'-biquinolyls. The reaction of 2,3'-biquinolyl with halo derivatives in the presence of metallic magnesium gives a mixture of products of addition at positions 2' and 4'. 1-Alkyl-3-(2-quinolyl)quinolinium halides and halo derivatives with metallic magnesium give 1'-alkyl-2'-R-1',2'-dihydro-2,3'-biquinolyls but form a complex mixture of substances when metallic lithium is used.

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

A series of methods for the synthesis of 4'-R-1',4'-dihydro-2,3'-biquinolyls **3** has been proposed based on the reactions of the 2,3'-biquinolyl dianion with halo derivatives [2, 3] or of 2,3'-biquinolyl with organometallic compounds [4, 5]. It was therefore of interest to develop a simpler synthetic method for **3** based on an investigation of the reaction of 2,3'-biquinolyl with halo derivatives in the presence of metals.

In the presence of metallic magnesium and lithium, pyridine reacts with halo derivatives to form addition (substitution) products at position 4 [6]. We expected that 2,3'-biquinolyl would behave similarly.

In fact, the reaction of 2,3'-biquinolyl **1** with halo derivatives in the presence of metallic lithium gives after work up with water the 4'-R-1',4'-dihydro-2,3'-biquinolyls **3a-d** but the use of halo derivative in the final stage gives the 1'-alkyl-4'-R-1',4'-dihydro-2,3'-biquinolyls **3f-h** (Scheme 1).

However, the use of metallic magnesium in this reaction gives a mixture of compounds **3** and 2'-R-1',2'-dihydro-2,3'-biquinolyls **4** in different ratios (**3a-4e** 0.82 : 1; **3d-4d** 0 : 1; **3a-4a** 5.5 : 1; **3b-4b** 1.6 : 1) (Scheme 2). It was interesting that Grignard and dialkylmagnesium reagents (with the exception of allylmagnesium chloride) gave exclusively the compound **3** [4].

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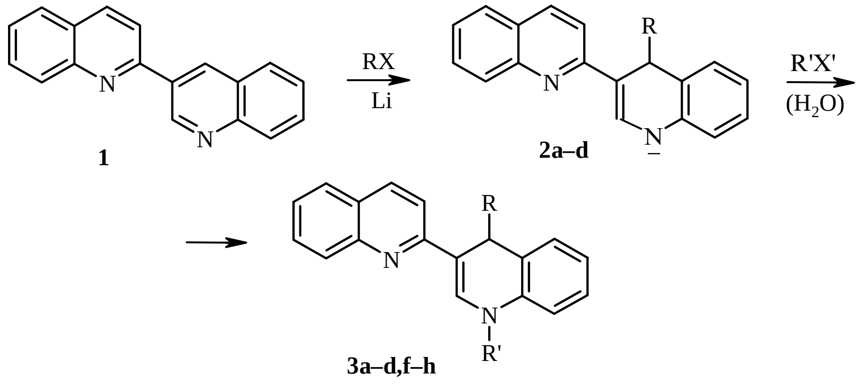
* For Communication 9, see [1].

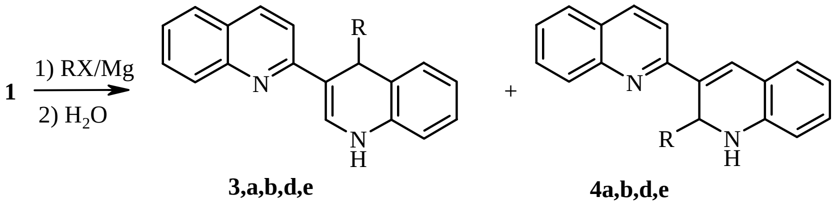
Stavropol State University, Stavropol 355009, Russia; e-mail: nauka@stavsu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1527-1531, November, 2000. Original article submitted February 24, 1999.

Scheme 1



2 **a** R = Ph; **b** R = 1-$C_{10}H_7$; **c** R = Pr; **d** R = CH_2CHCH_2; **3** **a** R = Ph, R' = H; **b** R = 1-$C_{10}H_7$, R' = H; **c** R = Pr, R' = H; **d** R = CH_2CHCH_2, R' = H; **f** R = Ph, R' = Me; **g** R = 1-$C_{10}H_7$, R' = Me; **h** R = 1-$C_{10}H_7$, R' = CH_2Ph

Scheme 2

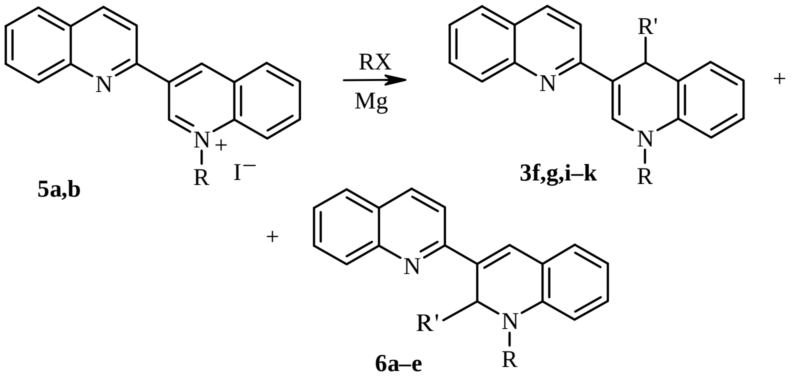


3, **4** **a** R = Ph; **b** R = 1-$C_{10}H_7$; **d** R = CH_2CHCH_2; **e** R = Me

The data obtained can be rationalized in the following way. Having a higher ionization potential, magnesium is less effective than lithium in donating electrons to 2,3'-biquinolyl and reacts with halo derivatives to form poorly associated, inflexible nucleophilic species. Reaction of the latter with compound **1** gives compound **4**.

The reaction of 1-alkyl-3-(2-quinolyl)quinolinium halides **5** with aryl and alkyl halides in the presence of metallic magnesium gives an increased amount of 1'-alkyl-2'-R-1',2'-dihydro-2,3'-biquinolyls **6** when compared with the use of a Grignard reagent [7]. However, in this reaction, benzyl chloride gives high yields of the products of alkylation at position 4' **3i,j** (Scheme 3).

Scheme 3



5 **a** R = Me; **b** R = CH_2Ph; **3** **i** R = Me, R' = CH_2Ph; **j** R = CH_2Ph, R' = CH_2Ph; **k** R = R' = Me;
6 **a** R = Me, R' = 1-$C_{10}H_7$; **b** R = Me, R' = Ph; **c** R = R' = Me; **d** R = Me, R' = CH_2Ph; **e** R = CH_2Ph, R' = CH_2Ph

The reaction of 1-alkyl-3-(2-quinolyl)quinolinium halides **5** with alkyl and aryl halides in the presence of metallic lithium gives a complex mixture of substances.

EXPERIMENTAL

^{1}H NMR spectra were recorded on Bruker WP-200 instruments using TMS as internal standard. Monitoring of the reaction course and the purity of the synthesized compounds was carried out on Silufol UV-254 plates in the solvent system ethyl acetate-hexane (1 : 1). Column chromatography was performed on L 40/100 silica gel. THF was purified by distillation over $LiAlH_4$ and then over benzophenone ketyl.

4'-Phenyl-1',4'-dihydro-2,3'-biquinolyl (3a, $C_{24}H_{18}N_2$). A mixture of 2,3'-biquinolyl (0.64 g, 2.5 mmol), bromobenzene (0.47 g, 3 mmol), and finely divided metallic lithium (0.046 g, 6.5 mmol) in THF (10 ml) was vigorously stirred under an argon atmosphere for 1.5 h. The mixture was poured into water (50 ml), extracted with benzene (3 × 30 ml), and the benzene extract was dried over sodium sulfate and evaporated. A yellow oil was obtained and this crystallized upon addition of a small amount of benzene and then hexane. Yield 0.79 g (95%); mp 213-214°C (benzene). According to data in [2], mp 213-214°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [2].

4'-(1-Naphthyl)-1',4'-dihydro-2,3'-biquinolyl (3b, $C_{28}H_{20}N_2$). Similarly to **3a** from 2,3'-biquinolyl (0.64 g, 2.5 mmol), bromonaphthalene (0.62 g, 3 mmol), and metallic lithium (0.046 g, 6.5 mmol). Yield 0.89 g (93%); mp 196-197°C (benzene). According to data in [2]; mp 196-197°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [2].

4'-Propyl-1',4'-dihydro-2,3'-biquinolyl (3c, $C_{21}H_{20}N_2$). Similarly to **3a** from 2,3'-biquinolyl (0.64 g, 2.5 mmol), 1-chloropropane (0.24 g, 3 mmol), and metallic lithium (0.046 g, 6.5 mmol). Yield 0.69 g (92%); mp 127-129°C (benzene–hexane). According to data in [4], mp 127-129°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [4].

4'-Allyl-1',4'-dihydro-2,3'-biquinolyl (3d, $C_{21}H_{18}N_2$). Similarly to **3a** from 2,3-biquinolyl (0.64 g, 2.5 mmol), metallic lithium (0.05 g, 7 mmol), and allyl chloride (0.34 g, 4.5 mmol). Yield 0.6 g (84%); mp 107-109°C (benzene–hexane). According to data in [3], mp 107-109°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [3].

1'-Methyl-4'-phenyl-1',4'-dihydro-2,3'-biquinolyl (3f, $C_{25}H_{20}N_2$). A mixture of 2,3'-biquinolyl (0.64 g, 2.5 mmol), bromobenzene (0.47 g, 3 mmol), and finely divided metallic lithium (0.046 g, 6.5 mmol) in THF (10 ml) was vigorously stirred under an argon atmosphere for 1.5 h. It was then cooled to room temperature, methyl iodide (0.71 g, 5 mmol) in THF (2 ml) added, and the product was stirred for 1 h. The mixture was poured into water (50 ml), extracted with benzene (3 × 30 ml), and the benzene extract was dried over sodium sulfate and evaporated to give a yellow oil which crystallized upon addition of hexane. Yield 0.79 g (91%); mp 173-174°C (alcohol). According to data in [2], mp 173-174°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [2].

1'-Methyl-4'-(1-naphthyl)-1',4'-dihydro-2,3'-biquinolyl (3g, $C_{29}H_{22}N_2$). Similarly to **3f** from 2,3'-biquinolyl (0.64 g, 2.5 mmol), metallic lithium (0.046 g, 6.5 mmol), 1-bromonaphthalene (0.62 g, 3 mmol), and methyl iodide (0.71 g, 5 mmol). Yield 0.88 g (88%); mp 151-153°C (benzene–hexane). According to data in [2], mp 151-153°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [2].

1'-Benzyl-4'-(1-naphthyl)-1',4'-dihydro-2,3'-biquinolyl (3h, $C_{35}H_{26}N_2$). Similarly to **3f** from 2,3'-biquinolyl (0.64 g, 2.5 mmol), metallic lithium (0.046 g, 6.5 mmol), 1-bromonaphthalene (0.62 g, 3 mmol), and benzyl chloride (0.44 g, 3.5 mmol). Yield 1 g (84%); mp 143-144°C (alcohol). According to data in [2], mp 143-144°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in the report [2].

General Method for the Alkylation (Arylation) of 2,3'-Biquinolyl Using Halo Derivatives in the Presence of Metallic Magnesium. A mixture of 2,3'-biquinolyl (0.32 g, 1.25 mmol), the halo derivative (2.5 mmol of bromobenzene, 1-bromonaphthalene, or methyl iodide), and metallic magnesium (0.07 g, 2.91 mmol) in THF (10 ml) was vigorously stirred for 3 h under an argon atmosphere. After addition of water (50 ml) which contained acetic acid (2 ml), the product was extracted with benzene (3 × 30 ml). The benzene extracts were combined, washed with aqueous ammonia solution (5%, 50 ml), dried over sodium sulfate, and evaporated. The residue was dissolved in benzene (5 ml) and column chromatographed using the solvent system benzene-ethyl acetate (10 : 1), collecting the first colored fraction. The solvent was evaporated to give compound **4**. Further elution with ethyl acetate, collection of the second colored fraction, and evaporation gave compound **3**.

2'-Phenyl-1',2'-dihydro-2,3'-biquinolyl (4a, $C_{24}H_{18}N_2$) and 4'-Phenyl-1',4'-dihydro-2,3'-biquinolyl (3a, $C_{24}H_{18}N_2$). Yield of compound **4a** 0.06 g (14%); mp 207-209°C (alcohol). According to data in [5], mp 207-209°C. Yield of compound **3a** 0.32 g (77%); mp 213-214°C (benzene). According to data in [2], mp 213-214°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectra were identical.

2'-(1-Naphthyl)-1',2'-dihydro-2,3'-biquinolyl (4b, $C_{28}H_{20}N_2$) and 4'-(1-Naphthyl)-1',4',-dihydro-2,3'-biquinolyl (3b, $C_{28}H_{20}N_2$). Yield of compound **4b** 0.14 g (29%); mp 166-167°C (alcohol). According to data in [5], mp 166-167°C. Yield of compound **3b** 0.23 g (48%); mp 196-197°C (benzene). According to data in [2], mp 196-197°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectra were identical.

2'-Allyl-1',2'-dihydro-2,3'-biquinolyl (4d, $C_{21}H_{18}N_2$). Yield 0.35 g (94%); mp 104-105°C (alcohol). According to data in [4], mp 104-105°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectra were identical.

2'-Methyl-1',2'-dihydro-2,3'-biquinolyl (4e, $C_{19}H_{16}N_2$) and 4'-Methyl-1',4'-dihydro-2,3'-biquinolyl (3e, $C_{19}H_{16}N_2$). Yield of compound **4e** 0.17 g (50%); mp 138-139°C (alcohol). According to data in [5], mp 138-139°C. Yield of compound **3e** 0.14 g (41%); mp 148-149°C (benzene). According to data in [4], mp 148-149°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectra were identical.

General Method for Alkylation (Arylation) of 1-Alkyl-3-(2-quinolyl)quinolinium Halides Using Halo Derivatives in the Presence of Metallic Magnesium. A mixture of 1-alkyl-3-(2-quinolyl)quinolinium halide (2.5 mmol), the halo derivative (5 mmol), and metallic magnesium (0.15 g, 6.25 mmol) in THF (20 ml) was vigorously stirred for 3 h under an argon atmosphere. Water (50 ml) containing acetic acid (2 ml) was added and the product was extracted with benzene (3 × 30 ml). The benzene extracts were combined, washed with aqueous ammonia (5%, 50 ml), dried over sodium sulfate, and evaporated to give a yellow oil which crystallized upon addition of hexane.

1'-Methyl-2'-(1-naphthyl)-1',2'-dihydro-2,3'-biquinolyl (6a, $C_{29}H_{22}N_2$). From 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and 1-bromonaphthalene (1 g, 5 mmol). Yield 0.88 g (88%); mp 225-226°C (alcohol). According to data in [7], mp 225-226°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in [7].

1'-Methyl-2'-phenyl-1',2'-dihydro-2,3'-biquinolyl (6b, $C_{25}H_{20}N_2$). From 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and bromobenzene (0.78 g, 5 mmol). Yield 0.72 g (83%); mp 138-139°C (alcohol). According to data in [7], mp 138-139°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in [7].

1',2'-Dimethyl-1',2'-dihydro-2,3'-biquinolyl (6c, $C_{20}H_{18}N_2$). From 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and methyl iodide (0.71 g, 5 mmol). Yield 0.62 g (86%); mp 168-169°C (benzene–hexane). According to data in [7], mp 168-169°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in [7].

1'-Methyl-4'-benzyl-1',4'-dihydro-2,3'-biquinolyl (3i, $C_{26}H_{22}N_2$). From 1-methyl-3-(2-quinolyl)quinolinium iodide (1 g, 2.5 mmol) and benzyl chloride (0.63 g, 5 mmol). Yield 0.82 g (91%); mp 136-137°C (alcohol). According to data in [3], mp 136-137°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in [3].

1',4'-Dibenzyl-1',4'-dihydro-2,3'-biquinolyl (3j, $C_{32}H_{26}N_2$). From 1-benzyl-3-(2-quinolyl)quinolinium iodide (1.19 g, 2.5 mmol) and benzyl chloride (0.63 g, 5 mmol). Yield 0.84 g (83%); mp 133-134°C (hexane). According to data in [3], mp 133-134°C. The melting point was not depressed by the addition of a known sample. The ^{1}H NMR spectrum was identical to that given in [3].

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