

Sodium Hydride as a Nucleophilic Agent. Part 1. A New Synthesis of 2,3'-Biquinolyls

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An effective synthesis has been developed for 2,3'-biquinolyls using nucleophilic addition of sodium hydride to quinoline and its alkyl derivatives.

Although quinoline reacts with metallic sodium (molar ratio 2.3:1) at 160 °C to yield 2,3'-biquinolyl (30–40% yield),¹ Osborne and Staley have shown recently that its reaction with metallic calcium (molar ratio 0.45:1) at 220 °C yields 2,2'-biquinolyl (18% yield).² In the present work, we have attempted both to account for these findings and to develop new approaches to the synthesis of 2,3'-biquinolyls.

By electron donation to quinoline, calcium generates a radical anion **2**, for which the maximal spin density in the pyridine nucleus is localised in positions 1 and 4 (see Fig. 1). Steric hindrance hampers recombination of the radical anions **2** to give 1,1'- and 4,4'-diquinolyls, 2,2'-biquinolyls being formed preferentially as a result of favourable spatial and spin density factors.

A similar mechanism has been postulated earlier for pyridine dimerisation.³

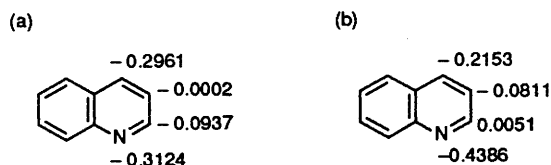
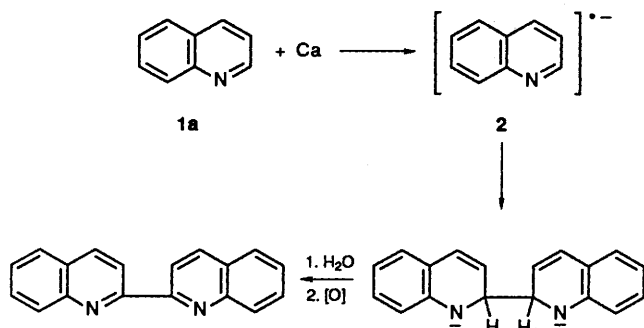


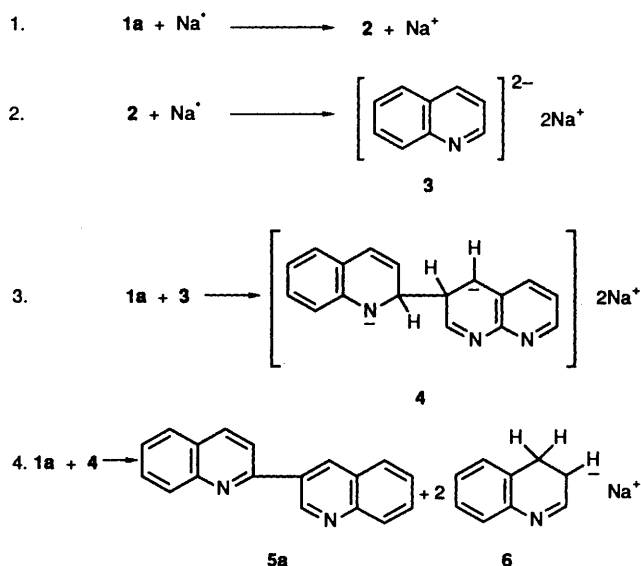
Fig. 1 (a) Spin density distribution in the radical anion **2** as calculated using the MNDO method; (b) charge distribution in the dianion **3** according to MNDO calculations



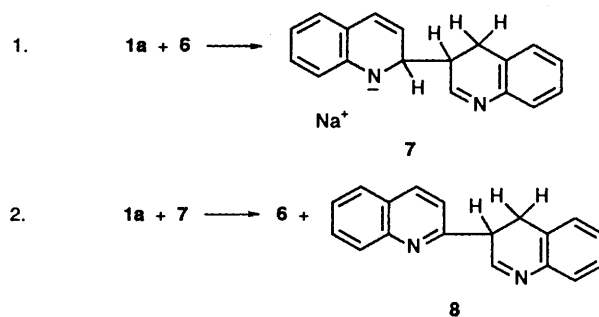
Scheme 1

For the reaction with sodium, we propose the mechanism outlined in Schemes 2 and 3.

Thus, as a result of its lower ionisation potential, sodium can reduce the primarily generated radical anion **2** to a dianion **3**, the maximal charge in the pyridine nucleus of which is localised on atoms 1, 4 and 3 [see Fig. 1(b)]. Although the charge in positions 1 and 4 is greater than that in position 3, position 1 is less nucleophilic as compared to 3 as a result of steric hindrance. Being a potent C-nucleophilic agent, the dianion **3** adds nucleophilically to quinoline (see Scheme 2). A chain mechanism results. Chain initiation steps (1–4, Scheme 2) yield 2,3'-biquinolyl and the anion **6**. The latter, being a strong C-nucleo-



Scheme 2 Chain initiation



Scheme 3 Chain elongation

phile, adds to quinoline (step 1 in chain elongation) to generate the anion **7**.

The latter, acting as a hydride-ion donor, reacts with quinoline (step 2 in chain elongation), to produce the dimer **8** and to regenerate the anion **6** which participates in step 1 of the chain elongation (Scheme 3). The dimer **8** is, presumably, readily oxidized by air to 2,3'-biquinolyl **5a**.

The validity of the above chain mechanism was established by dimerisation of the quinoline **1a** to the dimer **8** with catalytic quantities of sodium. Thus, 40 mmol of quinoline when heated with 2 mmol of sodium at 160 °C for 2 h under argon and then exposed to air gave 2,3'-biquinolyl (36%).†

† Here and below, the yields are calculated for the quinoline added to the reaction mixture. The yields for the quinoline that has reacted are given in the Experimental section.

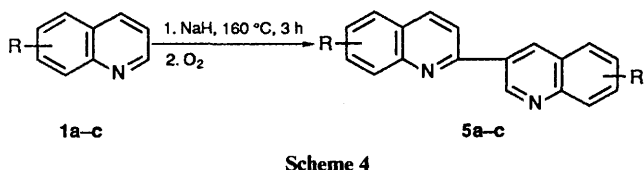
Table 1 Representative results in the dimerisation of quinolines

Substrate	R	Product	R	Yield (%)
1a	H	5a	H	36
1b	6-Me	5b	6-Me	32
1c	7-Me	5c	7-Me	32

Table 2 Effect of reaction conditions on dimerisation of quinoline to 2,3'-biquinolyl

No.	Reaction time (h)	NaH (mol)	Temp. (°C)	Yield (%)
1	1.5	0.002	160	36
2	3.0	0.002	160	36
3	1.5	0.002	239	10
4	3.0	0.002	239	10
5	1.5	0.004	160	36
6	1.5	0.004	239	10
7	1.5	0.002	160	10
	1.5		239	10
8	1.5	0.002	239	36
	1.5		160	36

Compounds other than the anions **4** and **7** can act as hydride donors in the reaction with quinoline, catalytic quantities of sodium hydride allowing generation of the anion **6*** and subsequent dimerisation. Sodium hydride can also be used for dimerisation of alkyl substituted quinolines, and the yields are sometimes even higher than those with metallic sodium.



For instance, dimerisation of 6- and 7-methylquinolines with sodium gives a 5% yield and with sodium hydride a 32% yield. The yields of 2,3'-biquinolyls (calculated for the quinoline added to the reaction mixture; see Table 1) are not high, 32–36%. In trying to establish the reason for this, we found that quinoline dimerisation to give compound **8** is an equilibrated exothermic reaction (see Table 2). The following results for 2,3'-biquinolyl support this. (1) Its yield is unchanged for reaction times > 1.5 h, equilibrium being established within this time (experiments 1–4). (2) Its yield is unchanged with additional sodium hydride, the catalyst exerting no effect on the equilibrium (experiments 1 and 5, 3 and 6). (3) The yield is decreased for reaction temperatures > 160 °C, the equilibrium in exothermic reactions being shifted towards the starting compounds as the temperature is raised (experiments 1 and 4). (4) If the reaction temperature is varied (160 °C for 1.5 h and then 239 °C for 1.5 h or 239 °C for 1.5 h and then 160 °C for 1.5 h), the yields of 2,3'-biquinolyl depend on the temperature of the last 1.5 h, equilibrium being established during this period (experiments 7 and 8).

Sodium ion complexation with the quinoline nitrogen is an important factor in the dimerisation process, no reaction occurring with 8-methylquinoline. The presence of a crown ether also inhibits dimerisation, as a result of competitive binding of sodium ions by the crown ether.†

* Generation of the anion **6** from quinoline and sodium hydride at 30–60 °C in HMPT has been described.⁴

† The inhibition of the amide anions addition because of its complexation with crown ether has already been described.⁵

Dimerisations were carried out both in the absence of solvent and in dimethylene glycol dimethyl ether, the product being easier to isolate in the latter case, but the yield dropping to 32%.

Experimental

NMR spectra were recorded on a WP-200 Bruker spectrometer and chemical shifts are reported in ppm (δ) relative to Me₄Si as an internal standard. *J* Values are given in Hz. Mass spectra were obtained on a Varian CH 7 spectrometer.

Quinolines were dried over molecular sieves (pore diameters 3 Å).

2,3'-Biquinolyl 5a.—*Method A.* A mixture of quinoline (10 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol) was heated at 160 °C in an atmosphere of argon for 2 h. The reaction mixture was allowed to cool to room temperature in the air. Ether (10 ml) was added to the solid reaction mixture and the latter was filtered off (3.58 g, 36%; 95% for the reacted quinoline), m.p. 175–176 °C (benzene) (lit.,¹ m.p. 175–176 °C). Then the ether was removed and the residue distilled at 114 °C/17 mmHg to recover unchanged quinoline (6.2 g).

Method B. A mixture of quinoline (10 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol) in dry diethylene glycol dimethyl ether (10 ml) was heated at 160 °C in an atmosphere of argon for 3 h. The reaction mixture was allowed to cool to room temperature in the air, when addition of water (10 ml) precipitated yellow crystals (3.2 g, 32%; or 95% for the reacted quinoline); $\delta_{\text{H}}(\text{CDCl}_3)$ 8.04 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.55, 3-H), 8.2 (8 H, m, ArH), 8.32 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.54, 4-H), 8.93 (1 H, d, $J_{2\text{H},4\text{H}}$ 2.28, 4'-H) and 9.76 (1 H, d, $J_{2\text{H},4\text{H}}$ 2.28, 4'-H). Then the filtrate was extracted with ether (3 × 50 ml). The combined extracts were dried (MgSO₄), the ether was removed, and the residue distilled at 114 °C/17 mmHg to recover unchanged quinoline (6.6 g).

6,6'-Dimethyl-2,3'-biquinolyl 5b.—*Method A.* This compound was prepared as described for 2,3'-biquinolyl (Method A) from 6-methylquinoline (11 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol); Yield 3.51 g (32%; 90% for the reacted 6-methylquinoline), m.p. 206–207 °C (from benzene) (lit.,⁶ m.p. 206–207 °C).

Method B. This compound was prepared as described for 2,3'-biquinolyl (Method B) from 6-methylquinoline (11 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol) in dry diethylene glycol dimethyl ether (10 ml); yield 3.3 g (30%; 90% for the reacted 6-methylquinoline); $\delta_{\text{H}}[(\text{CD}_3)_2\text{CO}]$ 2.57 (6 H, s, CH₃), 7.66 (1 H, c, $J_{7\text{H},8\text{H}}$ 8.54, $J_{5\text{H},7\text{H}}$ 2.14, 7'-H), 7.67 (1 H, c, $J_{7\text{H},8\text{H}}$ 8.54, $J_{5\text{H},7\text{H}}$ 2.14, 7-H), 7.77 (1 H, d, $J_{5\text{H},7\text{H}}$ 2.14, 5-H), 7.87 (1 H, d, $J_{5\text{H},7\text{H}}$ 2.14, 5'-H), 8.02 (1 H, d, $J_{7\text{H},8\text{H}}$ 8.54, 8'-H), 8.08 (1 H, d, $J_{7\text{H},8\text{H}}$ 8.54, 8-H), 8.26 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.54, 3-H), 8.40 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.54, 4-H), 8.99 (1 H, d, $J_{2\text{H},4\text{H}}$ 2.44, 4'-H) and 9.78 (1 H, d, $J_{2\text{H},4\text{H}}$ 2.44, 2'-H); *m/z* = (70 eV) 284 (M⁺, 100%).

7,7'-Dimethyl-2,3'-biquinolyl 5c.—*Method A.* This compound was synthesized as described for 2,3'-biquinolyl (Method A) from 7-methylquinoline (11 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol); yield 3.51 g (32%; 90% for the reacted 7-methylquinoline), m.p. 215–217 °C (from benzene).

Method B. The compound was synthesized as described for 2,3'-biquinolyl (method B) from 7-methylquinoline (11 g, 77.5 mmol) and sodium hydride (0.05 g, 2.1 mmol) in dry diethylene glycol dimethyl ether (10 ml); yield 3.3 g (30%; 90% for the reacted 7-methylquinoline); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.61 (6 H, s, CH₃), 7.40 (1 H, c, $J_{5\text{H},6\text{H}}$ 8.04, $J_{6\text{H},8\text{H}}$ 2.01, 6-H), 7.44 (1 H, c, $J_{5\text{H},6\text{H}}$ 8.41, $J_{6\text{H},8\text{H}}$ 2.01, 6'-H), 7.76 (1 H, d, $J_{5\text{H},6\text{H}}$ 8.41, 5'-H), 7.87 (1 H, d, $J_{5\text{H},6\text{H}}$ 8.04, 5-H), 7.95 (1 H, d, $J_{6\text{H},8\text{H}}$ 2.01, 8'-H), 7.96 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.71, 3-H), 8.01 (1 H, d, $J_{6\text{H},8\text{H}}$ 2.01, 8-H), 8.25 (1 H, d, $J_{3\text{H},4\text{H}}$ 8.71, 4-H), 8.86 (1 H, d, $J_{2\text{H},4\text{H}}$ 1.91, 4-H) and 9.69 (1 H, d,

$J_{2\text{H},4\text{H}}$ 1.91, 2'-H); $\delta_{\text{C}}(\text{CDCl}_3)$ 21.89 (q, CH_3), 21.99 (q, CH_3), 117.84 (d, ArC), 125.38 (s, ArC), 125.92 (s, ArC), 127.22 (d, ArC), 128.24 (d, ArC), 128.40 (d, ArC), 128.78 (d, ArC), 128.96 (d, ArC), 129.29 (d, ArC), 131.58 (s, ArC), 134.17 (d, ArC), 136.76 (d, ArC), 140.31 (s, ArC), 140.53 (s, ArC), 148.62 (s, ArC), 148.72 (s, ArC), 149.86 (d, ArC) and 154.81 (s, ArC); m/z (70 eV) 284 (M^+ , 100%) (Found: C, 84.9; H, 5.5; N, 9.6. Calc. for $\text{C}_{20}\text{H}_{16}\text{N}_2$: C, 84.51; H, 5.63; N, 9.86%).

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