Nucleophilic coupling of alkali 2-naphthoxides with 1-bromo-2-naphthols. Ion-pairing and halogen dance in the formation of 1,1′-binaphthalene-2,2′-diols

Martin Bělohradský, Petr Holý and Jiří Závada *
Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 166 10 Prague 6, Czech Republic

A very pronounced effect of solvent and cation has been found in the investigated reaction, indicating that ion-pairing is indispensable in the title product formation. A simple rationale has been provided assuming self-assembly of the complementary reactants driven by hydrogen bonding and ion-pairing interactions. Concomitantly, halogen exchange between the reaction partners has been demonstrated to be a concurrent pathway, resulting from the nucleophilic 2-naphthoxide attack at the bromine terminus of the C_α–Br bond in the participating 1-bromo-2-naphthol.

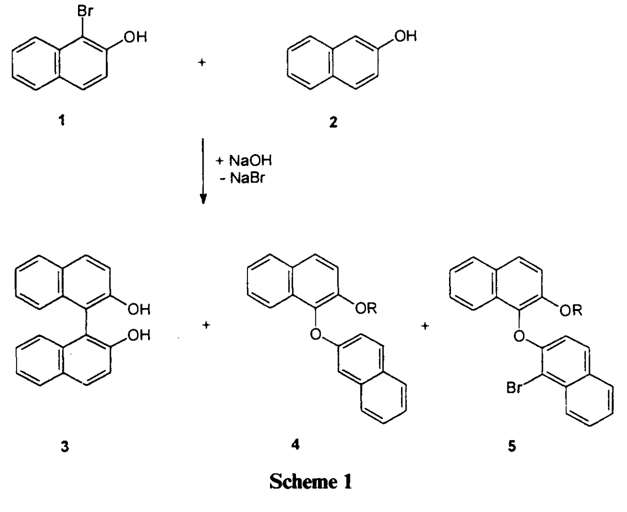
Introduction

Oxidative coupling of naphthols represents the most straightforward synthetic route to 1,1′-binaphthalene-2,2′-diols (binaphthols).[1-3] As a rule, such methodology leads to satisfactory yields of the symmetrically substituted products from homocoupling of a single naphthol. In contrast, oxidative cross-coupling of two different naphthols has been successful only in a few instances,[4] a low cross-coupling selectivity or exclusive formation of the corresponding homo-coupled products being the usual obstacle.

In order to overcome the apparent limitation, we have looked for alternative procedures which would be based on different coupling principles. Along these lines, we have investigated the title reaction. Enhanced reactivity of 1-bromo-2-naphthol towards nucleophiles has been already reported on several occasions.[5-8]

Results and discussion

Hinsberg in 1916 noted[5] that an equimolar mixture of 1-bromo-2-naphthol **1** and 2-naphthol **2** on heating with sodium hydroxide gave binaphthol **3** in an unspecified yield. Our re-examination of the old, until now unexploited and apparently forgotten reaction confirmed the original observation and showed (Scheme 1) that the binaphthol **3** is the main identifiable product, accompanied by traces of the ethers **4** and **5** and intractable tars. A closer investigation revealed that the prevailing binaphthol **3** formation is confined within remarkably narrow limits of reaction conditions.



Scheme 1

Table 1 Effect of base stoichiometry on binaphthol **3** formation from naphthols **1** and **2** in toluene

1:**2**:NaOH (Molar equiv.)	Conversion[a] (%)[b]
1:1:0	0.2
1:1:1	58.0
1:1:2	30.3
1:1:10	4.3

[a] After 1 h, 100 °C. [b] %Conversion = %**3** × 100/(%**2** + %**3**).

Table 2 Effect of solvent on the overall rate and product composition in the reaction of naphthols **1** and **2**

Solvent	Conversion[a] (%)[b]	Product composition (molar ratio **3**:**4**)
—	83.5	57.4
Toluene	68.5	37.2
Water	58.5	10.0
Dioxane	6.7	4.5
Ethylene glycol	6.7	3.0
DMSO	2.6	0.4
DMF	2.1	0.5

[a] After 4 h, 100 °C; **1**:**2**:NaOH ratio was 1:1:1. [b] %Conversion = (%**3** + %**4**) × 100/(%**2** + %**3** + %**4**).

Effects of base stoichiometry, solvent and cation

(*a*) Stoichiometry of the base employed to generate naphthoxide anion from the free 2-naphthol affects strongly the rate of the binaphthol formation. No reaction occurs in the absence of base. The coupling rate is at a maximum when the molar ratio of the starting naphthols and the participating base is 1:1:1. Further increase of the base proportion results in a gradual reduction of the reaction rate (Table 1).

(*b*) Also, solvent exhibits a strong effect on the reaction rate. On solvent addition to the 1:1:1 bromonaphthol **1**:naphthol **2**:NaOH mixture, a stepwise slowing down of the reaction is observed following the order: no solvent ~ toluene > water > dioxane ~ ethylene glycol ≫ DMSO ~ DMF. Simultaneously, the binaphthol **3**:ether **4** ratio decreases in the same solvent order (Table 2).

(*c*) At the same time, a remarkably large cation effect on the

Table 3 Effect of cation (M^+) on the rate of binaphthol **3** formation from naphthols **1** and **2** in toluene

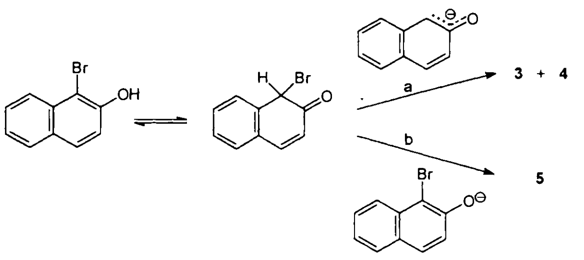
M^+	Conversion[a] (%)[b]
Na^+	54.0
K^+	34.5
Me_4N^+	1.8
K^+/18-crown-6	0.8

[a] After 1 h, 100 °C; molar ratio **1**:**2**:MOH was 1 : 1 : 1. [b] For calculation of %conversion see footnote in Table 1.

rate of binaphthol **3** formation occurs in the coupling reaction. On replacement of the sodium counterion by bulkier cations, a very steep retardation of the reaction has been found in toluene (Table 3) following the order $Na^+ > K^+ \gg Me_4N^+ \sim K^+$ (18-crown-6-ether).

Mechanistic scheme

A plausible explanation of the experimental findings can be given in terms of a nucleophilic substitution mechanism (Scheme 2) involving a tautomeric keto–enol equilibrium[6] of



Scheme 2

the bromonaphthol **1**. The ambident 2-naphthoxide nucleophile **2** attacks the α-carbon of the keto-form of **1** yielding the alternative products **3** and **4** . Such an ionic mechanism may well account for the observed rate dependence on the stoichiometry† of the base (Table 1) as well as for the solvent effect on the **3**:**4** ratio‡ (Table 2).

In order to rationalize the observed effects of solvent and cation on the rate of binaphthol **3** formation (Tables 2 and 3, respectively) one has to take into account the relative acidities of the participating naphthols **1** and **2**. It is known[10] that introduction of an *ortho*-bromine in a series of phenols increases the acidity by 1.58 p*K* units. Accordingly, the equilibrium (1) is shifted to the right side, reducing strongly the

$$o\text{-BrArOH} + \text{ArO}^- \rightleftharpoons o\text{-BrArO}^- + \text{ArOH} \qquad (1)$$

effective concentration of the reactive species *o*-BrArOH and ArO^- in the reaction (Scheme 2). Such an unfavourable situation is assumed to occur only under conditions supporting separation of ion pairs (*e.g.*, in protic or dipolar aprotic solvents and/or with the bulky tetraalkylammonium or crown-complexed cations). In the absence of such ion-separating factors, formation of complexes driven by hydrogen-bonding and ion-pairing interactions between the reaction partners can be anticipated, giving rise to the equilibrium (2).§

$$\begin{array}{ccc} o\text{-BrArO}^-\text{–M}^+ & \rightleftharpoons & o\text{-BrArO}\cdots\text{M}^+ \\ \vdots\quad\vdots & & |\quad\ | \\ \text{H–OAr} & & \text{H}\cdots\text{O}^-\text{Ar} \end{array} \qquad (2)$$

Both the alternative complexes in the equilibrium (2) resemble the transition state geometry for the binaphthol coupling differing each from the other merely by position of the hydrogen bond.

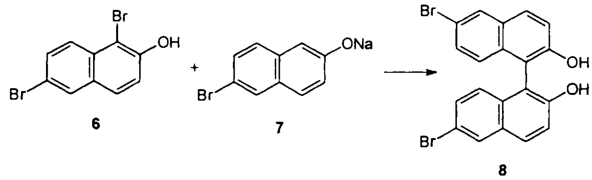
Occurrence of radical mechanisms in the coupling reactions

Earlier, it was reported[11–13] that polymerization of 4-bromo-2,6-dimethylphenoxide ion occurs under very mild conditions in the presence, but not in the absence, of air and a single electron transfer (SET) mechanism was proposed for the reaction. Since such a mechanism might be operative also in the present study, we have examined the effect of air on the coupling reaction. Whereas there was no effect of air on the rate of binaphthol formation, the amount of the tarry by-products was suppressed substantially when the reaction was performed under an argon blanket.

Also a photostimulated SET mechanism (occurring in the absence of air) has been previously demonstrated[14–16] in nucleophilic substitutions of several aryl halides. However, the rate of the present reaction was unaffected by light. Except for an elusive non-stimulated[17] SET, a radical mechanism can thus be dismissed from consideration in the present reaction.

Binaphthol coupling *vs.* halogen exchange reaction

In order to assess the synthetic scope of the revisited reaction, we have examined the effect of substituents on the binaphthol formation. A smooth formation of the symmetrically substituted 6,6′-dibromo-1,1′-binaphthol **8** from the corresponding 1,6-dibromo-2-naphthol **6** and 6-bromo-2-naphthol **7** has taken place (Scheme 3). By contrast, an unexpected complication has been encountered in the analogous reaction directed to the unsymmetrically substituted binaphthol **9** (Scheme 4). Examining the coupling of dibromonaphthol **6** with 2-naphthoxide ion **2**, a concurrent (minor) formation of two symmetrically substituted binaphthols **3** and **8** along with the expected product **9** has been found (Table 4). Identical by-products **3** and **8** have been obtained also from the corresponding reaction of the alternative naphthol pair **1** + **7** (Scheme 4).



Scheme 3

Formation of the by-products **3** and **8** can be rationalized in terms of a halogen exchange ('halogen dance'[18]) between the reaction partners **2** and **6** (or **1** and **7**), followed by their promiscuous coupling to the binaphthols **3**, **8** and **9**. The occurrence of such halogen exchange has been demonstrated by product analysis performed at the early stage of the coupling

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† The observed reduction of reaction rate at high base:(**1** + **2**) ratios is assumed to be caused by a gradual conversion of both the participating naphthols into their anions, which cannot then react. Analogous dependence of reaction rate on base stoichiometry has been recently observed in the self-condensation of 1-bromo-2-naphthol yielding the ether **5** (ref. 8). In the present reaction, formation of the ethers **4** and **5** (Scheme 2, pathway a and b, respectively) proceeds at a comparable rate.

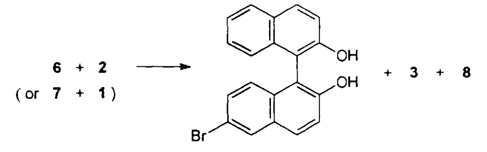
‡ Analogous solvent effect on product composition has been demonstrated earlier in C/O benzylation of the 2-naphthoxide ion (ref. 9) and interpreted in terms of a selective ion pairing and hydrogen bonding at the alternative reaction sites of the ambident nucleophile.

§ The actual situation may be more complex, with higher ionic aggregates than ion pairs being also involved in the equilibrium (2). This, however, cannot affect substantially the present discussion.

Table 4 Halogen dance accompanying binaphthol formation in toluene

	Product distribution[a]		
Educts	%**3**	%**9**	%**8**
6 + 7	0	0	100
1 + 7	14.3	80.1	5.6
2 + 6	9.0	73.3	17.7

[a] After 16 h, 100 °C; molar ratio of starting naphthols and NaOH was 1 : 1 : 1. Approximately the same product distribution was found in the absence of toluene.



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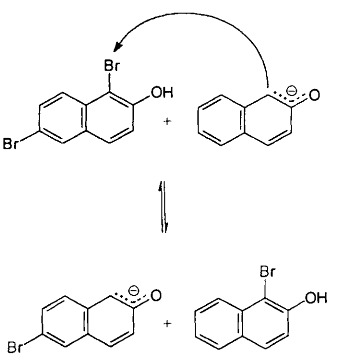
Scheme 4



Scheme 5

reaction (Scheme 5). Mechanistically, the halogen exchange can be interpreted as a displacement of one carbanion by another *via* nucleophilic attack at bromine. In this way, dichotomy of the nucleophilic attack on the α-carbon *vs.* bromine atom can influence product composition in the coupling reaction.

Experimental

Materials

Naphthols **1**, **2**, **6** and **7** were of the purest grade available (Aldrich). Ethylene glycol was distilled immediately before use. Other solvents were used as supplied.

Instruments

Mass spectra (EI) were recorded with a ZAB-EQ VG Analytical instrument. NMR spectra were measured on a Unity 200 Varian spectrometer (values of interaction constants *J* are in Hz). GLC analyses were performed with a Hewlett Packard 5890 gas chromatograph equipped with FID detector and 50% phenyl methyl silicone capillary column (10 m), using naphthalene as internal standard (injection temperature 250 °C, detector temperature 300 °C, time program 120 °C/5 °C min^{-1}/300 °C). Melting points are uncorrected and were determined on a micro heating plate apparatus.

Preparative experiments

Procedure A. 1-Bromo-2-naphthol **1** (2.23 g, 10 mmol) and 2-naphthol **2** (1.44 g, 10 mmol) were dissolved in methanol (50 cm^3) and aqueous NaOH (1.1 cm^3, 11 mmol; 10 mol dm^{-3}) was added. Methanol was evaporated *in vacuo* and the semi-solid reaction mixture was heated for 4 h at 100 °C under argon. After cooling, ethyl acetate (50 cm^3) and aqueous HCl (50 cm^3; 0.1 mol dm^{-3}) were added. The separated aqueous layer was extracted with ethyl acetate (3 x 30 cm^3), the combined organic layers were dried ($MgSO_4$) and the solvent was evaporated. The obtained crude product (2.86 g, 99%, GLC purity 87%) was crystallized from toluene (80 cm^3) to give binaphthol **3** as white needles (2.19 g, 77%, GLC purity 99%), mp 216–218 °C (lit.,[19] mp 214–216 °C). Column chromatography of the mother liquors (silica gel, light petroleum–diethyl ether–acetone, 90 : 5 : 5, as the eluent) afforded an inseparable mixture of ethers **4** and **5**. Acetylation (*vide infra*) of this mixture followed by chromatography (silica gel, light petroleum–ether–acetone, 96 : 2 : 2, as the eluent) gave the individual acetates **10** and **11**. 2-Acetoxy-1-(2-naphthyloxy)naphthalene **10**: mp 110–112 °C (lit.,[5] 115 °C); δ_H(200 MHz; $CDCl_3$) 2.03 (3 H, s, CH_3CO), 7.04 (1 H, d, *J* 3.4, Ar-H), 7.30–7.64 (7 H, m, Ar-H) and 7.76–8.10 (5 H, m, Ar-H); *m/z* 328 (M^+, 32%), 286 (100) and 128 (36) [Found (HRMS): 328.1102. $C_{22}H_{16}O_3$ requires 328.1099]. 2-Acetoxy-1-(1-bromo-2-naphthyloxy)naphthalene **11**: δ_H(200 MHz; $CDCl_3$) 2.03 (3 H, s, CH_3CO), 6.77 (1 H, d, *J* 8.8, Ar-H), 7.32–8.12 (10 H, m, Ar-H) and 8.37 (1 H, dd, *J* 8.8 and 0.5, Ar-H); *m/z* 406 (M^+ + 2, 38%), 404 (M^+, 36), 366 (87), 364 (87), 286 (86), 285 (100), 284 (40), 241 (32) and 128 (32) [Found (HRMS): 406.0168. $C_{22}H_{15}BrO_3$ requires 406.0204]. Acetate **11** was identical (GLC) with the acetylated authentic sample of **5**.[8]

Procedure B. A deaerated mixture of **1** (2.23 g, 10 mmol), **2** (1.44 g, 10 mmol), toluene (50 cm^3) and aqueous NaOH (1.1 cm^3, 11 mmol; 10 mol dm^{-3}) was stirred at 100 °C for 4 h under argon. After cooling, aqueous HCl (50 cm^3; 0.1 mol dm^{-3}) was added and the toluene layer separated. The aqueous phase was extracted with ethyl acetate (3 × 30 cm^3). The same work-up as in procedure *A* afforded crude product (2.86 g, 99%, GLC purity 86%) which on crystallization yielded binaphthol **3** (2.04 g, 71%, GLC purity 99%).

Procedure B was used for preparation of 6,6′-dibromo-1,1′-binaphthalene-2,2′-diol **8** from **6** and **7**. Crystallization of the crude product (4.40 g, 99%, GLC purity 81%) from benzene gave **8** (2.2 g, 50%, 98% GLC purity) mp 205–206 °C, (lit.,[19] mp 208–209 °C, lit.,[20] mp 199–199.5 °C). ^1H NMR and mass spectra are in agreement with ref. 19).

Procedure *A* was used for preparation of 6-bromo-1,1′-binaphthalene-2,2′-diol **9** from **6** and **2**. An inseparable mixture of **9** (77% by GLC), **8** (13% by GLC) and **3** (10% by GLC) was obtained after column chromatography and crystallization of the crude reaction mixture (from ethanol). Compound **9** was characterized by recording the ^1H NMR and MS spectra of the binaphthol mixture and subtracting the signals of the known minor components **3** and **8**.

9: *m/z* 366 (M^+ + 2, 100%), 364 (M^+, 100), 239 (25) and 120 (30); δ_H(200 MHz, $CDCl_3$) 4.98 (1 H, s, OH), 5.08 (1 H, s, OH), 6.96–7.22 (7 H, m, Ar-H) and 7.92–8.05 (4 H, m, Ar-H).

Analytical experiments (Tables 1–4)

To a mixture of the appropriate 2-naphthols (0.2 mmol of each) in a given solvent (1 cm^3) was added a calculated amount of the requisite aqueous base (10 mol dm^{-3}) by micropipette and the mixture was stirred and heated at 100 °C. After the period indicated, the reaction mixture was cooled and directly acetylated (1 cm^3 of pyridine containing a known amount of naphthalene as the internal standard, 0.5 cm^3 of acetanhydride, stirring for 2 h at room temp.). In the experiments described in Table 2, HCl (1 cm^3; 0.1 mol dm^{-3}) was added to the reaction mixture, the products were extracted with chloroform (3 × 1 cm^3) and the solvent was evaporated prior to the acetylation. The acetylated reaction mixture was mixed with ethyl acetate (8 cm^3) and aqueous HCl (8 cm^3; 5 mol dm^{-3}) and stirred vigorously for 5 min. The organic layer was separated, dried ($MgSO_4$) and a sample analysed by GLC. Molar percentages of the individual products were determined and employed in calculation of the data in Tables 1–4.

Acknowledgements

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