# Self-condensation of 1-Bromo-2-naphthol: Mechanism of Formation of a 1,4-Dinaphthodioxin

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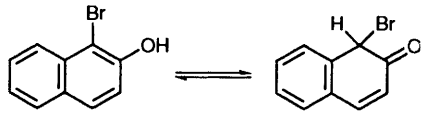
The reaction of 1-bromo-2-naphthol with its conjugated base (sodium 1-bromo-2-naphthoxide) affords 1-bromo-2'-hydroxy-2,1'-dinaphthyl ether and follows a second-order kinetic law. The bromo ether can be cyclised to a 1,4-dioxin derivative through a radical *ipso*-substitution reaction, predominantly. Some mechanistic implications are discussed.

Several years ago we investigated the reaction of halogenonaphthols with nucleophilic reagents, *viz.* thiophenoxide ions,[1] that yielded naphthols through a dehalogenation reaction and aromatic[2] or aliphatic[3] amines, which afforded halogen-substitution products. In the starting molecules, the presence of the hydroxy group enhances the reactivity of the bromine atom bonded to the naphthalene:[4] this is an unusual activation of a strong electron-donating group of an aryl halide in reactions with nucleophiles. This effect was not observed in 1-bromo-2-methoxynaphthalene and sodium (or ammonium) naphthoxide.[1-3,5] All the results support an ionic mechanism,[1-3,5] although a homolytic pathway cannot be ruled out.[6]

This reactivity has been explained by assuming a tautomeric equilibrium that leads to a halogen atom in a benzylic position and α to a carbonyl group: Scheme 1 shows the tautomers of 1-bromo-2-naphthol.

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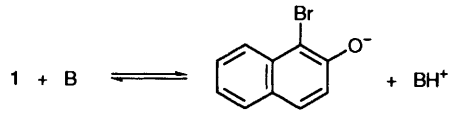
**Scheme 1**

The reaction of aliphatic amines, *e.g.* piperidine, has shown that the reactivity of the halogenonaphthols is affected strongly by the presence of a salification equilibrium like that illustrated in Scheme 2. The presence of the naphthoxide ion depresses the

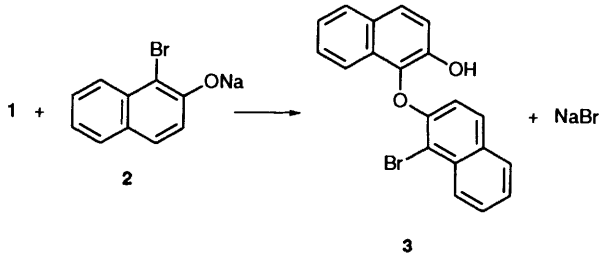



**Scheme 2**

rate of the reaction by lowering the amount of the keto-form, which is the reactive species of the halogenonaphthol.

This paper presents some new details on the condensation of 1-bromo-2-naphthol **1** with its anion (sodium 1-bromo-2-naphthoxide **2**) in ethylene glycol at 100 °C; this reaction gives 1-bromo-2'-hydroxy-2,1'-dinaphthyl ether **3** (Scheme 3).

It is well known that the synthesis and analytical determinations[7,8] of 1,4-dioxins (polychloro-dibenzodioxins, particularly) present problems in monitoring pollutants;[9] therefore, we also report some data on the ring-closure reaction of the bromo ether **3**, resulting in an unusual dinaphthodioxin.




**Scheme 3**

## Results and Discussion

When an excess of sodium glycoxide in ethylene glycol was added to a solution of **1** in ethylene glycol and the mixture was heated at 100 °C (or refluxed for several days) no reaction occurred, and the naphthol was quantitatively recovered unchanged by acidification of the reaction mixtures. The low $pK_a$ of naphthols (relative to alcohols)[10] indicates that, under these experimental conditions, all the halogenonaphthol was salified.

On the contrary, 0.01 mmol of bromide ion was obtained in *ca.* two days by adding a solution of sodium ethylene glycoxide (0.01 mmol) in ethylene glycol (10 $cm^3$) to a solution of **1** (0.02 mmol) in ethylene glycol (10 $cm^3$) at 100 °C. The reaction mixture was poured into ice and compound **3** precipitated as a pale-brown solid. This product is the same as that recovered in low yields from some reaction mixtures of 1-bromo-2-naphthol and piperidine.[3] When $[\mathbf{1}]_0 > [\mathbf{2}]_0$ ($[\ ]_0$ indicates the initial concentration), the condensation of 1-bromo-2-naphthol stops in the usual reaction times at the amount of bromide ion (and compound **3**) equivalent to $[\mathbf{2}]_0$—the concentration of 'free' 1-bromo-2-naphthol $[\mathbf{1}]_0$ is the difference between [stoichiometric $\mathbf{1}]_0$ and [sodium ethylene glycoxide]$_0$. Under the same experimental conditions, 2-bromophenol gave a very feeble appearance of the bromide ion at a very low rate.

We were not able to detect the presence of isomers of **3** in the reaction mixtures. One can expect that these compounds also could arise from a 1,4-addition to the C–C double bond of the keto-form of **1**, as suggested by a Referee. However, this reaction is hardly conceivable, because the 1,4-attack involves a loss of conjugation between the condensed phenyl ring and the α,β-unsaturated carbonyl.

When **2** largely predominated over **1**, it reacted with the bromo ether **3** to afford small amounts of a compound ($M^+$, 506, yield lower than 4%) to which structure **4** was tentatively assigned.

Table 1 reports some kinetic data that were obtained up to 30–50% of conversion to avoid the presence of compound **4**; $k_{obs}$ values ($s^{-1}$ $mol^{-1}$ $dm^3$) may refer to the formation of **3**, and were

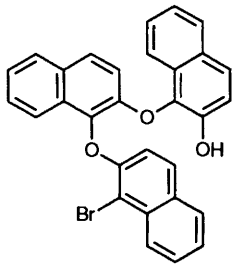



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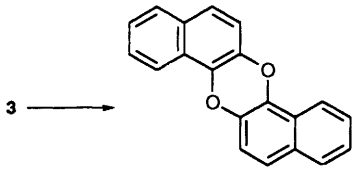
**Table 1** Rates of the reactions of **1** with **2** in ethylene glycol at 100 °C

| $[1]_0/10^{-2}$ mol dm$^{-3}$ | $[2]_0/10^{-2}$ mol dm$^{-3}$ | $k_{obs}/10^{-4}$ s$^{-1}$ mol$^{-1}$ dm$^3$ |
|---|---|---|
| 0.732 | 1.34 | 1.94 |
| 2.90 | 0.087 | 2.00 |
| 3.29 | 0.83 | 2.10 |
| 3.29 | 3.70 | 1.95 |
| 3.29 | 8.70 | 1.95 |
| 3.38 | 1.35 | 1.89 |
| 3.40 | 2.45 | 1.87 |
| 3.40 | 1.34 | 1.85 |
| 5.98 | 1.34 | 1.96 |
| 6.05 | 3.68 | 1.85 |
| 8.47 | 3.70 | 1.95 |

calculated under both experimental conditions, *viz.* $[1]_0 > [2]_0$ and $[1]_0 < [2]_0$. Although some pre-equilibria are present (Schemes 1 and 2), the kinetic behaviour implies that the formation of **3** follows a second-order law, as is usual in the bimolecular processes of nucleophilic substitution reactions. Under the same experimental conditions reported in Table 1, a $k_{obs}$ lower than $1 \times 10^{-7}$ ($s^{-1}$ $mol^{-1}$ $dm^3$) was estimated for 2-bromophenol by monitoring the appearance of the bromide ion.

The reactivity of sodium naphthoxide **2** ($k_{obs}$ of Table 1) is lower than that reported previously for piperidine[3] ($k = 1.2 \times 10^{-3}$ $s^{-1}$ $mol^{-1}$ $dm^3$ in ethylene glycol at 100 °C). In the present case, the nucleophilic power of the alkoxides, which is usually higher than that of neutral nitrogen compounds, is probably depressed by steric hindrance.

When mixtures of **1** and **2** were allowed to react at 100 °C for a long time (4–5 days), the GC–MS analyses showed the presence of small amounts (less than 5%) of dioxin **5** ($M^+$, 284) (Scheme 4); this compound was also observed by TLC analysis of the reaction mixtures.

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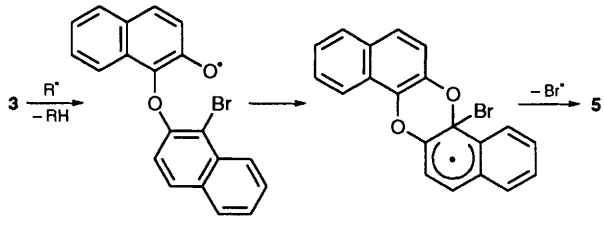
**Scheme 4**

The presence of **5** in the GC–MS analyses cannot be due to a thermal cyclisation of the starting bromonaphthol in the injector—both in the presence or in the absence of bases—because TLC and GC inspections of the reaction mixtures at zero reaction time did not reveal the presence of the dioxin **5**, as well as the ether **3**. Although thermal formation of **5** from **3** could not be completely ruled out, this possibility should be rejected because, after 48 h, TLC analyses of the reaction mixtures showed the presence of **3** but the absence of **5**; this finding was then confirmed by GC–MS. Therefore, one can conclude that **5** was not formed during GC–MS analyses.

The dioxin **5** probably arises from a further intramolecular attack to the α-position of the naphthyl ether **3**, which obviously cannot exist in the keto-form. The reaction is very slow, as proved by the low yield of **5** and the very slow increase of bromide ion concentration observed when the reactant present in smaller amounts (**1** or **2**) was completely consumed. This reactivity agrees with that of 1-bromonaphthalene, which has been indicated to react *via* a direct aromatic nucleophilic substitution;[4] on the contrary, halogenobenzenes prefer other reaction pathways.[6]

In some syntheses of polychlorinated 1,4-dibenzodioxins, the heterocyclic ring closure has been explained through a Smiles rearrangement mechanism.[11] However, our system is too poorly activated to support the negative charge of the possible spiro-intermediate. Under the drastic conditions of incinerators, the mechanism of formation of polichlorinated 1,4-dibenzodioxins cannot be considered a simple problem,[9] and several reaction pathways are conceivable, *e.g.* aromatic nucleophilic substitutions, radical chain mechanisms and *via* carbenes or arynes.

In our case, the main reaction pathway of the ring-closure process probably entails a homolytic mechanism. We suggest it might involve an *ipso*-attack of the phenoxy radical **6** to the aromatic carbon bearing the bromine, followed by β-fragmentation of the cyclohexadienyl radical **7** and displacement of the halogen atom (Scheme 5).

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**Scheme 5**

The feasibility of this mechanism is supported by the reaction of **3** with di-*tert*-butyl peroxide (TBP), which gave **5** in good yield. In this case, the *tert*-butoxy radicals, arising from thermolysis of the peroxide, readily abstract the phenolic hydrogen; the resulting intermediate **6** gives a six-membered ring closure to **5** through the cyclic radical **7**.

Homolytic *ipso*-substitutions on halogenoaromatics are well documented;[12] however, we know of a unique example of attack of an oxygen-centred radical to an aromatic halide. It is concerned with the gas-phase reaction of hydroxyl radicals with halogenobenzenes, which affords phenol in the minor product-forming pathway.[13] Therefore, it is worth pointing out that the above reaction appears to be the first example of a radical cyclisation involving an aromatic *ipso*-substitution of a bromine atom with a stable aryloxy radical. The intramolecularity of this cyclisation is probably the driving force of the *ipso*-substitution.

Although our model is a simplification, this study indicates clearly that the initial step of the self-condensation of bromonaphthol **1** is a nucleophilic attack to the keto–enol tautomeric system, which is quite inconceivable in the benzene series. On the contrary, the cyclisation step of the bromo ether follows a radical pathway. Indeed, the intramolecular aromatic nucleophilic substitution is unlikely for naphthalenes, as well as for the unactivated-benzenes series.

## Experimental

*Materials.*—1-Bromo-2-naphthol was obtained by described procedures.[1,2] Ethylene glycol was distilled under

vacuum; the middle fraction was dried over sodium sulfate and distilled immediately before use, b.p. 115–116 °C (25 mmHg).[14] *tert*-Butylbenzene was commercially available (Aldrich) and used without further purification. Di-*tert*-butyl peroxide (TBP, Aldrich) was distilled before use, b.p. 109–110 °C. Sodium ethylene glycoxide was prepared by adding the appropriate amount of sodium to ethylene glycol under a nitrogen atmosphere. The concentration of sodium glycoxide was determined by usual acid–base titrations.

*Kinetic Measurements.*—The appearance of the halide ion was titrimetically monitored with the Volhard method. The amount of the component that was present in smaller amounts (**1** or **2**) corresponded to the hypothetical highest concentration of bromo ether **3**—or bromide ion—in the condensation reaction (Scheme 3). The titration of the halide ion, together with the TLC analysis, indicated the end of the reaction. Runs carried out in sealed tubes under nitrogen and in a refluxing apparatus showed $k_{obs}$ within the experimental reproducibility (±4%).

*Instruments.*—Mass spectra and high resolution mass spectra (HRMS) were recorded by electron impact with a VG 7070E spectrometer. GC–MS analyses were performed with an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and an HP-5970 mass detector. Melting points are uncorrected and were determined with a Buchi apparatus.

*Self-condensation of* 1-*Bromo*-2-*naphthol* **1**.—Sodium ethylene glycoxide (0.5 equiv.) in ethylene glycol (10 $cm^3$) was added to a solution of **1** (4.0 g, in 40 $cm^3$ of ethylene glycol). The reaction mixture was placed in a thermostatic bath at 100 °C. The conversion was monitored, on acidified samples of the mixture, *via* GC–MS, TLC on silica gel—hexane–diethyl ether (10:3) as the eluent—and titration of bromide ion with the Volhard method. After 48 h, the reaction mixture was poured into a diluted, cold hydrogen chloride solution. The resulting solid was filtered and purified with a silica gel column—hexane–diethyl ether (10:3) as the eluent—to eliminate small amounts of tars and unreacted **1**. Compound **3** was obtained in 60% yield (3.9 g), m.p. 134–135 °C (decomp.) (Found: C, 66.0; H, 3.5; Br, 21.6. $C_{20}H_{13}BrO_2$ requires C, 65.8; H, 3.6; Br, 21.9); *m/z* 366 ($M^+ + 2$, 65%), 364 ($M^+$, 63), 285 (100), 268 (30), 267 (24), 257 (23), 255 (14), 241 (40) and 239 (27); the molecular ion was unsuitable to obtain the exact mass. When the amount of **2** exceeded that of **1**, the GC–MS analyses showed the presence of small amounts (less than 4%) of a compound with *m/z* 508 ($M^+ + 2$) and 506 ($M^+$), to which structure **4** is tentatively assigned.

*Reaction of* **3** *with Di*-tert-*butyl Peroxide.*—A solution of **3** (50 mg, 0.14 mmol) and TBP (30 mg, 0.21 mmol) in *tert*-butylbenzene (5 $cm^3$) was kept at 120 °C for 24 h. The solvent was then removed *in vacuo* and the residue analysed by GC–MS and TLC on silica gel—light petroleum (b.p. 40–60 °C)–diethyl ether (9:1) as the eluent. Compound **5** (28 mg, 70%) was obtained by chromatography with a silica gel column—light petroleum (b.p. 40–60 °C)–diethyl ether gradient (from 9:1 to 1:1) as the eluent—m.p. 183–184 °C (Found: C, 84.3; H, 4.1. $C_{20}H_{12}O_2$ requires C, 84.5; H, 4.25); *m/z* 284 ($M^+$, 100%), 255 (31), 227 (11), 226 (19), 142 (8), 113 (11) [Found (HRMS): 284.0831. $C_{20}H_{12}O_2$ requires 284.0837]. Under the same experimental conditions and after longer reaction times, **1** yielded a lot of undefined and tarry products.

## Acknowledgements

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