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C-C Coupling Reaction of 1,5-Dibromo-2,6-dihydroxynaphthalene with Alkali 2-Naphthoxide. Opposite Effects of Counterion Coordination and Hydrogen Bonding on Stereoselectivity in the Formation of cis- and trans-1,1':5',1''-Ternaphthyls

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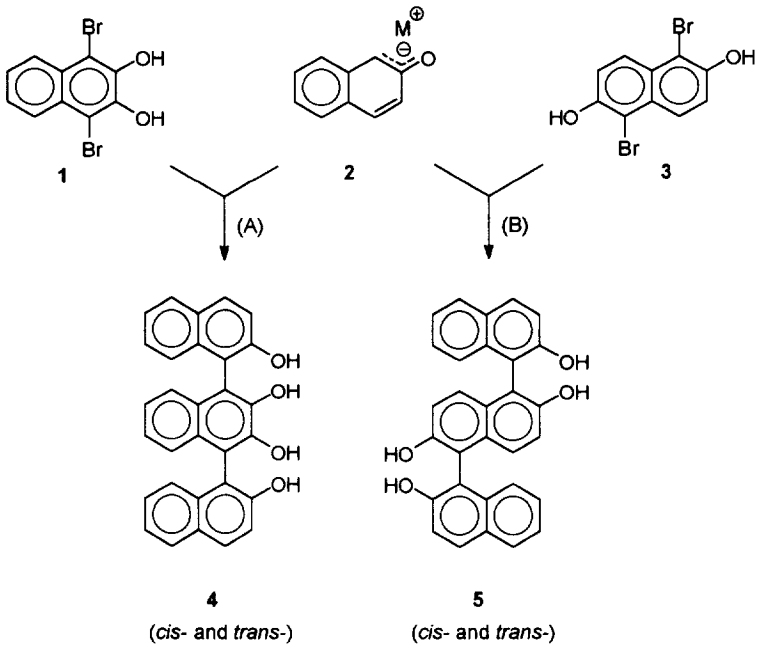
Abstract: The title reaction yields *cis*- and *trans*-2,2',6',2''-tetrahydroxy-1,1':5',1''-ternaphthyls as the main products. In contrast to non-selective distribution of the stereoisomers in the thermodynamic equilibrium, very high selectivity can be attained under conditions of kinetic control. The observed values of *cis*-/*trans*- ratios range between the extremes 94:6 and 6:94, depending on the solvent and counterion employed. The coordination of the metal counterion plays a key role in the reaction performed in toluene, supporting formation of the *cis*-stereoisomer. When the coordination ability of the counterion is supressed by 18-crown-6, intramolecular hydrogen bonding of the departing bromide group prevails in the stereocontrol, providing support for the *trans*-stereoisomer formation.

INTRODUCTION

Ternaphthyls represent simple models of stereoregulated oligomers and/or polymers with a conformationally locked arrangement of the neighbouring aryls. Recently,[1] we have investigated the reaction of 1,4-dibromo-2,3-dihydroxynaphthalene **1** with 2-naphthoxide ion **2** and demonstrated pronounced stereoselectivity in the formation of *cis*- and *trans*-2,2',3',2''-tetrahydroxy-1,1':4',1''-ternaphthyls **4** (Scheme 1; A). In this paper we report an extension of the novel C-C coupling process to the formation of the positionally isomeric *cis*- and *trans*-2,2',6',2''-tetrahydroxy-1,1':5',1''-ternaphthyls **5** (Scheme 1; B). Further information concerning the mechanism and stereoselectivity of the investigated reaction has been obtained in the course of the study.



Scheme 1

RESULTS AND DISCUSSION

Effect of Solvents

The reaction of 1,5-dibromo-2,6-dihydroxynaphthalene **3** with potassium 2-naphthoxide **2** ($M^+ = K^+$) proceeds in a variety of solvents. However, the reaction rate, overall yields and also stereoselectivity (ratios *cis*-**5**/*trans*-**5**) depend strongly on the nature of the solvent employed. On going from the aprotic non-polar toluene to the protic polar ethylene glycol, the rate of the coupling decreases by a factor >>100. The overall yields and the values of *cis*-**5**/*trans*-**5** ratios follow similar declining trends (Table 1).

Table 1. Effect of solvent on the *cis*-**5** : *trans*-**5** ratios and the overall yield in the reaction of **2** ($M^+ = K^+$) and **3**

Solvent	*cis*-**5** : *trans*-**5**	Overall yield (in %)
toluene[a]	90 : 10	74
-[b]	72 : 28	44
H_2O[c]	66 : 34	40
ethylene glycol[d]	47 : 53	35

[a] 50°C, 50 hrs. [b] 100°C, 16 hrs. [c] 90°C, 50 hrs. [d] 90°C, 40 hrs.

Stereochemical Assignment

NMR spectroscopy failed to determine configuration of the *cis*- and *trans*-**5** stereoisomers. None of the two stereoisomers provided crystals of X-ray quality. Finally, the single crystal analysis of the tetraacetoxy derivative of *trans*-**5** allowed an unambiguous stereochemical assignment (Fig. 1).

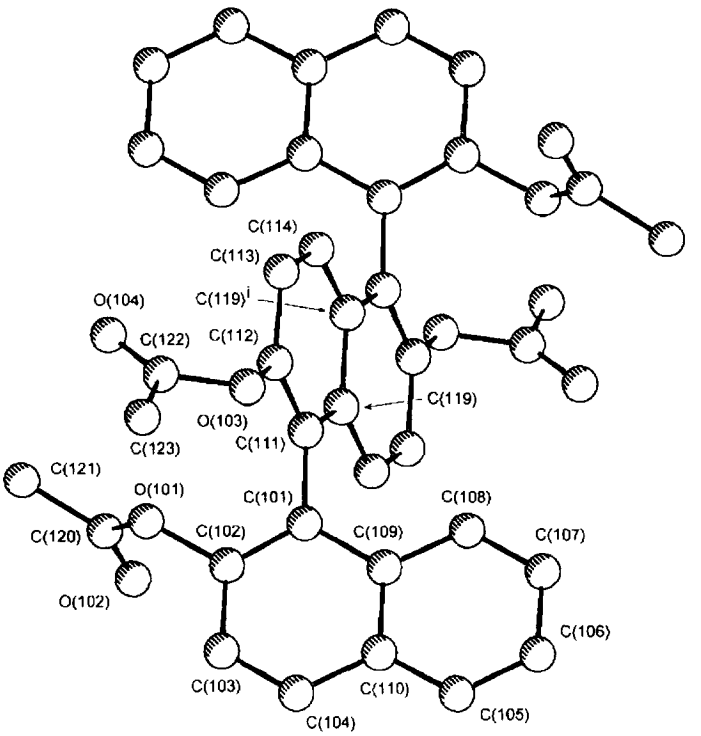
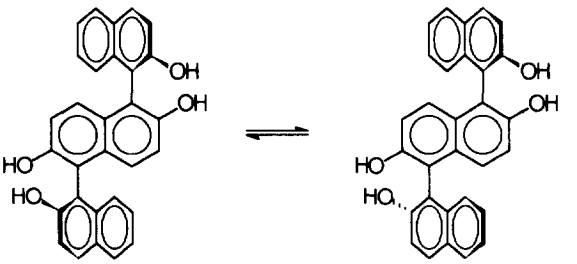


Fig. 1. Perspective view (PLUTO) of tetraacetate of *trans*-**5** with atom labelling. Hydrogen atoms are omitted for clarity.

The chromatographic behaviour of the *cis*- and *trans*-**5** stereoisomers on a CHIRALPAK OP(+) HPLC column has been found to be in accord with the X-ray analysis. The *trans*-**5** stereoisomer, which is centrosymmetric, appeared as a single peak, whereas the *cis*-**5** stereoisomer, which is axially chiral (C_2 symmetry), was cleanly resolved into the enantiomers. The absolute configuration of the individual enantiomers has not yet been determined.

Thermal Interconversion of cis- *and* trans-*5 Stereoisomers*

Refluxing *cis*-**5** and *trans*-**5** individually in pyridine led to an equilibrium mixture[2] (Scheme 2), in which the stereoisomers were distributed in the ratio 42:58, indicating a slight preference of the centrosymmetric isomer. In nonbasic solvents the interconversion was much slower.

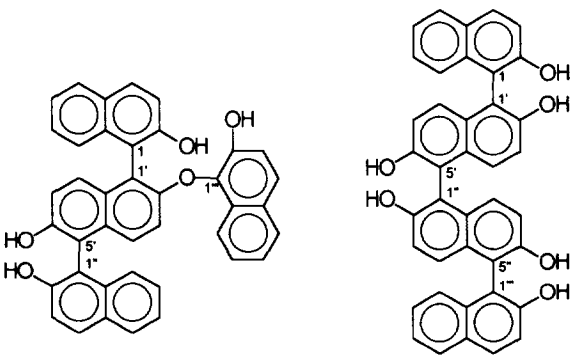


cis-**5** *trans*-**5**

Scheme 2

Higher Oligomers in the Reaction of **2** *and* **3**

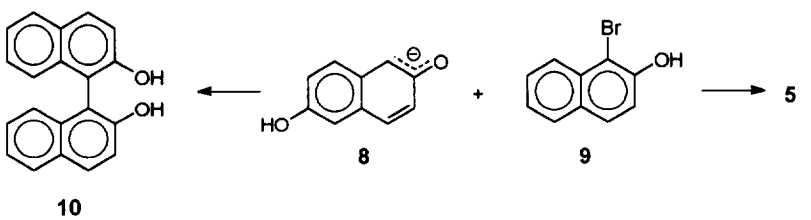
HPLC analysis of the acetylated crude reaction mixture on a silica gel column revealed the presence of several side products with longer elution times. The two most prominent peaks were separated and their structure was determined from ^{13}C NMR and EI MS spectra as **6** and **7**. Both the isolated by-products were found to be stereochemically uniform; upon refluxing in pyridine they interconverted into the expected number of stereoisomers (*cis*- and *trans*-**6**; *cis-cis*-, *cis-trans*- and *trans-trans*-**7**). On the basis of subsidiary evidence, the starting isomers have been assigned tentatively *cis*- configuration (*cis*-**6**, *cis-cis*-**7**).



6 **7**

Predominant Formation of 2,2'-Dihydroxy-1,1-binaphthyl in the "Inverse" Reaction of 8 and 9

Complementary to the main reaction between **2** and **3**, we have examined also the "inverse" reaction between **8** and **9** (Scheme 3). The expected ternaphthyls *cis*- and *trans*-**5** were formed only in minor amounts; surprisingly, 2,2'-dihydroxy-1,1'-binaphthyl **10** arose, under more forcing conditions, as the main product in the reaction.



10 **8** **9**

Scheme 3

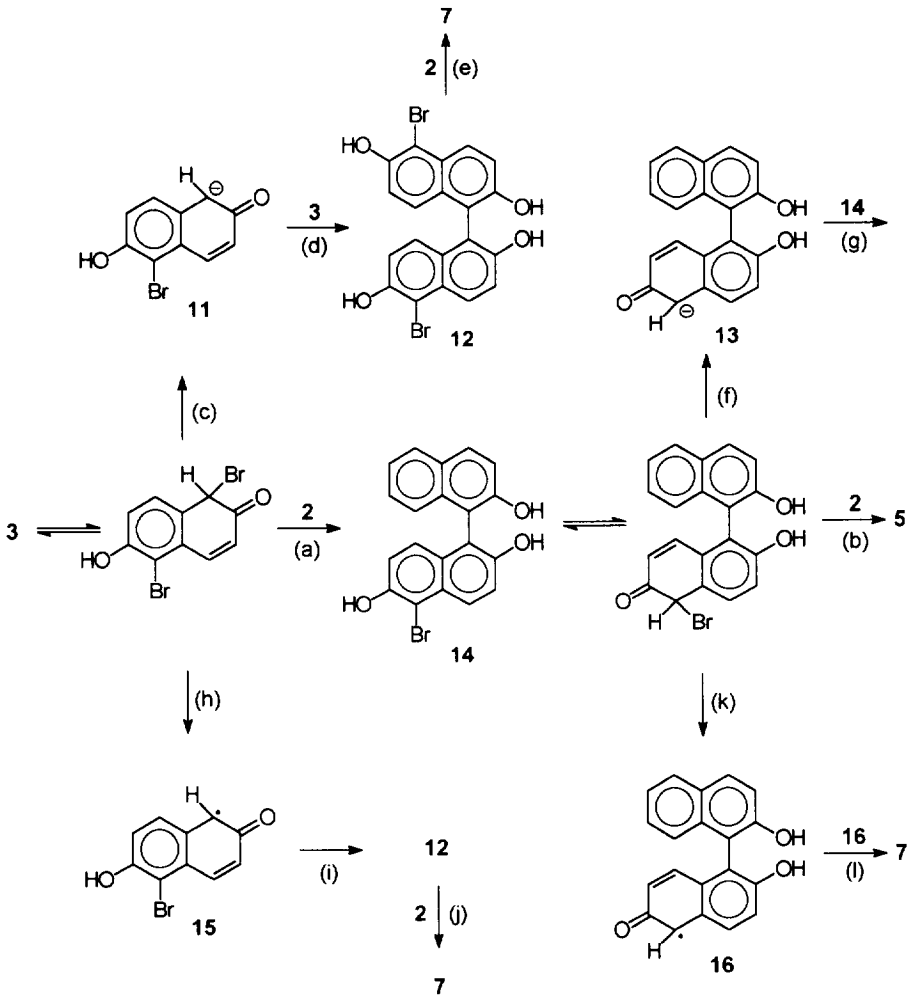
Gross Mechanism of the Coupling Reaction

Investigating earlier the C-C coupling of 1-bromo-2-naphthol with 2-naphthoxide ion we have already demonstrated[3] that the reaction proceeds via an S_N mechanism involving the reactive keto form of the 1-bromo-2-naphthol. A quite analogous mechanism is expected to operate also in the present reaction, accounting for the formation of the *cis*- and *trans*-**5** ternaphthyls (Scheme 4, pathways a and b).

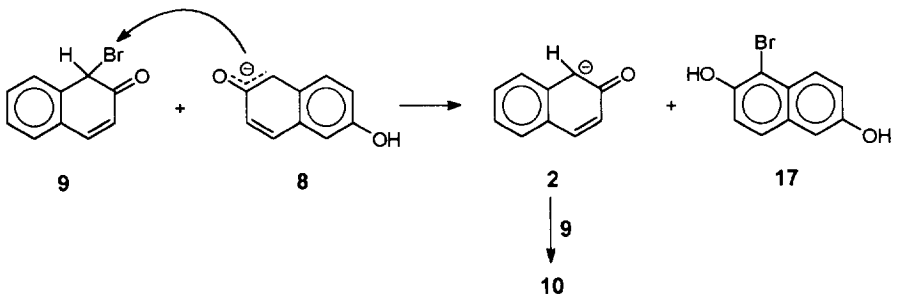
A concurrent nucleophilic attack by the 2-naphthoxide ion **2** at the bromine terminus of the C-Br bond in **3** is proposed to promote the observed side formation of the quaternaphthyl **7** in the reaction. The attack at the bromine atom may involve[1] either a nucleophilic displacement of one carbanion by another ($Ar_1X + Ar_2^- \rightarrow Ar_1^- + Ar_2X$; Scheme 4, pathways c,f) accompanied by halogen exchange between the two, or a single electron transfer (SET) followed by loss of the halide anion from the intermediary radical ($Ar_1X + Ar_2^- \rightarrow Ar_1X^{\cdot-} + Ar_2^{\cdot} \rightarrow Ar_1^{\cdot} + X^-$, Scheme 4, pathways h,k). Further coupling of the debrominated species **11**,**13** and/or **15**,**16** may give rise to the quaternaphthyl **7** (Scheme 4, pathways d,e,g,i,j,l).

A similar nucleophilic attack at the bromine atom operates assumedly also in the "inverse" reaction of **8** and **9** leading to the binaphthol **10**. In this particular case, an unambiguous distinction can be made between the halogen exchange and SET mechanism, since the intermediary product of the halogen exchange **2** (Scheme 5) has been identified at the early stage of the reaction. A subsequent (slower) coupling of **2** with **9** yields **10**, in accord with the earlier investigation.[3]

In principle, also occurence of the ether **6** in the reaction between **2** and **3** might be accounted by a nucleophilic attack at the bromine atom in **3**. We have found, however, that the ether **6** arises also upon heating ternaphthyl **5** with 2-naphthoxide ion **2** under comparable conditions, presumably via an oxidative (free radical) coupling triggered by O_2 persisting in the reaction medium.[4] In toluene, *cis*-**5** yielded exclusively *cis*-**6**, whereas *trans*-**5** afforded a mixture of *cis*-**6** and *trans*-**6**.



Scheme 4



Scheme 5

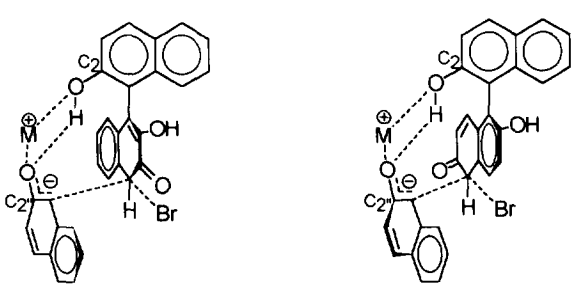
Counterion Effect

As it was shown in Table 1, the stereoselectivity of ternaphthyl **5** formation from **2** and **3** ($M^+ = K^+$) depends markedly on polarity of the solvent employed. A much more pronounced effect can be produced, however, by a simple variation of the counterion M^+ in a single (non-polar) solvent. Table 2 indicates that in toluene the *cis*-**5**/*trans*-**5** ratio decreases in the order $Cs^+ > K^+ > Na^+ > Li^+ >> K^+$(18-crown-6), ranging between the extremes 94:6 and 6:94. Stereoselectivity in the reaction can thus be completely reversed by the counterion.

Table 2. Effect of the counterion (M^+) on *cis*-**5** : *trans*-**5** ratios in the reaction of **2** and **3** in toluene at 50°C

M^+	*cis*-**5** : *trans*-**5**
Cs^+	94 : 6
K^+	90 : 10
Na^+	70 : 30
Li^+	58 : 42
K^+(18-crown-6)	6 : 94

We have earlier demonstrated a similar but somewhat weaker counterion effect also in the corresponding reaction of 1,4-dibromo-2,3-dihydroxynaphthalene **1** with **2**; it has been interpreted[1] in terms of a metal coordination which promotes the preferential formation of the *cis*-stereoisomer (*cis*-**4**). Inspection of the alternative transition states leading to *cis*-**4** and *cis*-**5** (Scheme 6; A and B, respectively) suggests that the steric arrangement of the proximal oxygen donors at C_2 and C_2'' participating in the metal coordination in both the two compared systems is similar. Optimal steric fit is attained assumedly with the bulkiest alkali metal ion (Cs^+) and it deteriorates gradually upon diminishing the ionic diameter of M^+.



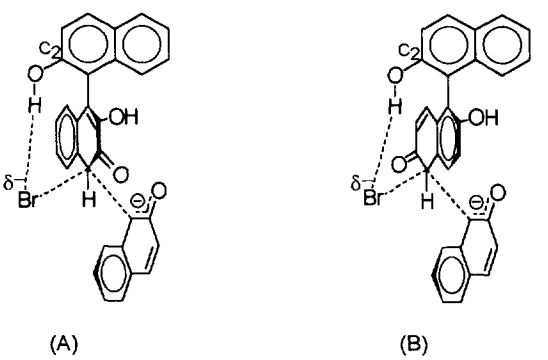
(A) (B)

Scheme 6

Effect of Hydrogen Bonding

The predominant or almost exclusive *trans*-stereoisomer formation, observed in the coupling reaction of **1** as well as **3** with **2** in the presence of stoichiometric amounts of 18-crown-6, cannot be explained merely by a suppression of the metal ion coordination visualized in the Scheme 6. Absence of the metal ion coordination alone should produce a loss of *cis*-stereoselectivity in the reaction and lead accordingly to a non-selective distribution of the corresponding *cis*- and *trans*-isomers. Some other factor must therefore be involved in the reaction which supports the *trans*-isomer formation.

As a simple explanation, we propose operation of a selective hydrogen bonding in the reaction. Intramolecular hydrogen bonding between the incipient bromide anion and the proximate phenolic group at C_2 may occur in the transition state leading to *trans*- but not to the *cis*-stereoisomer of **4** and **5** (Scheme 7; A, B). This may provide driving force for the preferential *trans*-isomer formation when the (stronger) metal coordination is excluded from reaction.



Scheme 7

In accord with the proposed explanation is the observation that the investigated reactions of **1** as well as **3** with **2** proceed much slower (by a factor >>100) in the presence than in the absence of the macrocyclic polyether.

EXPERIMENTAL

General

Melting points were taken on a Kofler block and are uncorrected; analytical samples were dried at 120°C/20Pa for 36 h. ^1H and ^{13}C NMR spectra (500 MHz and 125.7 MHz respectively, FT mode) were recorded in $CDCl_3$ (except of ^{13}C NMR spectra of low soluble *cis*-**5** and *trans*-**5** which were run in $CDCl_3$ + CD_3SOCD_3 (5:1) and CD_3SOCD_3, resp.) with TMS as the internal standard. EI MS spectra were obtained at 70 eV; FAB MS spectra were measured in thioglycerol-glycerol (1:3) matrix in methanol as solvent. Flash chromatography was performed on Silpearl silica gel (5-40 mm, Kavalier Votice, Czech Republic) with chloroform - methanol

mixtures (97:3 to 90:10) as eluents. HPLC analyses of acetylated samples were carried out on silica gel (Lichrosorb 5 Si 100, column 250x4.6 mm), using a petroleum ether - ethyl acetate gradient. Quantitative evaluation of the chromatograms was made using an internal standard (2,3-dihydroxynaphthalene). Racemic ternaphthyls were resolved on chiral phase CHIRALPAK OP (+) (Daicel Chemical Ind., Ltd) in methanol.

Reaction of 1,5-dibromo-2,6-dihydroxynaphthalene* 3 *with naphthoxide* 2 *($M^+ = K^+$)

Procedure A. To a deaerated suspension of 1,5-dibromo-2,6-dihydroxynaphthalene (0.8 g, 2.5 mmol) and 2-naphthol (0.72 g, 5 mmol) in dry toluene (50 mL) was added *t*-BuOK (0.85 g, 7.5 mmol) and the heterogeneous mixture was stirred at 50°C for 3 days under argon. After cooling, ethyl acetate (200 mL) and 2M aqueous HCl (200 mL) were added, the organic layer was separated and dried over $MgSO_4$. Evaporation of volatiles afforded a solid residue (1.30 g). Flash chromatography of the bulk product gave ternaphthols *cis*-**5** (0.74 g, 67%) and *trans*-**5** (0.08 g, 7%).

cis-**5**: mp 324-327°C (ethyl acetate); ^{1}H NMR δ 4.93 (2xOH), 5.14 (2xOH), 7.21 (3',7'), 7.26 (8,8"), 7.30 (4',8'), 7.40 (7,7"), 7.41 (6,6"), 7.42 (3,3"), 7.93 (5,5"), 8.02 (4,4"); ^{13}C NMR (in $CDCl_3$ + CD_3SOCD_3 (5:1)) δ 113.68 (1',5'), 114.15 (1,1"), 117.80 (3,3"), 118.02 (3',7'), 122.06 (6,6"), 124.36 (8,8"), 125.44 (7,7"), 125.58 (4',8'), 127.14 (5,5"), 128.00 (9',10'), 128.60 (4,4"), 128.65 (10,10"), 133.49 (9,9"), 150.16 (2',6'), 152.21 (2,2"); EI MS *m/z* (rel intensity), 444 (M^+, 100), 301 (5), 256 (9), 149 (16). Anal. Calcd for $C_{30}H_{20}O_4$: C, 81.06; H, 4.54. Found: C, 81.05; H, 4.66.

Tetraacetate of cis-**5**: mp 235-237°C (ethyl acetate - petroleum ether); ^{1}H NMR δ 1.78 (2xOAc), 1.85 (2xOAc), 7.22 (3',7'), 7.35 (4',8'), 7.36 (8,8"), 7.41 (7,7"), 7.46 (3,3"), 7.52 (6,6"), 7.97 (5,5"), 8.03 (4,4"); ^{13}C NMR δ 20.39 and 169.08 (2xOAc), 20.43 and 169.10 (2xOAc); 121.80 (3,3"), 122.66 (3',7'), 123.18 (1',5'), 123.66 (1,1"), 125.82 (8,8"), 126.14 (6,6"), 126.97 (7,7"), 127.70 (4',8'), 128.04 (5,5"), 129.68 (4,4"), 131.36 (9',10'), 131.48 (10,10"), 133.20 (9,9"), 146.69 (2',6'), 146.72 (2,2"); EI MS *m/z* (rel intensity), 612 (M^+, 10), 570 ($C_{36}H_{26}O_7$, 22), 528 ($C_{34}H_{24}O_6$, 81), 486 ($C_{32}H_{22}O_5$, 54), 444 ($C_{30}H_{20}O_4$, 100). Anal. Calcd for $C_{38}H_{28}O_8$ + 1/2 H_2O: C, 73.88; H, 4.61. Found: C, 73.95; H, 4.59.

Trans-**5**: mp 341-344°C (ethyl acetate); ^{1}H NMR δ 4.93 (2xOH), 5.16 (2xOH), 7.21 (3',7'), 7.24 (8,8"), 7.30 (4',8'), 7.38 (7,7"), 7.42 (6,6"), 7.43 (3,3"), 7.93 (5,5"), 8.02 (4,4"); ^{13}C NMR (in CD_3SOCD_3) δ 115.85 (1',5'), 116.20 (1,1"), 118.50 (3,3"), 118.75 (3',7'), 122.40 (6,6"), 124.98 (8,8"), 125.39 (7,7"), 125.86 (4',8'), 127.94 (5,5"), 128.31 (9',10'), 128.64 (4,4"), 128.96 (10,10"), 134.46 (9,9"), 150.50 (2',6'), 153.16 (2,2"); EI MS *m/z* (rel intensity), 444 (M^+, 100), 301 (5), 256 (10), 149 (10). Anal. Calcd for $C_{30}H_{20}O_4$ + 1/2 H_2O: C, 79.46; H, 4.67. Found: C, 79.04; H, 4.42.

Tetraacetate of trans-**5**: mp 286-289°C (ethyl acetate - petroleum ether); ^{1}H NMR δ 1.80 (2xOAc), 1.93 (2xOAc), 7.21 (3',7'), 7.22 (8,8"), 7.33 (4',8'), 7.34 (7,7"), 7.47 (3,3"), 7.50 (6,6"), 7.96 (5,5"), 8.03 (4,4"); ^{13}C NMR δ 20.52 and 169.21 (2xOAc), 20.59 and 169.37 (2xOAc), 121.91 (3,3"), 122.72 (3',7'), 123.23 (1',5'), 123.66 (1,1"), 125.79 (8,8"), 125.98 (6,6"), 126.86 (7,7"), 127.76 (4',8'), 128.14 (5,5"), 129.74 (4,4"), 131.48 (9',10'), 131.55 (10,10"), 133.30 (9,9"), 146.76 (2',6'), 146.83 (2,2"); EI MS *m/z* (rel intensity), 612 (M^+, 10),

570 ($C_{36}H_{26}O_7$, 22), 528 ($C_{34}H_{24}O_6$, 81), 486 ($C_{32}H_{22}O_5$, 54), 444 ($C_{30}H_{20}O_4$, 100). Anal. Calcd for $C_{38}H_{28}O_8$ + 1/2 H_2O: C, 73.88; H, 4.61. Found: C, 73.42; H, 4.70.

Procedure B. To a deaerated suspension of 1,5-dibromo-2,6-dihydroxynaphthalene (0.8 g, 2.5 mmol) and 2-naphthol (0.72 g, 5 mmol) in water (20 mL) was added *t*-BuOK (0.85 g, 7.5 mmol) and the heterogeneous reaction mixture was stirred at 90°C for 3 days under argon. The same work-up as in procedure A afforded a solid residue (1.48 g). Flash chromatography gave ternaphthols *trans*-**5** (0.22 g, 20%), *cis*-**5** (0.43 g, 39%) and quaternaphthol **7** (0.06 g, 4%). A minor chromatographic fraction (0.1 g) preceding *cis*-**5** which contained **6** as the main component was acetylated (vide infra) and subjected to preparative HPLC (silica gel, petroleum ether - ethyl acetate gradient) affording tetraacetate of **6** (0.04 g, 2%)

Quaternaphthol **7**: mp 288-292°C (ethyl acetate); ^{1}H NMR δ 5.02 (2xOH), 5.18 (4xOH), 7.00 (3',7"), 7.19 (7',3"), 7.22 (4',8"), 7.27 (3,3"',8,8"'), 7.34 (8',4"), 7.40 (7,7"'), 7.42 (6,6"'), 7.91 (5,5"'), 7.97 (4,4"'); ^{13}C NMR δ 110.95 (1,1"'), 112.15 (1',5"), 112.18 (5',1"), 117.71 (3,3"'), 118.92 (7',3"), 119.14 (3',7"), 124.23 (6,6"',8,8"'), 127.58 (4',8"), 127.60 (7,7"'), 127.67 (8',4"), 128.52 (5,5"'), 129.31 (10',9"), 129.39 (9',10"), 129.52 (10,10"'), 131.62 (4,4"'), 133.39 (9,9"'), 151.27 (6',2"), 151.48 (2',6"), 152.61 (2,2"'); EI MS *m/z* (rel intensity), 602 (M^+, 75), 444 (100), 316 (60); HREIMS, found m/z 602.1753, calcd for $C_{40}H_{26}O_6$ (M^+) 602.1729.

Hexaacetate of **7**: mp 260-263°C (ethyl acetate - petroleum ether); ^{1}H NMR δ 1.80 (2xOAc), 1.83 (2xOAc), 1.86 (2xOAc), 7.26 (3',7"), 7.35 (7',3"), 7.38 (8,8"'), 7.40 (4',8"), 7.44 (7,7"'), 7.47 (3,3"'), 7.54 (6,6"'), 7.55 (8',4"), 7.99 (5,5"'), 8.05 (4,4"'); ^{13}C NMR δ 20.36 and 168.87 (2xOAc), 20.44 and 169.13 (2xOAc), 20.52 and 169.18 (2xOAc), 121.87 (3,3"'), 122.76 (7',3"), 123.05 (3',7"), 123.21 (1,1"'), 123.55 (1',5"), 123.84 (5',1"), 125.92 (8,8"'), 126.18 (6,6"'), 127.10 (7,7"'), 127.73 (4',8"), 127.98 (8',4"), 128.14 (5,5"'), 129.81 (4,4"'), 131.36 (10',9"), 131.49 (10,10"'), 131.56 (9',10"), 133.27 (9,9"'), 146.80 (2',6',2",6"), 146.89 (2,2"'); EI MS *m/z* (rel intensity), 854 (M^+, 15), 812 ($C_{50}H_{36}O_{11}$, 20), 770 ($C_{48}H_{34}O_{10}$, 81), 728 ($C_{46}H_{32}O_9$, 69) 686 ($C_{44}H_{30}O_8$, 79), 644 ($C_{42}H_{28}O_7$, 50), 602 ($C_{40}H_{26}O_6$, 100); HREIMS, found m/z 854.2503, calcd for $C_{52}H_{38}O_{12}$ (M^+) 854.2363; found m/z 770.2114, calcd for $C_{48}H_{34}O_{10}$ (M^+ - 2 CH_3CO) 770.2152

Tetraacetate of **6**: mp 325-326°C; ^{1}H NMR δ 1.79 (OAc), 1.84 (OAc), 1.90 (OAc), 1.95 (OAc), 6.69 (3'), 7.12 (4'), 7.15 (3"'), 7.22 (7'), 7.30 (7"'), 7.36 (7",8"), 7.39 (3",6"'), 7.44 (8'), 7.46 (3), 7.48 (6"), 7.49 (7), 7.53 (6), 7.57 (4"'), 7.64 (8), 7.74 (5"'), 7.90 (8"'), 7.91 (5"), 7.96 (5), 7.97 (4"), 7.98 (4); ^{13}C NMR δ 20.42, 20.47 (3x), 168.29, 168.82, 168.90 and 169.25 (4xOAc), 115.65 (3'), 117.55 (1'), 121.75 (3"'), 121.97 (3), 122.05 (3"), 122.28 (4'), 122.84 (7'), 123.43 (1"), 123.46 (5'), 124.24 (1), 125.32 (8"'), 125.74 (8"), 125.79 (8), 126.06 (6), 126.17 (6"), 126.21 (6"'), 126.26 (7"'), 126.66 (7"), 126.77 (7), 127.24 (5"'), 127.74 (8'), 128.06 (5"), 128.08 (5), 128.32 (10"'), 128.41 (4"'), 129.16 (9'), 129.61 (4,4"), 131.53 (10), 131.91 (10"), 131.93 (10'), 132.58 (9"'), 133.27 (9), 133.62 (9"), 139.34 (2"'), 140.16 (1"'), 145.74 (6'), 146.70 (2"), 147.11 (2), 153.26 (2'); EI MS *m/z* (rel intensity), 754 (M^+, 12), 712 ($C_{46}H_{32}O_8$, 33), 670 ($C_{44}H_{30}O_7$, 71), 628 ($C_{42}H_{28}O_6$, 100), 586 ($C_{40}H_{26}O_5$, 98); HREIMS, found m/z 754.2210, calcd for $C_{48}H_{34}O_9$ (M^+) 754.2202.

Procedure C. To a deaerated solution of 1,5-dibromo-2,6-dihydroxynaphthalene (80 mg,0.25 mmol) and 2-naphthol (72 mg, 0.5 mmol) in methanol (3 mL) was added *t*-BuOK (85 mg, 0.75 mmol) and the mixture was evaporated to dryness. The semi-solid reaction mixture was heated at 100°C under argon overnight. After cooling, ethyl acetate (20 mL) and 2M aqueous HCl (20 mL) were added, the organic layer was separated and dried over $MgSO_4$. Evaporation of volatiles afforded a solid residue (132 mg). Flash chromatography of the bulk product gave *trans*-**5** (13 mg, 12%) and *cis*-**5** (30 mg, 27%).

Reaction of 1-bromo-2-naphthol with potassium salt of 2,6-dihydroxynaphthalene

To a deaerated solution of 2,6-dihydroxynaphthalene (40 mg,0.25 mmol) and 1-bromo-2-naphthol (112 mg, 0.5 mmol) in methanol (3 mL) was added *t*-BuOK (85 mg, 0.75 mmol). The reaction mixture was further treated as described in procedure C affording a solid residue (120 mg). A small sample was acetylated (*vide infra*) and subjected to HPLC analysis (41% of 2,2'-dihydroxy-1,1'-binaphthyl **10**, 8% of *cis*-**5** and 4% of *trans*-**5**). Flash chromatography of the bulk product gave binaphthol **10** (27 mg, 38%), m.p. 213-216°, identical with an authentic sample.[5]

Equilibration of Stereoisomers

Individual stereoisomers of **5** (0.1 mmol) were heated in dry pyridine (0.5 mL) at 115°C for 12 h under argon. After cooling, the reaction mixtures were acetylated (*vide infra*) and subjected to HPLC analysis. The ratio *trans*-**5** : *cis*-**5** was 58 : 42.

Acetylation

Individual naphthols (*cis*-**5**, *trans*-**5** and **7**) or naphthol fractions (0.2 mmol) were dissolved in pyridine (2 mL) and acetic anhydride (1 mL) was added. After 2 h at room temperature, ethyl acetate (10 mL) and 5M aqueous HCl (10 mL) were added and the mixture was stirred vigorously for 5 min. The organic layer was separated, washed with H_2O (2 x 5 mL) and dried over $MgSO_4$. After evaporation of volatiles the crude acetate was purified by crystallization or preparative HPLC.

Solvent and Counterion Effects (Tables 1,2)

1,5-Dibromo-2,6-dihydroxynaphthalene (16 mg, 0.05 mmol) and 2-naphthol (14.5 mg, 0.1 mmol) were dissolved or suspended in the given solvent (1 mL) containing in some instances 18C6 (0.2 mmol), and appropriate alkali metal *tert*-butoxide (0.15 mmol) was added. Caesium *tert*-butoxide was generated by an *in situ* metathesis of potassium *tert*-butoxide and caesium chloride (2 eqs.). The reaction mixture was stirred at 50°C (unless otherwise indicated in the Tables) for a convenient time period (16 - 160 hrs), diluted with ethyl acetate (2.5 mL) and acidified with 2M aqueous HCl (5 mL). The organic extract was dried with $MgSO_4$, filtered and adjusted to 5 mL. An aliquot (0.5 mL) was treated with pyridine (0.1 mL) containing an internal standard (2,3-dihydroxynaphthalene) and acetic anhydride (0.05 mL). The reaction mixture was heated at 50°C for 30 min, cooled, 5M aqueous HCl (0.5 mL) was added and the mixture was stirred vigorously for 5 min. The separated organic layer was dried over $MgSO_4$ and a sample subjected to HPLC analysis.

Single-crystal X-ray diffraction

$C_{38}H_{28}O_8$, m.w. 612.60, monoclinic, space group $P2_1/c$ (No.14), a = 19.039(2), b = 21.157(3), c = 21.620(1) Å, β = 100.50(1)°, V = 3035.0(7) Å^3, Z = 4 (eight halves constituting, through inversion centers, two pairs of crystallographically independent but chemically almost identical molecules), D_c = 1.341 gcm^{-3}, F(000) = 1280. A colorless crystal of the dimensions 0.07 x 0.2 x 0.5 mm was measured at 20 °C on a CAD4 diffractometer with a graphite-monochromated MoK$_\alpha$ radiation (λ = 0.71073 Å). Absorption was neglected (μ = 0.09 mm^{-1}). The lattice parameters were determined from 25 reflections in the 12-16° Θ-range. The intensities of the reflections were measured using the θ-2θ scan between 1-23 θ, h<0,20>, k<0,23>, l<-8,8>. Three standard reflections monitored every 1 h showed 3% intensity variation during the measurement. From 3157 measured reflections, 3057 were unique (R_{int} = 0.021) and 2045 of them were regarded as "observed" according to the the $I \geq 4\sigma(I)$ criterion. The structure was solved by direct methods (SHELXS86[6]) and refined by full-matrix least squares based on F^2 (SHELXL93[7]). Hydrogen atoms were placed in theoretical positions and then refined with isotropic temperature factors of their bonding partners multiplied by 1.2. The function minimized was $\Sigma w(|F_o|-|F_c|)^2$ where $w = (\sigma^2_F \times |F_o|^2 + (0.0680P)^2 + 2.56P)^{-1}$, $P = (F_o^2 + 2F_c^2)/3$. Convergence was achieved at R = 0.0512, R_w = 0.1334, S = 1.11, GOF = 1.108 with $(\Delta/\sigma)_{max}$ = 0.05; -0.03 for non-H atoms. The final difference electron density map showed no peaks of chemical significance (extreme values of ±0.20 e Å^{-3}). Figure 1 shows the perspective view of one molecule with atom labeling. Further crystallographic details (as standard CIF files produced by SHELX93) have been deposited at the Cambridge Crystallization Data Centre, 12 Union Road - Cambridge, CB2 1EZ (UK) and are also available from J.P. on request.

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