Reaction of 1,4-Dibromo-2,3-dihydroxynaphthalene with 2-Naphthoxide Ion. Solvent and Cation Control in the Formation of the Conformationally Locked Stereoisomers of 2,2′,3′,2″-Tetrahydroxy-1,1′:4′,1″-ternaphthyl and 2,2′,3′,2″,3″,2‴-Hexahydroxy-1,1′:4′,1″:4″,1‴-quaternaphthyl

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The reaction of the dibromide **1** with the 2-naphthoxide ion **2** proceeds under remarkably mild conditions (25−50 °C), yielding all possible stereoisomers of ternaphthol **3** and quaternaphthol **4**. An unambiguous structure assignment has been made for the individual stereoisomers and conditions for their thermal interconversion have been established. In contrast to a nonselective distribution of stereoisomers found in the thermodynamic equilibrium mixture, a high stereoselectivity can be induced in the coupling reaction under kinetic control. The coordinating ability of the alkali metal counterion (M^+) of the participating 2-naphthoxide ion **2** has been found to play a key role in the stereocontrol, supporting strongly the formation of the *cis* stereoisomers of **3** and **4**. When the coordinating ability of M^+ is suppressed by an efficient solvation and/or by complexation with 18-crown-6, formation of the *trans* stereoisomers prevails in the reaction.

Introduction

p-Ter- and quateraryls represent important models and/or building blocks for the synthesis of long, rod-like molecules that cannot bend or coil and may thus possess unusual properties with a variety of applications.[1−6] In this context, the corresponding 1,4-oligonaphthalene derivatives, hitherto unreported in the literature, attracted our interest. A high rotational barrier along the main axis in these compounds permits the occurrence of conformationally locked stereoisomers. The stereoselective synthesis of these compounds poses an intriguing problem.

In this paper, we report a one-pot synthesis of all possible stereoisomers of 2,2′,3′,2″-tetrahydroxy-1,1′:4′,1″-ternaphthyl (**3**) and 2,2′,3′,2″,3″,2‴-hexahydroxy-1,1′:4′,1″:4″,1‴-quaternaphthyl (**4**) from 1,4-dibromo-2,3-dihydroxynaphthalene (**1**) and 2-naphthoxide ion (**2**). At the same time, the mechanism and stereoselectivity of this novel reaction is discussed.

Results and Discussion

Main Products and Reaction Conditions. The reaction of 1,4-dibromo-2,3-dihydroxynaphthalene (**1**) with 2-naphthoxide ion (**2**) (Scheme 1) proceeds in a variety of solvents under remarkably mild conditions (25−50 °C). However, the product composition strongly depends on the solvent employed in the reaction (Table 1).

In protic solvents (ethylene glycol, methanol, or water) the reaction affords the expected stereoisomers of 2,2′,3′,2″-tetrahydroxy-1,1′:4′,1″-ternaphthyl (ternaphthol), *cis*- and *trans*-**3**, as the main products, accompanied by the homologous stereoisomers of 2,2′,3′,2″,3″,2‴-hexahydroxy-1,1′:4′,1″:4″,1‴-quaternaphthyl (quaternaphthol), *cis*,*cis*-**4**, *cis*,*trans*-**4**, and *trans*,*trans*-**4**, together with trace amounts of the next higher homologues (quinquenaphthols, etc.). In aprotic solvents (toluene, DMSO) or in the absence of solvent, ternaphthols **3** and quaternaphthols **4** are only minor products, intractable tars being the major part of the reaction mixture.

Gross Mechanism of the Coupling Reaction. The coupling of 1-bromo-2-naphthols with 2-naphthoxide ion represents an almost unexplored reaction. In a recent study,[7] we have investigated the C−C coupling of 1-bromo-2-naphthol (**5**) with the ambident 2-naphthoxide ion (**2**) yielding 2,2′-dihydroxy-1,1′-binaphthyl (binaphthol) (**6**) and demonstrated that the reaction proceeds via an S_N mechanism involving the reactive keto form of **5** (Scheme 2). An analogous mechanism may also operate in the reaction of **1** with **2** (Scheme 3), accounting for the stepwise formation of the ternaphthols *cis*- and *trans*-**3** (pathways *a* and *b*). The intermediate 4-bromo-2,3,2′-trihydroxy-1,1′-binaphthyl (**7**) has been identified in the product mixture at the early stage of the coupling reaction.

In order to rationalize the unexpected formation of the quaternaphthols **4**, one has to take into account the possibility of a concurrent nucleophilic attack at the bromine terminus[8] of the reactive C−Br bond in the

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(1) Baum, R. *Chem. Eng. News* **1993**, (2), 30.
(2) Marin, G. H.; Horak, V. *J. Org. Chem.* **1994**, *59*, 4267.
(3) Unrau, C. M.; Campbell, M. G.; Sniekus, V. *Tetrahedron Lett.* **1992**, *33*, 2773.
(4) Tieke, B.; Bubeck, C.; Lieser, G. *Makromol. Chem., Rapid Commun.* **1992**, *3*, 261.
(5) Müller, U.; Adam, M.; Müller, K. *Chem. Ber.* **1994**, *127*, 437.
(6) Kreyenschmidt, M.; Baumgartner, M.; Tyutyulkov, N.; Müller, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1957.
(7) Bělohradský, M.; Holý, P.; Závada, J. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1853.

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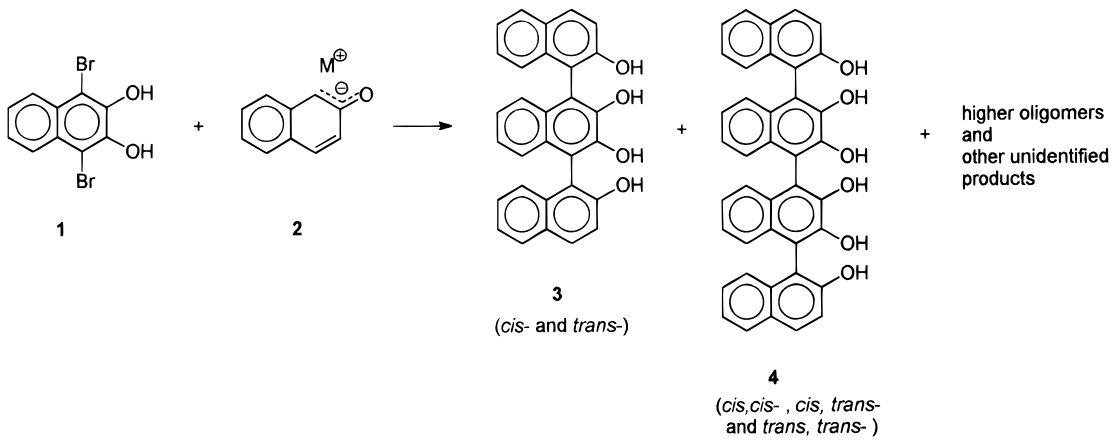
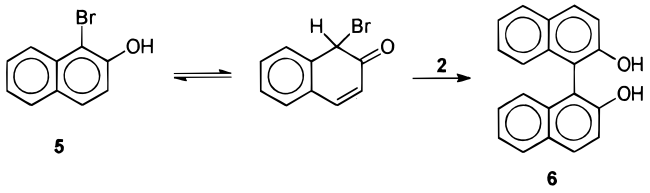
Scheme 1



Scheme 2



participating bromonaphthol **1** (and/or **7**). The attack at the bromine atom may involve either a nucleophilic displacement of one carbanion by another ($ArX + Nu^- \rightarrow Ar^- + NuX$), which is accompanied by halogen exchange between the two (pathways *c* and *d*), or a single electron transfer ($ArX + Nu^- \rightarrow ArX^{\bullet -} + Nu^{\cdot} \rightarrow Ar^{\cdot} + X^-$) followed by ejection of the halide anion from the intermediary radical anion (pathways *e* and *f*). The resulting debrominated species **8**−**11** may enter into a further coupling, giving rise ultimately to the quaternaphtols **4** (pathways *g*, *i*, and *j*).

In this way, the simultaneous formation of the ternaphthols **3** and quaternaphthols **4** outlined in Scheme 3 may be viewed to result from the competition between the nucleophilic attack at the carbon and at the bromine terminus of the C−Br bond.

As far as the role of the solvent is concerned in the nucleophilic competition (Table 1), protic solvents apparently support the attack at the carbon terminus of the C−Br bond, as evidenced by the prevailing formation of the ternaphthols **3**. Hydrogen bonding to the incipient bromide anion arising by the nucleophilic attack at the carbon atom of **1** presumably favors the C−C coupling over the debromination reaction. In the absence of the hydrogen bonding, the debromination may prevail, possibly also accounting for the formation of higher oligomers and/or polymers in the reaction.

Stereochemical Assignment. Due to a high rotational barrier along the aryl−aryl axis, two conformationally locked stereoisomers of the ternaphthol **3** (*cis*-**3** and *trans*-**3**) and three of quaternaphthol **4** (*cis*,*cis*-**4**, *cis*,*trans*-**4**, and *trans*,*trans*-**4**) may exist, as shown in Scheme 4.

The single-crystal X-ray analysis (Figure 1) unambiguously determined the stereochemistry of the ternaphthols *cis*-**3** and *trans*-**3**. In both the stereoisomers, the naphthyl groups are planar within ±0.07 Å. When labeled according to the pivot atoms, the dihedral angles between the individual planes (in degrees and with estimated standard deviations in parentheses) are C_1/C_{11}, 69(1), 74.7(4); C_{11}/C_{21}, 66(1), 72.2(4); C_1/C_{21}, 4(1), 4.2(4) for the isomers *cis*-**3** and *trans*-**3**, respectively. The chromatographic behavior of the two stereoisomers on a CHIRALPAK OP(+) HPLC column agrees well with the X-ray analysis; the *cis* isomer, which is the meso form, appeared as a single peak, whereas the racemic *trans* isomer was resolved into enantiomers. The absolute configuration of the individual enantiomers has not yet been determined.

None of the three isolated quaternaphthols **4** provided crystals of X-ray quality. However, an unambiguous stereochemical assignment for the *cis*,*cis* and *trans*,*trans* stereoisomers of **4** has been attained via the correlation of their ^{13}C NMR shifts with those observed for the corresponding ternaphthols *cis*-**3** and *trans*-**3**, respectively (cf. supporting information).

An independent stereochemical assignment for the remaining quaternaphthol, *cis*,*trans*-**4**, has been drawn from a comparison of the ^{13}C NMR spectra of the three stereoisomers of **4**. Only the *cis*,*trans*-**4** stereoisomer, by virtue of its irregular conformation, has been found to exhibit the full number of NMR signals, corresponding to all individual carbon atoms. Both the *cis*,*cis*-**4** and *trans*,*trans*-**4** isomers provided a reduced (one-half) number of NMR signals, in accord with their higher symmetry (cf. supporting information).

Thermal Interconversion of Stereoisomers. Refluxing the individual *cis*- and *trans*-ternaphthols **3** in pyridine[9] for 12 h led to an equilibrium mixture in which both stereoisomers were present in nearly equal proportions (49:51). Under analogous conditions, the corresponding quaternaphthols **4** gave an equilibrium mixture, in which the *cis*,*cis*, *cis*,*trans*, and *trans*,*trans* stereoisomers were represented in 22:46:32 ratio. This is again close to the statistical (1:2:1) distribution.

Effect of Solvent and Cation on Steroselectivity and Rate of the Coupling Reaction. In contrast to the nonselective distribution of stereoisomers in the

(8) The identity of the nucleophile participating in the proposed attack at the bromine atom has not been established. In addition to the 2-naphthoxide ion **2**, the conjugated base of the bromonaphthol **1** may also act as the nucleophile, as evidenced by the observed formation of **12** in the base-catalyzed disproportionation of **1** (cf. Experimental Section). Significantly, no side products which could be ascribed to halogen exchange between two naphthols have been observed in the course of the present study. This lends support to the view that single electron transfer rather than a halogen exchange mechanism operates in the quaternaphthol **4** formation. We thank to a referee for valuable discussion.

(9) In non-basic solvents, such as toluene or xylene, the thermal interconversion proceeds much more sluggishly. Apparently, the availability of the proton transfer between the equilibrated ter- or quaternaphthols and pyridine substantially lowers the interconversion barrier.

Scheme 3

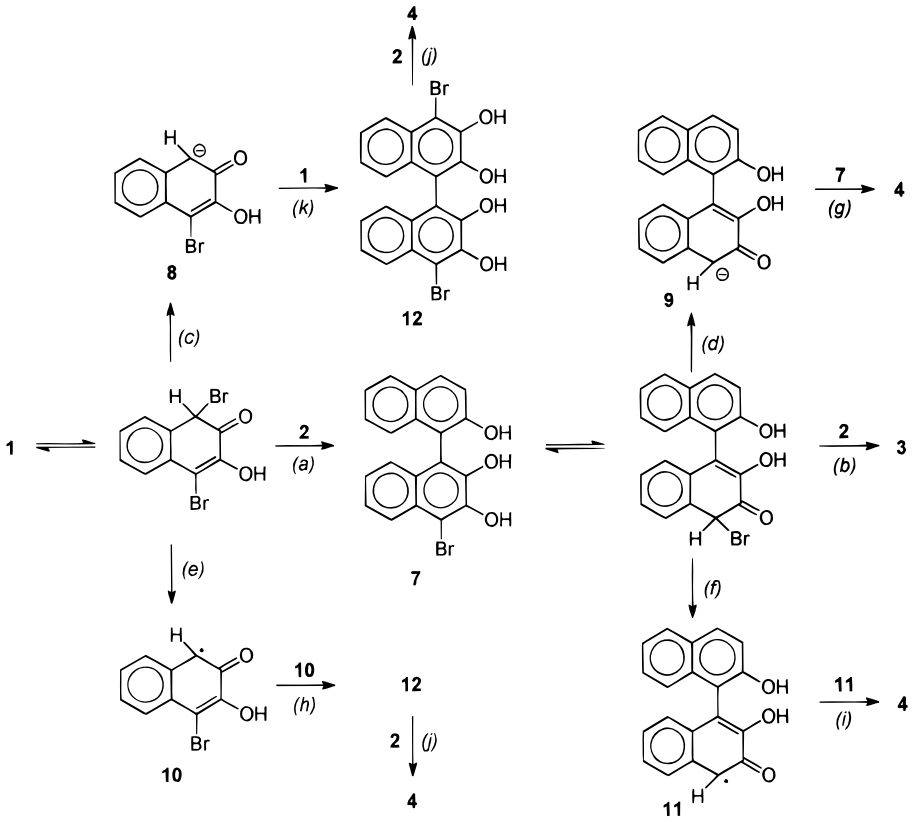


Table 1. Effect of Solvent on the Overall Yields of 3 and 4 in the Reaction of 1 with 2 ($M^+ = Na^+$)

solvent	**3** (%)[a]	**3**/**4**[b]
$HOCH_2CH_2OH$	53	5.8
CH_3OH	39	3.6
H_2O[c]	29	3.4
d	16	1.5
toluene	12	4.5
DMSO	8	2.5

[a] Percentage of the theoretical yield. [b] Molar ratio. [c] Heterogeneous reaction. [d] Reaction in the absence of solvent.

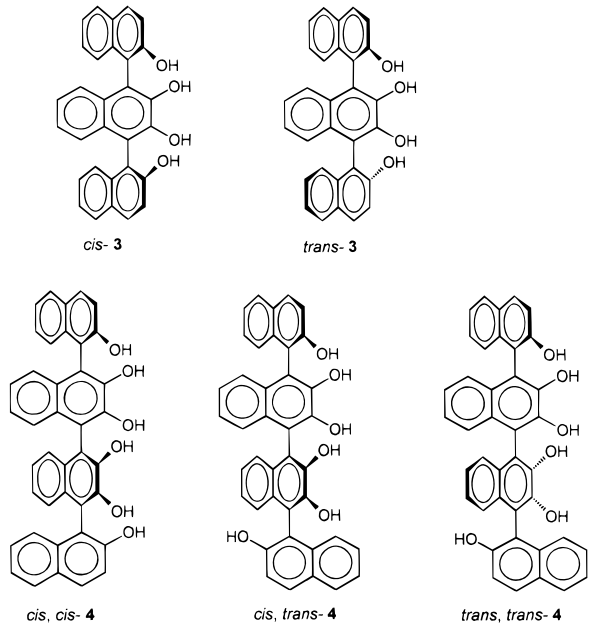
thermal equilibrium, a remarkably high stereoselectivity can be induced by variation of solvent and/or cation in the coupling reaction under conditions of a kinetic control.[10]

As Table 2 shows, the *cis*-**3** stereoisomer predominates over *trans*-**3** in the reaction of **1** with **2** ($M^+ = Na^+$) in toluene. By contrast, prevalence of the *trans*-**3** stereoisomer has been found in the reaction carried out in methanol or ethylene glycol. Intermediate results were obtained in DMSO and in the absence of a solvent and/or under heterogeneous conditions (in water).

The accompanying effect of the counterion M^+ of the participating 2-naphthoxide anion is summarized in Table 3. In toluene, replacement of the sodium ($M^+ = Na^+$) by the potassium ($M^+ = K^+$) ion results in an increase of the *cis*-**3**/*trans*-**3** ratio. Conversely, complexation of the alkali ions with 18-crown-6 reduces strongly the *cis*-**3**/*trans*-**3** ratio. A similar but less pronounced effect of the macrocyclic polyether is observed in methanol.

Also, the effect of 18-crown-6 on the stereoselectivity is accompanied by very substantial changes in the reaction rate. Noteworthy, the formation of **3** proceeds much *faster* in the *absence* of the macrocyclic ether (Table 4).

Scheme 4



An analogous counterion effect on the reaction rate has been observed by us previously[7] in the coupling of 1-bromo-2-naphthol (**5**) with 2-naphthoxide ion (**2**) (Scheme 2). As an explanation we have proposed a noncovalent self-assembly of the two reaction partners (driven by ion pairing and hydrogen bonding interactions) prior to the coupling reaction. We have suggested that the association enhances the effective concentration of both reactants, depending on the solvent and the counterion employed in the coupling reaction. Extension of this

(10) No interconversion of the stereoisomeric ternaphthols **3** as well as quaternaphthols **4** occurs under conditions of the coupling experiments summarized in Tables 2−5.

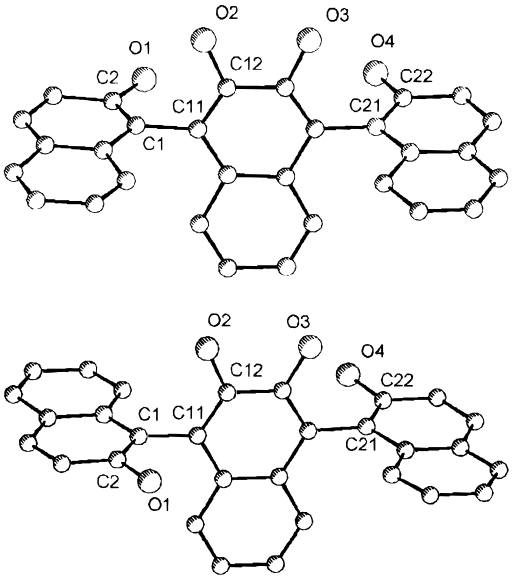


Figure 1. Perspective view (PLUTO) of *cis*- and *trans*-**3**.

Table 2. Effect of Solvent on the Distribution of Individual Stereoisomers of 3 and 4 in the Reaction of 1 with 2 ($M^+ = Na^+$)

	3		4		
solvent	*cis*	*trans*	*cis,cis*	*cis,trans*	*trans,trans*
toluene	69	31	47	31	22
H_2O[a]	66	34	40	43	17
b	58	42	35	41	23
DMSO	40	60	27	50	23
$HOCH_2CH_2OH$	34	66	22	47	31
CH_3OH	29	71	22	49	29

[a] Heterogeneous reaction. [b] Performed in the absence of solvent.

Table 3. Effect of Counterion (M^+) on the Distribution of Individual Stereoisomers of 3 and 4 in the Reaction of 1 with 2

	3		4		
M^+ (solvent)	*cis*	*trans*	*cis*,cis	*cis*,trans	*trans*,trans
Na^+ (toluene)	69	31	47	31	22
K^+ (toluene)	85	15	50	31	19
K^+/18C6 (toluene)	35	65	8	34	58
K^+ (CH_3OH)	25	75	15	46	39
K^+/18C6 (CH_3OH)	16	84	10	46	44

Table 4. Effect of Counterion (M^+) and Solvent on the Rate of Reaction of 1 with 2

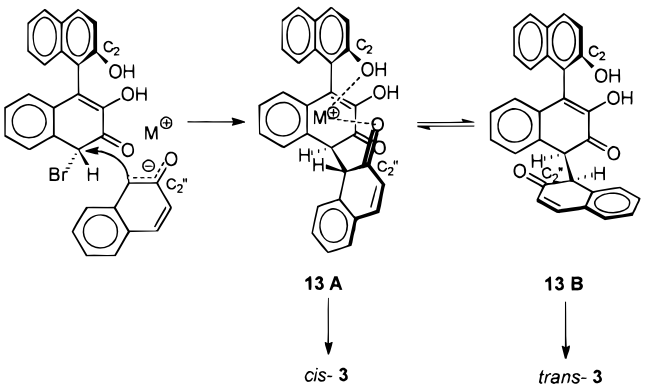
M^+ (solvent)	$t/2$[a] (temp, °C)
K^+(toluene)	1 min (25)
K^+/18C6 (toluene)	8 h (25)
K^+ (CH_3OH)	10 min (50)
K^+/18C6 (CH_3OH)	2 h (50)

[a] Approximate half-time of conversion of **1** into products.

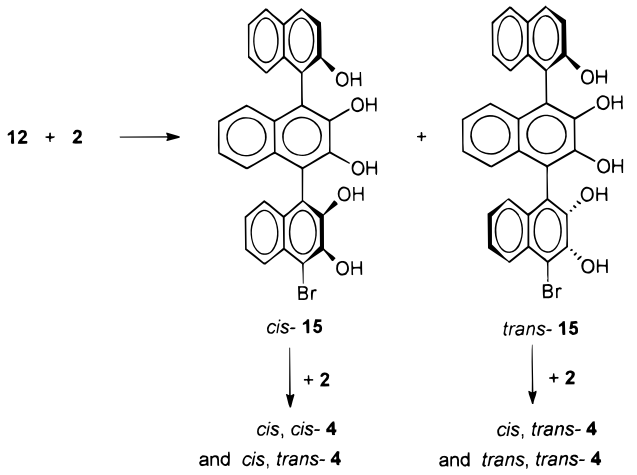
mechanistic concept, in which the organizing ability of the metal ion plays a key role, to the present reaction may well account for the observed effect of the counterion on both the rate and the stereoselectivity of the ternaphthol **3** formation.

In the terminal step of the ternaphthol **3** coupling (Scheme 5), the metal ion M^+ is proposed to support the attack of the 2-naphthoxide ion (**2**) from that side of 4-bromo-2,3,2′-trihydroxy-1,1′-binaphthyl (**7**), which allows the proximal oxygen at C_2 to participate in the metal ion coordination. The ensuing nucleophilic coupling leads to the diketo intermediate **13**.[11] The stereochemical fate of **13**, which is conformationally mobile (owing to the easy

Scheme 5



Scheme 6



rotation along the central sp^3-sp^3 hybridized C−C bond), depends assumedly upon the continuous coordination with the metal ion.

In the absence of 18-crown-6, the coordination in toluene (a nonpolar solvent) is expected to be strong enough to freeze the initial conformation **13A**, in which the opposing oxygens at C_2 and $C_{2''}$ are held in proximity to the metal ion M^+. Upon enolization,[12] the conformer **13A** collapses into the *cis*-**3** stereoisomer. On the other hand, in the presence of the macrocyclic polyether (or in the highly polar solvent, such as methanol), the organizing ability of M^+ vanishes, allowing other conformers which may lead to the *trans*-**3** stereoisomer (e.g., conformer **13B**) to prevail in the enolization.

Concerning the quaternaphthol **4** formation, the stereochemical situation is complicated by a possible operation of several contributing pathways (*g*, *i*, and *j* in Scheme 3). We examined separately the stereoselectivity of the last of the three reactions (*j*).

As follows from Scheme 6, the reaction of the dibromide **12** with the 2-naphthoxide ion (**2**) proceeds in two consecutive steps. The stereochemical control in each of these steps is expected to be similar to that outlined for the formation of ternaphthol **3** (Scheme 5). Accordingly, the prevalence of the *cis,cis*-**4** stereoisomer, which is

(11) Scheme 5 represents an oversimplification of the actual situation. In principle, two diastereoisomeric diketo intermediates, differing from each other in the configuration at $C_{1''}$, may arise by the attack of **2** from that side of **7** which allows the coordination of the metal ion. However, examination of models suggests that the stereochemical fate of the two diastereoisomers is similar. Accordingly, only one diastereoisomer (**13**) is shown in the scheme.

(12) Conceivably, the double enolization of **13** represents a concerted process which is triggered by an intramolecular proton transfer, e.g., from the hydroxyl at C_2 to the carbonyl oxygen at $C_{2''}$.

Table 5. Effect of Counterion (M^+) and Solvent on the Distribution of Individual Stereoisomers 4 in the Reaction of 12 with 2

	4		
M^+ (solvent)	*cis,cis*	*cis,trans*	*trans,trans*
K^+ (toluene)	44	42	14
K^+/18C6 (toluene)	7	47	46
K^+ (CH_3OH)	9	45	46
K^+/18C6 (CH_3OH)	3	30	67

observed in toluene in the absence of 18-crown-6 (Table 5), is attributed to a strong participation of the metal ion in both consecutive steps. Conversely, the dominant formation of the *trans,trans*-**4** stereoisomer, which is obtained in the presence of the macrocyclic polyether, can be ascribed to the absence of metal ion in the stereochemical control.

Conclusion

The reaction of the dibromide **1** with the 2-naphthoxide ion (**2**) proceeds under remarkably mild conditions, yielding all possible stereoisomers of the ternaphthol **3** and quaternaphthol **4**. An unambiguous configurational (conformational) assignment has been made for the individual stereoisomers by means of X-ray and NMR analysis. It has been shown that the stereochemical course of this novel reaction can be controlled efficiently by a judicious variation of solvent and/or cation to produce either mainly *cis* or mainly *trans* stereoisomers of **3** and **4**. On further elaboration, this reaction may provide access to the stereoregulated, functionalized 1,4-naphthalene oligomers and/or polymers.

Experimental Section

General. Melting points were determined on a Kofler block and are uncorrected. ^1H and ^{13}C NMR spectra (500 and 125.7 MHz, respectively, FT mode) were recorded in $CDCl_3$ with TMS as the internal standard. EI Mass spectra were obtained at 70 eV; FAB spectra were measured in thioglycerol−glycerol (1:3) matrix in methanol as solvent. Flash chromatography was performed with Silpearl silica gel (5−40 μm, Kavalier Votice, Czech Republic) with chloroform−methanol mixture (97:3 to 90:10) as eluent. HPLC analyses were carried out on silica gel, using a petroleum ether−ethyl acetate gradient. Quantitative evaluation of the chromatograms was made using an internal standard; correction was made for different responses of the individual compounds. Optical resolution of racemic compounds was performed on the chiral phase CHIRALPAK OP (+) (Daicel Chemical Ind., Ltd) in methanol.

Synthesis and Separation of the Individual Stereoisomers of 2,2′,3′,2″-Tetrahydroxy-1,1′:4′,1″-ternaphthyl (3) and 2,2′,3′,2″,3″,2‴-Hexahydroxy-1,1′:4′,1″:4″,1‴-quaternaphthyl (4). Procedure A. To a deaerated solution of dibromide **1**[13] (2.88 g, 10 mmol) and 2-naphthol (3.18 g, 20 mmol) in methanol (90 mL) was added a 3 M solution of $NaOCH_3$ in methanol (10 mL, 30 mmol). The homogenous mixture was heated at 50 °C for 16 h. After cooling, methanol was evaporated and 1 M aqueous HCl (300 mL) was added to the residue. After extraction with ethyl acetate (4 × 50 mL), the combined extracts were washed with H_2O (2 × 50 mL) and dried over $MgSO_4$ yielding, after evaporation, a solid residue (5.15 g). A small sample (50 mg) was acetylated (*vide infra*) and subjected to HPLC analysis [**2** (42%), *trans*-**3** (28%), *cis*-**3** (11%), *trans,trans*-**4** (7%), *cis,trans*-**4** (12%), and *cis,cis*-**4** (5%)]. Flash chromatography of the bulk product gave *trans*-**3** (1.22 g, 27%), *cis*-**3** (0.36 g, 8%), *trans,trans*-**4** (0.09 g, 4%), and *cis,trans*-**4** (0.20 g, 10%).

Procedure B. To a deaerated suspension of dibromide **1**[13] (3.18 g, 10 mmol) and 2-naphthol (2.88 g, 20 mmol) in water (200 mL) was added 10 M aqueous NaOH (3 mL, 30 mmol), and the heterogenous reaction mixture was stirred and heated at 50 °C for 24 h. To the cooled mixture were added ethyl acetate (150 mL) and 5 M aqueous HCl (100 mL), and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (2 × 50 mL), and the combined organic extracts were dried over $MgSO_4$. After evaporation a solid residue (5.08 g) was obtained. A small sample (50 mg) was acetylated (vide infra) and subjected to HPLC analysis [**2** (40%), *trans*-**3** (10%), *cis*-**3** (17%), *trans,trans*-**4** (7%), *cis,trans*-**4** (17%), and *cis,cis*-**4** (11%)]. Flash chromatography of the bulk product gave *trans*-**3** (0.37 g, 8%), *cis*-**3** (1.03 g, 23%), *trans, trans*-**4** (0.11 g, 6%), *cis,trans*-**4** (0.31 g, 16%), and *cis,cis*-**4** (0.22 g, 11%).

***trans*-3**: mp 335−337 °C (ethyl acetate); ^1H NMR δ 5.12 (s, 2 H), 5.35 (s, 2H), 7.22−8.01 (m, 16 H); ^{13}C NMR δ 111.91, 113.94, 117.89, 123.98, 124.40, 125.01, 125.68, 127.33, 128.48, 128.83, 129.40, 131.22, 133.23, 143.23, 152.17; EI MS *m/z* (rel intensity) 444 (M^+, 100), 271 (13), 255 (13), 215 (11); FAB MS *m/z* (rel intensity) 445 ($M^+ + 1$, 69), 444 (M^+, 100), 301 (40). Anal. Calcd for $C_{30}H_{20}O_6 + {}^1/_2H_2O$: C, 79.45; H, 4.67. Found: C, 80.02; H, 4.54.

Tetraacetate of *trans*-3: mp 257−258 °C (ethyl acetate−petroleum ether); ^1H NMR δ 1.82 (s, 6 H), 2.09 (s, 6 H), 7.23−8.04 (m, 16 H); ^{13}C NMR δ 19.92, 20.60, 121.99, 122.57, 125.82, 126.28, 126.41, 126.53, 126.57, 126.88, 128.01, 129.88, 131.27, 131.50, 133.09, 140.56, 146.89, 168.06, 169.57; EI MS *m/z* (rel intensity) 612 (M^+, 13), 570 ($C_{36}H_{26}O_7$, 40), 528 ($C_{34}H_{24}O_6$, 63), 486 ($C_{32}H_{22}O_5$, 63), 444 ($C_{30}H_{20}O_4$, 100). Anal. Calcd for $C_{38}H_{28}O_8$: C, 72.37; H, 4.79. Found: C, 72.47; H, 4.53.

***cis*-3**: mp 300−302 °C (ethyl acetate); ^1H NMR δ 5.34 (s, 2 H), 5.76 (s, 2 H), 7.24−8.01 (m, 16 H); ^{13}C NMR δ 112.98, 114.30, 117.98, 123.89, 124.51, 124.94, 125.27, 127.27, 128.36, 129.01, 129.27, 130.97, 133.49, 143.27, 152.59; EI MS *m/z* (rel intensity) 444 (M^+, 100), 271 (10), 215 (8); FAB MS *m/z* (rel intensity) 462 ($M^+ + H_2O$, 11), 445 ($M^+ + 1$, 99), 444 (M^+, 100), 301 (40), 215 (27). Anal. Calcd for $C_{30}H_{20}O_4$: C, 81.07; H, 4.54. Found: C, 80.88; H, 4.51.

Tetraacetate of *cis*-3: mp 292−294 °C (ethyl acetate−petroleum ether); ^1H NMR δ 1.83 (s, 6 H), 2.00 (s, 6 H), 7.25−8.04 (m, 16 H); ^{13}C NMR) δ 19.97, 20.56, 121.92, 122.54, 125.89, 126.28, 126.32, 126.41, 126.53, 127.09, 128.0, 129.84, 131.29, 131.48, 133.20, 140.52, 146.78, 168.03, 169.40; EI MS *m/e* (rel intensity) 612 (M^+, 10), 570 ($C_{36}H_{26}O_7$, 26), 528 ($C_{34}H_{24}O_6$, 34), 486 ($C_{32}H_{22}O_5$, 45), 444 ($C_{30}H_{20}O_4$, 100). Anal. Calcd for $C_{38}H_{28}O_8 + H_2O$: C, 72.37; H, 4.79. Found: C, 72.51; H, 4.83.

***trans,trans*-4**: mp 289−291 °C (ethyl acetate); ^1H NMR δ 5.5 (bs, 6 H), 7.24−8.02 (m, 20 H);^{13}C NMR δ 111.77, 113.36, 115.26, 117.88, 124.04, 124.50, 124.93, 125.31, 125.41, 125.47, 127.42, 128.32, 128.59, 128.97, 129.43, 131.29, 133.26, 142.76, 143.08, 152.26; EI MS *m/z* (rel intensity) 602 (M^+, 100), 368 (11), 257 (12); FAB MS *m/z* (rel intensity) 603 ($M^+ + 1$, 63), 602 (M^+, 100), 460 (26), 301 (63), 271 (74). Anal. Calcd for $C_{40}H_{26}O_6 + 2H_2O$: C, 75.22; H, 4.75. Found: C, 75.08; H, 4.25.

Hexaacetate of *trans,trans*-4: mp 304−306 °C (ethyl acetate−petroleum ether); ^1H NMR δ 1.86 (s, 6 H), 2.04 (s, 6 H), 2.10 (s, 6 H), 7.24−8.05 (m, 20 H); ^{13}C NMR) δ 19.96, 19.99, 20.61, 121.98, 122.53, 125.54, 126.16, 126.55 (2×), 126.72, 126.76, 126.93 (2×), 128.06, 128.85, 129.96, 131.04, 131.30, 131.52, 133.08, 140.67, 140.70, 146.89, 168.11, 168.24, 169.55; EI MS *m/z* (rel intensity) 854 (M^+, 16), 812 ($C_{50}H_{36}O_{11}$, 54), 770 ($C_{48}H_{34}O_{10}$, 57), 728 ($C_{46}H_{32}O_9$, 66), 686 ($C_{44}H_{30}O_8$, 58), 644 ($C_{42}H_{28}O_7$, 30), 602 ($C_{40}H_{26}O_6$, 100). Anal. Calcd for $C_{52}H_{38}O_{12} + 2H_2O$: C, 70.11; H, 4.73. Found: C, 69.61; H, 4.30.

***cis,trans*-4**: mp 246−248 °C (ethyl acetate); ^1H NMR δ 5.28−5.97 (bs, 6 H), 7.18−8.00 (m, 20 H); ^{13}C NMR δ 112.21, 112.63, 113.37, 114.24, 114.88, 115.28, 117.83, 118.18, 123.77, 123.83, 124.55, 124.78, 124.90, 124.95 (3×), 125.06, 125.10, 125.18, 125.29, 127.04, 127.22, 128.30, 128.70, 128.86, 129.00, 129.02, 129.19, 129.22, 129.28, 130.82, 130.90, 133.39, 133.54, 142.76, 143.07, 143.13, 143.49, 151.97, 152.42; EI MS *m/z* (rel intensity) 602 (M^+, 100), 271 (10); FAB MS *m/z* (rel intensity) 620 ($M^+ + H_2O$, 12), 603 ($M^+ + 1$, 100), 602 (M^+, 98), 460 (15), 301 (33), 271 (33), 215 (96). Anal. Calcd for $C_{40}H_{26}O_6 + {}^1/_2H_2O$: C, 78.55; H, 4.45. Found: C, 78.84; H, 4.29.

(13) Zincke, T.; Fries, K. *Liebigs Ann. Chem.* **1904**, *334*, 342.

Hexaacetate of *cis,trans*-4: mp 322−325 °C (ethyl acetate−petroleum ether); ^{1}H NMR δ 1.84 (s, 3 H), 1.85 (s, 3 H), 1.95 (s, 3 H), 2.02 (s, 3 H), 2.06 (s, 3 H), 2.11 (s, 3H), 8.06 (bd, 2 H), 7.97 (bt, 2 H), 7.25−7.54 (m, 16 H); ^{13}C NMR δ 19.88, 19.94, 19.98, 20.06, 20.56, 20.62, 121.98 (2×), 122.41, 122.50, 125.33, 125.60, 125.86, 125.91, 126.24, 126.34, 126.43, 126.55 (2×), 126.62, 126.67, 126.69, 126.78, 126.82, 126.87, 126.93, 126.98, 127.11, 128.03 (2×), 129.89, 129.95, 131.07, 131.23, 131.31, 131.33, 131.49, 131.50, 133.07, 133.14, 140.58, 140.63, 140.69, 140.71, 146.79, 146.88, 167.99, 168.06 (2×), 168.12, 169.35, 169.56; EI MS *m/z* (rel intensity) 854 (M^+, 12), 812 ($C_{50}H_{36}O_{11}$, 44), 770 ($C_{48}H_{34}O_{10}$, 45), 728 ($C_{46}H_{32}O_9$, 54), 686 ($C_{44}H_{30}O_8$, 56), 644 ($C_{42}H_{28}O_7$, 38), 602 ($C_{40}H_{26}O_6$, 100). Anal. Calcd for $C_{52}H_{38}O_{12} + {}^1/_2H_2O$: C, 72.30; H, 4.55. Found: C, 72.36; H, 4.51.

***cis,cis*-4**: mp 324−326 °C (ethyl acetate); ^{1}H NMR δ 5.58 (s, 2 H), 5.74 (s, 2 H), 5.99 (s, 2 H), 7.21−8.01 (m, 20 H); ^{13}C NMR δ 112.3, 114.14, 115.33, 118.38, 123.98, 124.46, 124.96, 125.09, 125.22, 125.30, 127.30, 128.36, 129.01, 129.20, 129.41, 131.03, 133.49, 142.16, 142.85, 152.27; EI MS *m/z* (rel intensity) 602 (M^+, 100), 460 (6), 271 (6); FAB MS *m/z* (rel intensity) 620 ($M^+ + H_2O$, 10) 603 ($M^+ + 1$, 100), 602 (M^+, 100), 460 (14), 301 (36), 271 (25). Anal. Calcd for $C_{40}H_{26}O_6 + 2H_2O$: C, 75.22; H, 4.75. Found: C, 75.99; H, 4.28.

Hexaacetate of *cis,cis*-4: mp 246−248 °C (ethyl acetate−petroleum ether); ^{1}H NMR δ 1.84 (s, 6 H), 1.98 (s, 6 H), 2.02 (s, 6 H), 7.26−8.05 (m, 20 H); ^{13}C NMR δ 19.95, 19.98, 20.57, 121.97, 122.43, 125.37, 125.91, 126.33, 126.43, 126.60, 126.72, 126.78, 126.93, 127.11, 128.03, 129.88, 131.23, 131.35, 131.49, 133.16, 140.58, 140.62, 146.79, 167.92, 168.09, 169.39; EI MS *m/z* (rel intensity) 854 (M^+, 2), 812 ($C_{50}H_{36}O_{11}$, 19), 770 ($C_{48}H_{34}O_{10}$, 24), 728 ($C_{46}H_{32}O_9$, 32), 686 ($C_{44}H_{30}O_8$, 45), 644 ($C_{42}H_{28}O_7$, 38), 602 ($C_{40}H_{26}O_6$, 100). Anal. Calcd for $C_{52}H_{38}O_{12} + H_2O$: C, 71.52; H, 4.62. Found: C, 71.82; H, 4.46.

Triacetate of 4-Bromo-2,3,2′-trihydroxy-1,1′-binaphthyl (7). Dibromide **1**[13] (48 mg, 0.15 mmol) and 2-naphthol (43 mg, 0.3 mmol) were dissolved in methanol (2.5 mL), *t*-BuOK (45 mg, 0.4 mmol) was added, and the reaction mixture was heated at 50 °C for 15 min and acetylated (vide infra). The crude product was separated on a preparative HPLC column, and the triacetate of **7** was isolated (15 mg, 22%): mp 150−153 °C (ethyl acetate); ^{1}H NMR δ 1.84 (s, 3 H), 1.98 (s, 3 H), 2.41 (s, 3 H), 7.16 (m, 1 H), 7.20 (dq, 1 H), 7.30 (m, 1 H), 7.32 (m, 1 H), 7.44 (d, 1 H), 7.47 (m, 1 H), 7.60 (m, 1 H), 7.92 (m, 1H), 8.01 (dd, 1 H), 8.36 (m, 1H); ^{13}C NMR δ 19.81, 20.45, 20.62, 117.20, 121.80, 121.95, 125.90, 126.02, 126.20, 126.71, 127.03, 127.28, 127.33, 127.67, 127.98, 130.00, 130.66, 131.39, 131.70, 132.96, 140.54, 140.58, 146.78, 167.50, 167.86, 169.55; EI MS *m/z* (rel intensity) 506 (M^+, 16), 464 (40), 422 (49), 380 (100); HRMS for $C_{26}H_{19}BrO_6$, observed mass 506.026.

4,4′-Dibromo-2,3,2′,3′-tetrahydroxy-1,1′-binaphthyl (12). Procedure A. A suspension of 2,3,2′,3′-tetrahydroxy-1,1′-binaphthyl[14] (2.2 g, 6.91 mmol) in acetic acid (20 mL) was heated to 55 °C under vigorous stirring, and bromine (2.2 g, 13.8 mmol) in acetic acid (10 mL) was added during 1 h. The reaction mixture was stirred for 30 min and cooled down and the acetic acid evaporated. Chloroform (100 mL) was added, and the insoluble residue was filtered off. The clear chloroform solution was concentrated to ca. 20 mL and left overnight. The deposited crystals of **12** were collected, washed with a small amount of cold chloroform, and dried (2.97 g, 62%): mp 214−216 °C; ^{1}H NMR δ 5.66 (bs, 2 H), 6.26 (bs, 2 H), 7.13 (m, 2 H), 7.23 (m, 2 H), 7.48 (m, 2 H), 8.14 (m, 2 H); ^{13}C NMR δ 107.01, 113.29, 124.99, 125.71, 125.95, 125.99, 127.83, 128.83, 141.85, 142.39; EI MS *m/z* (relative intensity) 478 (M^++ 4, 50), 476 (M^++ 2, 100), 474 (M^+, 50), 398 (45), 396 (50), 82 (90), 80 (86). Anal. Calcd for $C_{20}H_{12}Br_2O_4$: C, 50.45; H, 2.54; Br, 33.57. Found: C, 50.55; H, 2.76; Br, 33.42.

Tetraacetate of 12: mp 140−145 °C; ^{1}H NMR δ 1.94 (s, 6 H), 2.40 (s, 6 H), 7.19 (m, 2 H), 7.34 (m, 2 H), 7.60 (m, 2 H), 8.34 (m, 2 H); ^{13}C NMR δ 19.91, 20.46, 117.97, 124.42, 126.73, 127.32, 127.59, 127.86, 130.62, 131.33, 140.53, 140.66, 167.44, 167.89; EI MS *m/z* (relative intensity) 642 (M^+, 9), 640 (18), 638 (9), 603 (21), 601 (40), 599 (21), 561 (36), 559 (71), 557 (36), 519 (26), 517 (50), 515 (26), 478 (52), 476 (100), 474 (52). Anal. Calcd for $C_{28}H_{20}Br_2O_8$: C, 52.20; H, 3,13; Br, 24.81. Found: C, 51.99; H, 3.11; Br, 24.69.

Procedure B (Base-Catalyzed Disproportionation of 1). Dibromide **1**[13] (31.8 mg, 0.1 mmol) was dissolved in toluene (1 mL), *t*-BuONa (7.2 mg, 0.05 mmol) was added, and the reaction mixture was stirred at 50 °C for 1 h. The formation of **12** as the main product was confirmed by HPLC comparison of the acetylated samples, obtained by procedures A and B.

Equilibration of Stereoisomers. An appropriate stereoisomer of **3** or **4** (0.1 mmol) was heated in dry pyridine (0.5 mL) at 115 °C for 12 h under argon. After cooling, the reaction mixture was acetylated (vide infra) and subjected to HPLC analysis.

Acetylation. An appropriate naphthol (0.2 mmol) was dissolved in pyridine (2 mL), and acetic anhydride (1 mL) was added. After 2 h at room temperature, ethyl acetate (10 mL) and 5 M 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 × 5 mL), and dried over $MgSO_4$. After evaporation of volatiles the crude acetate was purified by crystallization.

Solvent and Counterion Effects (Tables 1−5). Dibromide **1**[13] (32 mg, 0.1 mmol) or **12** (47 mg, 0.1 mmol) and 2-naphthol (29 mg, 0.2 mmol) were dissolved or suspended in a given solvent (1 mL) containing in some cases 18-crown-6 ether (0.4 mmol), and an appropriate alkali metal *tert*-butoxide (0.3 mmol) was added. The reaction mixture was stirred at 50 °C (unless otherwise indicated in the tables) for a convenient time period (4−60 h), diluted with ethyl acetate (5 mL), and acidified with a 5 M aqueous solution of HCl (10 mL). The organic extract was dried over $MgSO_4$, filtered, and adjusted to 10 mL. An aliquot (0.5 mL) was treated with pyridine (100 μL) containing an internal standard and acetic anhydride (50 μL). The reaction mixture was heated at 50 °C for 30 min and cooled, 5 M 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 was subjected to HPLC analysis.

X-ray Analysis. Single crystals of *trans*-**3** were grown at room temperature by vapor diffusion of pentane into the concentrated acetone solution. Considerable difficulties were encountered in obtaining single crystals of *cis*-**3**. With a number of solvents and their combinations, solvent molecules exhibited the notorious tendency to penetrate into crystals, leading to materials of low diffraction power and air instability. Eventually, acceptable crystals were formed by very slow diffusion of petroleum ether into a solution in ethyl acetate at 0−5 °C. By X-ray analysis, these crystals were shown to contain seriously disordered solvent molecules. The disorder, together with poor diffraction by the crystals, resulted in low precision of this structure determination (R = 0.13); the chemical picture is, however, unequivocal.[15]

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Supporting Information Available: ^{13}C and ^{1}H NMR shift assignments for the bi-, ter-, and quaternaphthalene derivatives (4 pages). This material is contained in libraries on microfiche, immmediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1989**, *54*, 3007.

(15) Atomic coordinates and bond lengths and angles for the compounds *trans*-**3** and *cis*-**3** have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.