Atropisomerization Barriers of Configurationally Unstable Biaryl Compounds, Useful Substrates for Atroposelective Conversions to Axially Chiral Biaryls†

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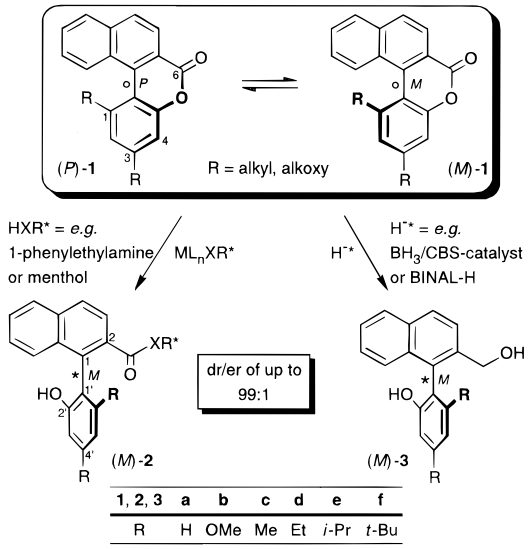
Configurationally unstable biaryl lactones of type (*M*)-**1** ⇌ (*P*)-**1** and ring-opened 2-acyl-2′-hydroxy biaryl compounds of type (*M*)-**4** ⇌ (*P*)-**4** are versatile precursors for the atroposelective preparation of axially chiral biaryls. The activation barriers of their atropisomerization process, which constitutes a fundamental precondition for the dynamic kinetic resolution, were determined by dynamic NMR spectroscopy for rapid processes and by HPLC-monitored racemization of enantiomerically enriched material for smaller interconversion rates. For the lactones, the free activation energies $\Delta G^{\ddagger}_{298}$ increase with the steric demand of the substituent R *ortho* to the biaryl axis in the series H < OMe ($t_{1/2} \approx$ ms) < Me ($t_{1/2} \approx$ s) < Et < *i*-Pr ($t_{1/2} \approx$ min) < *t*-Bu ($t_{1/2} \approx$ d). The formally ring-opened 2-acyl-2′-hydroxy biaryls, which interconvert via the lactol isomers **5** as the cyclic (and thus configurationally less stable) intermediates, have a significantly slower atropisomerization rate as a result of the high loss in activation entropy $\Delta S^{\ddagger}$ as a consequence of the required intermediate ring closure **4** → **5**.

Introduction

A most efficient method for the stereoselective construction of axially chiral biaryls is the "lactone approach",[1] which is based on the dynamic kinetic resolution of configurationally unstable biaryl lactones[2] of type **1** (Scheme 1). As a consequence of the steric repulsion between the naphthalene moiety and the *ortho* substituent R in the phenolic part, the lactones **1** are helically distorted and thus exist as a racemic mixture of their two enantiomeric forms, (*M*)-**1** and (*P*)-**1**.[1,3] The bridging lactone function, however, dramatically lowers the atropisomerization barrier compared with that of the ring-opened target molecules, so that the two lactone enantiomers interconvert more or less rapidly. Out of this enantiomeric equilibrium, **1** can be cleaved atropselectively by using chiral *O*- or *N*-nucleophiles[4] or hydride transfer reagents[5] to give the corresponding esters, amides, or alcohols, **2** or **3**, in excellent atropisomeric ratios of up to 99:1.[1] The scope of this method has meanwhile been proven in the atroposelective synthesis of a broad series of naturally occurring biaryls and axially chiral auxiliaries.[1]

Scheme 1



Like the lactones **1**, but in contrast to the amides and esters **2**,[6] the formally related 2-acyl-2′-hydroxy biaryls

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(1) (a) Bringmann, G.; Breuning, M.; Tasler, S. *Synthesis* **1999**, 525. (b) Bringmann, G.; Tasler, S. In *Current Trends in Organic Synthesis*; Scolastico, C., Nicotra, F., Eds.; Plenum Publishing Corporation: New York, 1999; p 105. (c) Bringmann, G.; Schupp, O. *S. Afr. J. Chem.* **1994**, *47*, 83.

(2) Bringmann, G.; Hartung, T.; Göbel, L.; Schupp, O.; Ewers, C. L. J.; Schöner, B.; Zagst, R.; Peters, K.; von Schnering, H. G.; Burschka, C. *Liebigs Ann. Chem.* **1992**, 225.

(3) For the now recommended *M*/*P*-denotion for axially chiral compounds, see: Helmchen, G. In *Methods of Organic Chemistry* (Houben Weyl), 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E21a, p 11.

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(5) (a) Bringmann, G.; Hartung, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 761. (b) Bringmann, G.; Hartung, T. *Tetrahedron* **1993**, *49*, 7891. (c) Bringmann, G.; Breuning, M. *Tetrahedron: Asymmetry* **1999**, *10*, 385.

(6) Since a "chemical" atropisomerization via cyclic intermediates as for the acyl compounds **4** is less feasible for the corresponding less reactive esters and amides **2**, these compounds are usually configurationally stable (for an exception involving esters of MeOH as a very small alcohol, see: Bringmann, G.; Reuscher, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1672).

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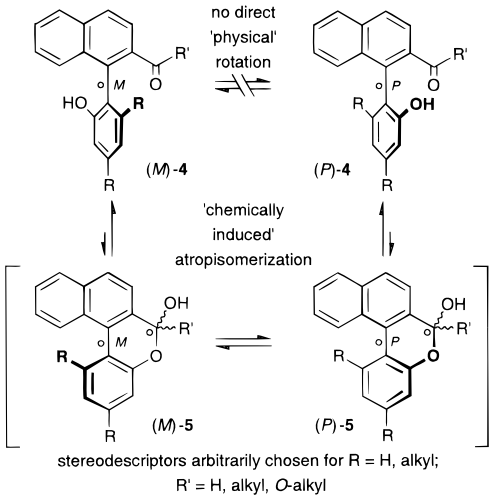
Scheme 2



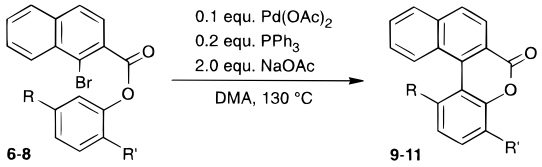
4, as the primary cleavage products of **1** with *H*- and *C*-nucleophiles, are configurationally unstable at the axis (Scheme 2).[1] Their atropisomerization, however, does not proceed via a direct, "physical" rotation around the biaryl axis but is a consequence of a ring-closure → atropisomerization → ring-opening process (*M*)-**4** ⇌ (*M*)-**5** ⇌ (*P*)-**5** ⇌ (*P*)-**4**, which involves the bridged and thus again configurationally unstable lactols **5**.[7−9] Like the lactones **1**, biaryls of type **4** have also been used successfully as precursors for atroposelective biaryl synthesis, e.g., for atroposelective CBS-reductions,[10] including applications in natural products synthesis.[11]

The configurational instability of the biaryl lactones **1** and of the hydroxyaldehyde/lactol intermediates, as well as related 2-acyl-2′-hydroxy biaryls in general, is thus a fundamental basis for these atropenantiomer-differentiating reactions. For this reason, an investigation of the isomerization barriers of these processes is a crucial precondition for directed further improvements of this remarkably efficient methodology. In this paper, we thus report on the atropisomerization barriers of several configurationally unstable biaryls of types **1**, **4**, and **5**, which vary by the degree of steric hindrance at the axis (due to the different sizes of the *ortho* substituent R), the nature of the bridge (lactone vs lactol), and the mechanism of isomerization (merely "physical" rotation around the axis, cp. Scheme 1, vs the "chemical" three-step mechanism of the ring-opened biaryls, cp. Scheme 2). In the case of the configurationally unstable lactones, the activation parameters were determined by dynamic NMR spectroscopy (DNMR) and for the enantiomerically enriched, less rapidly isomerizing biaryls prepared by HPLC measurement of the rates of decrease in enantiomeric purity. For the former purpose, new lactones were synthesized, equipped with suitably located ethyl or isopropyl groups as the "DNMR probes".

Results and Discussion

1. Synthesis of Biaryl Lactones 9−11. For the observation of enantiomerization processes via DNMR,

Scheme 3



Ester	**6d**	**6e**	**7b**	**7c**	**8a**	**8b**	**8c**	**8d**
Lactone	**9d**	**9e**	**10b**	**10c**	**11a**	**11b**	**11c**	**11d**
R	Et	*i*-Pr	OMe	Me	H	OMe	Me	Et
R'	Me	Me	Et	Et	*i*-Pr	*i*-Pr	*i*-Pr	*i*-Pr
yield [%]	73	70	73	62	77	84	76	69

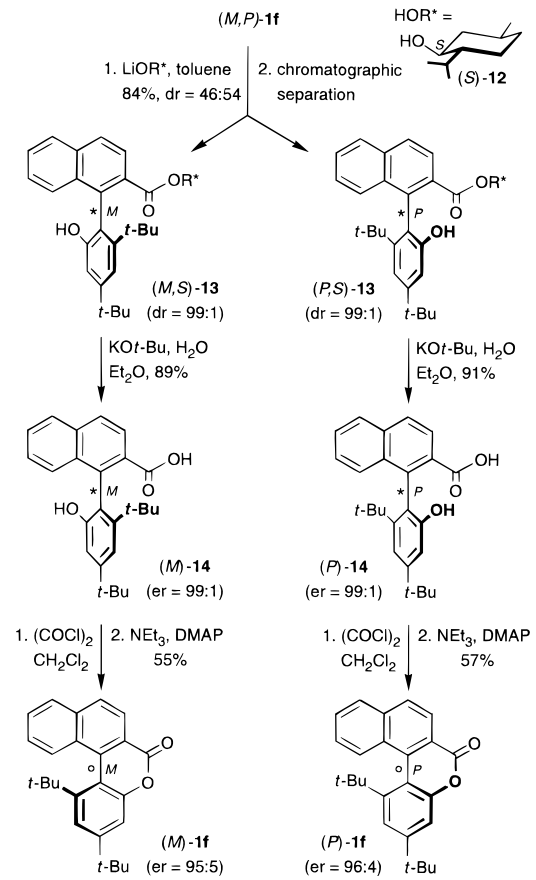
the presence of a pair of diastereotopic groups in the molecule, which serve as an internal DNMR probe, is essential. Among the standard lactones **1** (Scheme 1) previously introduced,[2] only two representatives, **1d** (R = Et) and **1e** (R = *i*-Pr), fulfill this basic requirement. For this reason, we synthesized a new type of biaryl lactones **9**−**11** with two different substituents in the phenolic part providing three advantages simultaneously (Scheme 3): first, the variation of the *ortho* substituent R allows a stepwise enhancement of the steric hindrance at the biaryl axis; second, the dynamic behavior is monitored by the diastereotopic group R′ (or, alternatively, by R); and third, with the 1,4-substitution pattern chosen, a regioselectivity in the coupling of the esters **6**−**8** is guaranteed by blocking one of the two *ortho* positions in the phenolic part. By Pd-catalyzed aryl coupling the preparation of the lactones **9** (R′ = Me), **10** (R′ = Et), and **11** (R′ = *i*-Pr) was achieved smoothly and in good yields (62−84%).

2. Preparation of the Enantiomerically Enriched Biaryls. The activation parameters of the more hindered, less rapidly atropisomerizing biaryls were determined by HPLC measurement of the racemization rates of (almost) enantiomerically pure samples, which were prepared in different ways. Lactone (*P*)-**9e** (see Scheme 3) was obtained by simple crystallization of racemic **9e** from petroleum ether/dichloromethane,[12] whereas the sterically even more highly hindered and thus only very slowly helimerizing lactones (*M*)-**1f** and (*P*)-**1f** were synthesized in a three-step procedure starting from racemic **1f** (Scheme 4). Ring cleavage with the lithium alkoxide of (1*S*)-menthol [(*S*)-**12**] gave the configurationally stable diastereomeric esters (*M*,*S*)-**13** and (*P*,*S*)-**13** (dr = 54:46, 84% yield), which were separated by column chromatography.[13] Hydrolysis of the two separate atropisomers gave the acids (*P*)-**14** and (*M*)-**14** (er = 99:1 each), which were both recyclized back to the now enantiomerically enriched lactones (*P*)-**1f** (er = 96:4) and (*M*)-**1f** (er = 95:5), respectively.

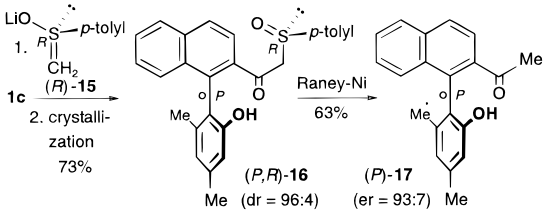
The enantiomerically enriched biaryl acetophenone derivative (*P*)-**17** (Scheme 5) was obtained by ring cleavage of the configurationally unstable racemic lactone **1c** with the homochiral lithium sulfoxide (*R*)-**15** and subsequent crystallization of the crude diastereomeric mixture, which gave the *β*-ketosulfoxide (*P*,*R*)-**16**[14] (dr = 96:4) in

(7) Bringmann, G.; Hartung, T. *Liebigs Ann. Chem.* **1994**, 313.
(8) Bringmann, G.; Breuning, M.; Endress, H.; Vitt, D.; Peters, K.; Peters, E.-M. *Tetrahedron* **1998**, *54*, 10677.
(9) Bringmann, G.; Vitt, D.; Kraus, J.; Breuning, M. *Tetrahedron* **1998**, *54*, 10691.
(10) Bringmann, G.; Breuning, M. *Synlett* **1998**, 634.
(11) Bringmann, G.; Saeb, W.; Rübenacker, M. *Tetrahedron* **1999**, *55*, 423.
(12) Peters, K.; Peters, E.-M.; von Schnering, H. G.; Bringmann, G.; Schupp, O. *Z. Kristallogr.* **1995**, *210*, 49.
(13) For a directed atropisomer-selective synthesis of **1f** by kinetic resolution of *rac*-**1f** using chiral *H*-nucleophiles, see ref 1a and: Bringmann, G.; Hinrichs, J.; Kraus, J.; Wuzik, A.; Schulz, T. *J. Org. Chem.*, submitted for publication.
(14) Peters, K.; Peters, E.-M.; Bringmann, G.; Schöner, B. *Z. Kristallogr. NCS* **1998**, *213*, 337.

Scheme 4



Scheme 5



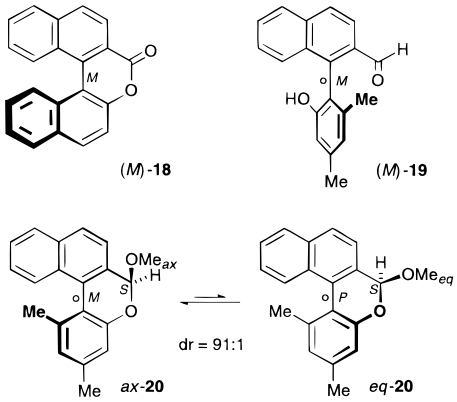
73% yield. Reductive removal of the sulfinyl group in (*P*,*R*)-**16** led to the target biaryl (*P*)-**17** with an er of 93:7 (yield 63%).

Upon standing in solution, the configurationally unstable biaryls (*M*)-**1f**, (*P*)-**1f**, (*P*,*R*)-**16**, and (*P*)-**17** started racemizing.

The biaryl compounds (*M*)-**18** and (*M*)-**19** (Scheme 6, top) were prepared according to literature procedures.[7,15] As a closely related analogue of the nondetectable lactol intermediates in the atropisomerization process of **19** (cp. Scheme 2), the *O*-protected and thus ring-opening hindered acetal **20** was synthesized.[8] In this case, the interconversion *ax*-**20** ⇌ *eq*-**20** constitutes a diastereomerization process, due to the additional stereocenter at the acetalic carbon atom (Scheme 6, bottom; only the 6-(*S*)-enantiomers are shown). Of the two diastereomeric forms, the isomer *ax*-**20**, which has the methoxy group in an axial position, is more stable in the equilibrium (dr = 91:9) than *eq*-**20**.[8]

3. Measurement of the Rate Constants. A precondition for DNMR investigations is a change in the spectra

Scheme 6



at different temperatures due to the presence of appropriate substituents (here Et or *i*-Pr), with nuclei that may serve as probes for a chiral vs achiral character of the molecules, by their diastereotopic vs enantiotopic character within the time scale of the exchange process. Depending on the steric demand of the substituent R *ortho* to the stereogenic axis, the ^{1}H DNMR spectra of compounds **9**−**11** showed different behaviors of these nuclei at room temperature: The signals of the diastereotopic protons in **10b**, **11a**, and **11b** were found to be isochronous (and thus formally, i.e., on an average, enantiotopic), indicating a fast exchange relative to the NMR time scale, while those in **1d**, **9d**, **9e**, **10c**, **11c**, and **11d** are clearly separated as the result of a very slow rate of exchange (or even configurational stability).

For the investigated lactones **11a** (R = H) and **11b** (R = OMe), the limit of slow exchange regimes (i.e., to attain decoalescence) could not be reached. The rates of **1d**−**f** (R = Et, *i*-Pr, and *t*-Bu), by contrast, were too slow for observation by DNMR. The signals of the diastereotopic ethyl CH_2 protons in **1e** did not appear completely separated because of the small shift difference even in the slow exchange region but remained superimposed, so that rate constants could not be evaluated from the DNMR spectra. The same problem occurred for the diastereotopic [$CH(CH_3)_2$] protons of the *i*-Pr group of **9d**.

The spectra of **10b**, **10c**, **11c**, **11d**, and **9e**, by contrast, proved to be well suited for DNMR investigations and were thus carefully simulated and iterated by line-shape analysis[16] to give the rate constants. Exemplarily for lactone **11d**, which is equipped with both types of probes, H atoms (R = Et) and methyl groups (R = *i*-Pr), selected parts of the experimental and the iterated proton spectra are depicted in Figure 1.

The activation parameters of the highly enantiomerically enriched biaryls **1f**, **9e**, and **17** were determined by HPLC measurements of the decrease of the er at different temperatures.[17] The quantitative evaluation of the activation parameters was done using a first-order rate equation, even for the ring-opened compounds **17** and **19** despite their three-step atropisomerization mechanism (cp. Scheme 2), because the population of the intermediate lactols of type **5** was undetectably low and thus negligible.[8]

(15) Bringmann, G.; Schöner, B.; Schupp, O.; Peters, K.; Peters, E.-M.; von Schnering, H. G. *Liebigs Ann. Chem.* **1994**, 91.

(16) (a) Binsch, G. *Band-Shape Analysis.* In *Dynamic Magnetic Resonance Spectroscopy*; Jackman, L. M., Ed.; Academic Press: New York 1975; p 45. (b) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press: New York 1980.

(17) For similar investigations on **18** and **19**, see refs 7 and 15, respectively.

Table 1. Activation Parameters[a] and Half-Lives ($t_{1/2}$) at 298 K of the Atropisomerization of Configurationally Unstable Biaryls

biaryl compound	*ortho* substituent next to axis	method	$\Delta H^{\ddagger}$ [kJ mol^{-1}]	$\Delta S^{\ddagger}$ [J K^{-1} mol^{-1}]	$\Delta G^{\ddagger}_{298}$ [kJ mol^{-1}]	$t_{1/2}$
11a	H	DNMR		*b*		
10b	OMe	DNMR	26.6 ± 0.3	−92.9 ± 0.2	54.4 ± 0.1	0.4 ms
11b	OMe	DNMR		*b*		
10c	Me	DNMR	57.9 ± 1.1	−47.4 ± 3.3	72.1 ± 0.2	0.5 s
11c	Me	DNMR	43.9 ± 0.4	−101 ± 1.2	73.9 ± 0.1	1.0 s
11d	Et	DNMR	71.8 ± 2.7[c]	−37.7 ± 7.1	83.0 ± 0.6	39.5 s
			75.3 ± 1.5[d]	−28.0 ± 4.0	83.7 ± 0.3	52.4 s
18[15]	"benzo"	HPLC	84.5 ± 0.9	−22.3 ± 3.1	91.1 ± 1.8	17.3 min
9e	*i*-Pr	DNMR	82.1 ± 9.7	−34.1 ± 35.1	92.3 ± 20.2	28.1 min
1f	*t*-Bu	HPLC	91.6 ± 3.6	−43.1 ± 10.8	104.4 ± 6.8	2.2 d
20 (*eq* → *ax*)	Me	DNMR	61.1 ± 0.4	−60.8 ± 3.1	79.2 ± 1.2	8.5 s
(*ax* → *eq*)			53.5 ± 0.2	−66.0 ± 1.1	73.2 ± 0.5	0.8 s
19[7]	Me	HPLC	54.9	−150	98.8	6.5 h
17	Me	HPLC	51.3 ± 0.3	−161 ± 1.0	99.2 ± 0.5	7.6 h

[a] The reported errors are statistical errors. [b] Limit of slow exchange could not been reached. [c] Using the ethyl group as the DNMR probe. [d] Using the isopropyl group as the DNMR probe.

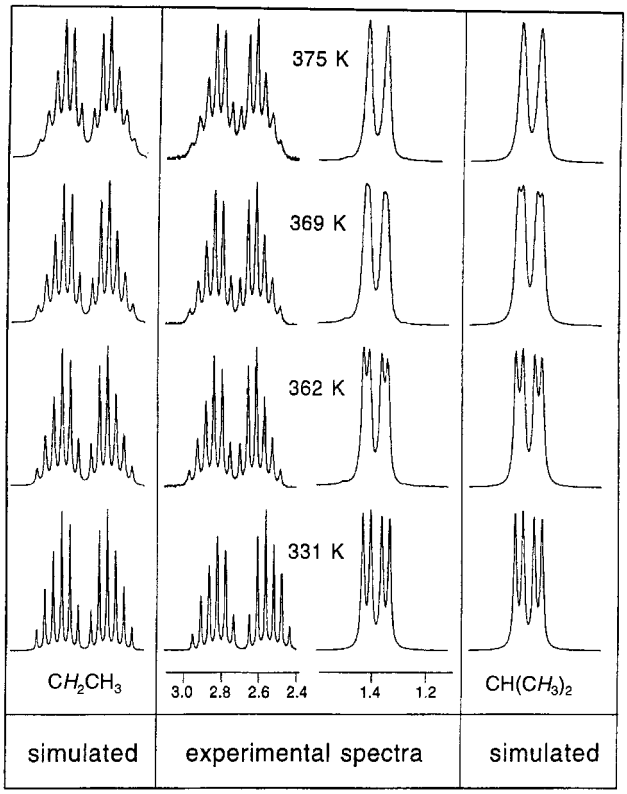


Figure 1. Selected parts of the experimental and iterated ^{1}H NMR spectra of the ethyl group (left side) and the isopropyl group (right side) of **11d** at different temperatures.

For a complete list of the activation parameters thus measured by DNMR and HPLC, see Table 1.

4. Discussion of the Activation Parameters. Exemplarily for the lactones **10c** and **11c**, which have comparable steric constraints at the biaryl axis (R = Me), we have investigated whether different substituents in other positions, here next to the phenolic oxygen, do significantly affect the exchange rate. Such an unfavorable influence was excluded because the free energies of activation $\Delta G^{\ddagger}_{298}$ showed very similar values [**10c** (R′ = Et) $\Delta G^{\ddagger}_{298}$ = 72.1 kJ mol^{-1} and **11c** (R′ = *i*-Pr) $\Delta G^{\ddagger}_{298}$ = 73.9 kJ mol^{-1}].

On this basis, the expected relation between the steric demand of the substituent R *ortho* to the axis and the rate of atropisomerization was found for the lactones. The free energy of activation $\Delta G^{\ddagger}_{298}$ increased within the sequence H < OMe < Me < Et < *i*-Pr < *t*-Bu. The methoxy-substituted compound **10b** showed the smallest measurable $\Delta G^{\ddagger}_{298}$ of 54.4 kJ mol^{-1}. For the lactones with R = alkyl, every carbon unit added raises the free activation energy $\Delta G^{\ddagger}_{298}$ by ca. 10 kJ mol^{-1}, from ca. 73 kJ mol^{-1} for R = Me up to 104 kJ mol^{-1} for R = *t*-Bu. As obvious from the $\Delta G^{\ddagger}_{298}$ value (91.1 kJ mol^{-1}) of the binaphthyl lactone **18**,[15] its annulated additional ring has a steric demand comparable to that of an isopropyl group. Furthermore, this series of activation barriers experimentally found qualitatively agrees with the one theoretically calculated for the lactones **1**.[18]

The influence of the biaryl structure on the atropisomerization rate was investigated for the compounds **10c**, **11c**, **17**, **19**, and **20**, all of which are identical with respect to the presence of a methyl group next to the biaryl axis. The enthalpies of activation $\Delta H^{\ddagger}$ are all in the same order of magnitude, between 44 and 60 kJ mol^{-1}, but the bridged biaryls **10c**, **11c**, and **20** differ remarkably from the ring-opened ones, **17** and **19**, in the entropies of activation $\Delta S^{\ddagger}$ (≥ −100 J K^{-1} mol^{-1} vs < −150 J K^{-1} mol^{-1}) and, thus, also in the free energies of activation ($\Delta\Delta G^{\ddagger}_{298} \approx 25$ kJ mol^{-1}). This jump in $\Delta S^{\ddagger}$ is caused by the different atropisomerization mechanisms. Whereas the enantiomeric forms of the lactones **10c** and **11c** and of the acetal **20** interconvert "physically", by direct rotation around the axis (cp. Scheme 1), the enantiomerization of the acyl compounds **17** and **19** occurs "chemically", via the cyclic lactol species of type **5** (cp. Scheme 2).[7−9] This ring closure strongly reduces the number of degrees of freedom and thus causes higher $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}_{298}$ values, which finally leads to a much slower isomerization process. If the phenolic OH-group in **19** is "sealed", e.g., by *O*-methylation, the "chemical" atropisomerization is blocked, and thus no atropisomerization is observed.[1,7]

Because the acetal **20**, whose structure is closely related to that of lactol **5**, possesses a $\Delta G^{\ddagger}_{298}$ value (73.2−79.2 kJ mol^{-1}) remarkably lower than that of the ring-opened compounds **17** and **19**, (≈ 99 kJ mol^{-1}) and, thus, an interconversion rate (*M*)-**20** ⇌ (*P*)-**20** corresponding to a half-life about 5000 times smaller than that of the

(18) Bringmann, G.; Busse, H.; Dauer, U.; Güssregen, S.; Stahl, M. *Tetrahedron* **1995**, *51*, 3149.

"complete" process of (*M*)-**17** ⇌ (*P*)-**17** and (*M*)-**19** ⇌ (*P*)-**19**, the rate-determining step of the latter atropisomerization processes as depicted in Scheme 2 must be the ring closure and the ring opening, respectively. These observations and the undetectably low concentrations of the intermediate lactol justify the former assumption (vide supra) made for the evaluation of the dynamic HPLC measurements, viz., to treat the overall interconversions of (*M*)-**17** ⇌ (*P*)-**17** and (*M*)-**19** ⇌ (*P*)-**19** as first-order processes.

It is noteworthy that the free activation energy $\Delta G^{\ddagger}_{298}$ of the acetal **20** ($\Delta G^{\ddagger}_{298} \approx 74-79$ kJ mol^{-1}) is very similar to that of corresponding lactones **10c** and **11c** ($\Delta G^{\ddagger}_{298} \approx 73$ kJ mol^{-1}), showing that the hybridization of the carbon atom in the bridge (sp^2 in the lactone group vs. sp^3 in the acetal group) does not remarkably influence the atropisomerization rate.

Conclusions

By variation of the substituents *ortho* to the biaryl axis, the interconversion rates of the lactones can be modified stepwise. The atropisomerization barriers measured increase with the steric demand of the substituents in the series H < OMe < Me < Et < *i*-Pr < *t*-Bu. Corresponding to these rates, the half-lives range from milliseconds (R = OMe) to days (R = *t*-Bu). As a consequence, lactones containing *ortho* substituents R < *i*-Pr can be cleaved atroposelectively to give configurationally stable axially chiral biaryls by a *dynamic* kinetic resolution (see introduction), whereas the largely helically distorted lactones with R = *t*-Bu (or even more bulky residues) are useful precursors for "normal" (i.e., nondynamic) kinetic resolutions.[1] The configurationally unstable ring-opened 2-acyl-2′-hydroxy biaryls, which show a slower isomerization as a result of the smaller entropies of activation, are suited for dynamic kinetic resolutions only if R has a very low steric demand (typically R = H).[10]

Experimental Section

Sources. Compounds **18**,[15] **19**,[8] **20**,[7] 1-bromo-2-naphthalenecarboxylic acid,[19] 5-ethyl-2-phenol,[20] 5-ethyl-2-methoxyphenol,[21] 2-hydroxy-4-methoxyacetophenone,[22] and 5-ethyl-2-isopropylphenol[23] were prepared according to literature procedures. The esters **6**−**8** were synthesized in analogy to ref 2; for details see Supporting Information.

Instrumentation. NMR: 600 MHz spectrometer equipped with a temperature control assembly (±0.1 K) and a probe head heater; 200 MHz spectrometer with a variable temperature unit (±1 K). HPLC−UV: columns, Chiracel OF (200 mm × 4.6 mm) and Chiracel OD (260 mm × 4.6 mm).

General Procedure for the Preparation of the Lactones 9−11 (2.5−30 mmol Scale). A mixture of the ester **6**, **7**, or **8**[24] (1.0 equiv), $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.2 equiv), and NaOAc (2.0 equiv) was added to *N*,*N*-dimethylacetamide (DMA, 7.5 mL/mmol ester, freshly distilled from CaH_2), and the reaction mixture was heated to 130 °C for 18 h. After removal of the solvent in vacuo, the residue was purified by column chromatographic filtration [charcoal (1 cm), silica gel (20 cm), eluent: petroleum ether → diethyl ether]. Crystallization from dichloromethane/petroleum ether gave the spectroscopically pure lactones **9**−**11** as colorless or slightly yellow solids. Yields are reported in Scheme 3.

1-Ethyl-4-methyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (9d). Mp 149 °C; IR (KBr) ν 3040, 2950, 2900, 1710 cm^{-1}; ^{1}H NMR (200 MHz, [D$_8$]toluene) δ 0.65 (t, 3H, J = 7.4 Hz), 2.30 (s, 3H), 2.22−2.62 (m, 2H), 6.90 (d, 1H, J = 7.9 Hz), 6.98 (d, 1H, J = 7.9 Hz), 7.06−7.24 (m, 2H), 7.40 (d, 1H, J = 8.4 Hz), 7.44 (d, 1H, J = 8.0 Hz), 7.78 (d, 1H, J = 8.2 Hz), 8.25 (d, 1H, J = 8.5 Hz); MS (EI) *m*/*z* 288 (100) [M$^+$], 273 (91) [M$^+$ − CH$_3$], 202 (33), 101 (33). Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 82.92; H, 5.31.

1-Isopropyl-4-methyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (9e). Mp 137−138 °C; IR (KBr) ν 3030, 2970, 2940, 1710 cm^{-1}; ^{1}H NMR (200 MHz, CDC1$_3$) δ 0.62 (d, 3H, J = 6.7 Hz), 1.53 (d, 3H, J = 6.7 Hz), 2.51 (s, 3H), 3.24 (sept, 1H, J = 6.7 Hz), 7.30 (d, 1H, J = 7.8 Hz), 7.38 (d, 1H, J = 7.8 Hz), 7.52 (ddd, 1H, J = 8.5, 7.2, 1.4 Hz), 7.63 (ddd, 1H, J = 8.6, 7.2, 1.2 Hz), 7.90 (d, 1H, J = 8.5 Hz), 7.92 (d, 1H, J = 8.6 Hz), 8.11 (d, 1H, J = 8.6 Hz), 8.28 (d, 1H, J = 8.6 Hz); MS (EI) *m*/*z* 302 (100) [M$^+$], 287 (71) [M$^+$ − CH$_3$], 272 (47) [M$^+$ − C$_2$H$_6$], 259 (38) [M$^+$ − C$_3$H$_7$]. Anal. Calcd for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.43; H, 6.17. Crystallization of the racemic mixture of **9e** from petroleum ether/dichloromethane resulted in crystals of enantiomerically pure (*P*)-**9e** and crystals of (*M*)-**9e**. Atropisomerization experiments were performed on (*P*)-**9e** (absolute configuration known from multiple scattering X-ray experiments).[12,25]

4-Ethyl-1-methoxy-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (10b). Mp 186−187 °C; IR (KBr) ν 3040, 2950, 2920, 1710 cm^{-1}; ^{1}H NMR (250 MHz, CDC1$_3$) δ 1.33 (t, 3H, J = 7.5 Hz), 2.93 (q, 2H, J = 7.5 Hz), 3.80 (s, 3H), 6.88 (d, 1H, J = 8.4 Hz), 7.37 (d, 1H, J = 8.4 Hz), 7.45−7.68 (m, 2H), 7.90 (d, 1H, J = 8.0 Hz), 7.94 (d, 1H, J = 8.5 Hz), 8.04 (d, 1H, J = 8.5 Hz), 8.37 (d, 1H, J = 8.5 Hz); MS (EI) *m*/*z* 304 (67) [M$^+$], 289 (100) [M$^+$ − CH$_3$], 273 (19) [M$^+$ − OCH$_3$], 189 (24). Anal. Calcd for $C_{20}H_{16}O_3$: C, 78.86; H, 5.26. Found: C, 78.58; H, 5.31.

4-Ethyl-1-methyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (10c). Mp 60−62 °C; IR (KBr) ν 3040, 2940, 2850, 1710 cm^{-1}; ^{1}H NMR (200 MHz, [D$_8$]toluene) δ 1.22 (t, 3H, J = 7.5 Hz), 1.88 (s, 3H), 2.59−2.96 (m, 2H), 6.81 (d, 1H, J = 7.8 Hz), 6.97 (d, 1H, J = 7.7 Hz), 7.02−7.27 (m, 2H), 7.41 (d, 1H, J = 8.2 Hz), 7.45 (br. d, 1H, J = 6.8 Hz), 7.58 (br. d, 1H, J = 8.2 Hz), 8.23 (d, 1H, J = 8.5 Hz); MS (EI) *m*/*z* 288 (100) [M$^+$], 273 (75) [M$^+$ − CH$_3$], 202 (28). Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31, H, 5.59. Found: C, 82.53; H, 5.44.

4-Isopropyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (11a). Mp 108 °C; IR (KBr) ν 3030, 2950, 2910, 2850, 1710 cm^{-1}; ^{1}H NMR (200 MHz, CDC1$_3$) δ 1.38 (d, 6H, J = 6.9 Hz), 3.79 (sept, 1H, J = 6.9 Hz), 7.37 (dd, 1H, J = 7.7, 7.7 Hz), 7.49 (dd, 1H, J = 7.7, 1.2 Hz), 7.69 (m, 2H), 7.93 (d, 1H, J = 8.6 Hz), 8.08 (m, 1H), 8.33 (d, 1H, J = 8.6 Hz), 8.35 (d, 1H, J = 7.7 Hz), 8.90 (m, 1H); MS (EI) *m*/*z* 288 (73) [M$^+$], 273 (100) [M$^+$ − CH$_3$], 202 (30) [M$^+$ − C$_4$H$_7$O$_2$]. Anal. Calcd for $C_2H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.64; H, 5.71.

4-Isopropyl-1-methoxy-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (11b). Mp 156−157 °C; IR (KBr) ν 3030, 2940, 1710 cm^{-1}; ^{1}H NMR (200 MHz, CDCI$_3$) δ 1.37 (d, 6H, J = 6.9 Hz), 3.72 (sept, 1H, J = 6.9 Hz), 3.76 (s, 3H), 6.87 (d, 1H, J = 8.6 Hz), 7.41 (d, 1H, J = 8.6 Hz), 7.47 (ddd, 1H, J = 7.5, 7 7, 1.4 Hz), 7.61 (ddd, 1H, J = 7.5, 7.5, 1.2 Hz), 7.85−8.02 (m, 3H), 8.26 (d, 1H, J = 8.6 Hz); MS (EI) *m*/*z* 318 (39) [M$^+$], 303 (100) [M$^+$ − CH$_3$], 287 (13) [M$^+$ − OCH$_3$]. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.23; H, 5.70. Found: C, 79.03; H, 5.96.

4-Isopropyl-1-methyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (11c). Mp 36 °C; IR (KBr) ν 3050, 2950, 1715 cm^{-1}; ^{1}H NMR (200 MHz, CDC1$_3$) δ 1.35 (d, 3H, J = 6.9 Hz), 1.38 (d, 3H, J = 6.9 Hz), 2.23 (s, 3H), 3.72 (sept, 1H, J = 6.9 Hz), 7.22 (d, 1H, J = 7.8 Hz), 7.40 (d, 1H, J = 7.8 Hz), 7.56 (ddd, 1H, J = 8.5, 6.7, 1.5 Hz), 7.66 (ddd, 1H, J = 8.2, 6.7, 1.4 Hz), 7.92−

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8.00 (m, 3H), 8.29 (d, 1H, J = 8.6 Hz); MS (EI) m/z 302 (56) [M^+], 287 (100) [$M^+ - CH_3$], 228 (18) [$287 - C_2H_3O_2$], 215 (33) [$M^+ - C_4H_7O_2$]. Anal. Calcd for $C_{21}H_{18}O_2$; C, 83.42; H, 6.00. Found: C, 83.24; H, 5.99.

1-Ethyl-4-isopropyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one (11d). Mp 90 °C; IR (KBr) ν 3040, 2910, 1710, 1580 cm^{-1}; ^1H NMR (200 MHz, $CDC1_3$) δ 0.90 (t, 3H, J = 7.5 Hz), 1.33 (d, 3H, J = 6.9 Hz), 1.40 (d, 3H, J = 6.9 Hz), 2.53 (m, 1H), 2.82 (m, 1H), 3.72 (sept, 1H, J = 6.9 Hz), 7.31 (d, 1H, J = 8.1 Hz), 7.49−7.58 (m, 1H), 7.60−7.73 (m, 1H), 7.94 (d, 1H, J = 7.8 Hz), 8.04 (d, 1H, J = 8.3 Hz) 8.30 (d, 1H, J = 8.6 Hz, 1 H); MS (EI) m/z 316 (62) [M^+], 301(100) [$M^+ - CH_3$], 273 (16), 215 (18). Anal. Calcd for $C_{22}H_{20}O_2$: C, 83.52; H, 6.37. Found: C, 83.65; H, 6.41.

(*P*,*R*)-1-(2′-Hydroxy-4′,6′-dimethylphenyl)-2-[2-(4-tolylsulfinyl)aceto]naphthalene [(*P*,*R*)-16]. A solution of (*R*)-methyl-*p*-toluyl sulfoxide (113 mg, 730 μmol) in absolute THF (3 mL) was added dropwise under argon to a solution of LDA·THF complex (1.5 M in cyclohexane) in absolute THF (1.5 mL) at −40 °C, stirred for 30 min at this temperature, and then gently warmed to 0 °C. After the mixture cooled to −40 °C, a solution of **1c**[2] in absolute THF (3 mL) was slowly added, and the mixture was stirred for 1 h at −40 °C and for 2 h at 0 °C. After hydrolysis with saturated aqueous NH_4Cl, the phases were separated, and the aqueous phase was extracted with diethyl ether (2 × 5 mL). The combined organic layers were dried with Na_2SO_4, and the solvent was evaporated to give a 50:50 diastereomeric mixture of (*M*,*R*)-**16** and (*P*,*R*)-**16**. Slow crystallization from petroleum ether/diethyl ether under isomerization of (*M*,*R*)-**16** to (*P*,*R*)-**16** yielded the pure (according to an X-ray structure analysis[14]) crystalline diastereomer (*P*,*R*)-**16** (314 mg, 730 μmol, 73%; initial dr in solution 96:4). Mp 139−140 °C; $[\alpha]^{23}_D$ +133.2 (*c* 0.50, dichloromethane/methanol 9:1); CD (ethanol) λ_{max} ($\Delta\epsilon$) 208 (+154), 253 (−138), 312 (+32); IR (KBr) ν 3080, 2930, 2670, 1600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.68 ppm (s, 3H), 2.30 (s, 3H), 2.38 (s, 3H), 3.48 (d, J = 14.4 Hz, lH), 4.03 (d, J = 14.4 Hz, IH), 5.79 (s, 1H), 6.67 (s, 2H), 7.24 (m, 2H), 7.39−7.60 (m, 5H), 7.68 (d, J = 8.6 Hz, 1H), 7.89 (m, 2H); MS (CI, ammonia) m/z 446 (100) [$M^+ + NH_4$], 429 (4) [$M^+ + H$], 308 (10), 289 (4) [$M^+ - C_7H_7SO$], 140 (5) [$C_7H_8SO^-$]. Anal. Calcd for $C_{27}H_{24}O_3S$: C, 75.68; H, 5.65. Found: C, 74.94; H, 5.43.

(*P*)-2-Aceto-1-(2′-hydroxy-4′,6′-dimethylphenyl)naphthalene [(*P*)-17]. Freshly prepared Raney-nickel (0.5 g) was added to a solution of (*P*)-**16** (25.0 mg, 58 μmol) in diethyl ether (70 mL), and the mixture was stirred at room temperature for 1 h. After removal of the catalyst by filtration, the solvent was evaporated, and the residue was purified by preparative TLC (silica 60 $F_{254}S$, 20 cm × 20 cm × 1 mm, diethyl ether/petroleum ether 3:1) to give (*P*)-**17** as a yellow oil. Crystallization from petroleum ether/dichloromethane yielded (*P*)-**17** (dr 93:7, 10.7 mg, 37 μmol, 63%) as a white solid. Mp 122−124 °C; CD (ethanol): λ_{max} ($\Delta\epsilon$) 203 (−59), 221 (+88), 235 (−22), 251 (+7); IR (KBr) ν 3260, 3030, 2900, 1660 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.80 (s, 3H), 2.17 (s, 3H), 2.39 (s, 3H), 6.72 (d, J = 0.6 Hz, 1H), 6.75 (d, J = 0.6 Hz, 1H), 7.40−7.60 (m, 3H), 7.76 (d, J = 8.6 Hz, 1H), 7.92 (m, 2H); MS (EI) m/z 290 (62) [M^+], 275 (100) [$M^+ - CH_3$], 247 (29). Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H 6.25. Found C, 82.85; H 6.31.

***n*-Butyl 1-(2,4-Di-*tert*-butyl-6-hydroxyphenyl)-2-naphthoate [(*M*,*S*)-13, (*P*,*S*)-13].** *n*-Butyllithium (2.5 M in hexane, 0.32 mL, 788 μmol) was added at 0 °C to (1*S*)-menthol (141 mg, 900 μmol) in absolute toluene (8.7 mL) and stirred for 1 h at room temperature. The mixture was added slowly at −78 °C to a solution of *rac*-**1f**[1,2] (161.3 mg, 450 μmol) in absolute toluene (27 mL) and stirred at −60 °C for 7 d. Glacial acetic acid (0.23 mL) was added at −78 °C, and the mixture was warmed to 0 °C. After removal of the solvent and the excess menthol in vacuo, the residue was purified by column chromatography (dichloromethane/petroleum ether 1:1) to yield successively *rac*-**1f** (22.8 mg, 63.5 μmol, 14%), (*M*)-**13** (107 mg, 208 μmol, 46%, dr 99:1), and (*P*)-**13** (87.4 mg, 170 μmol, 38%, dr 99:1). The esters were purified by recrystallization from dichloromethane/petroleum ether to give colorless crystals.

(*M*,*S*)-**13**: mp 134−135 °C; $[\alpha]^{20}_D$ +30.4 (*c* 0.64, chloroform); CD λ_{max} ($\Delta\epsilon$) 204 (+96.4), 213 (−193.7), 217 (−178.0), 225 (−223.7) 249 (+93.2), 261 (+40.7), 278 (+89.6); IR (KBr) ν 3280, 2940, 1680, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.68 (d, J = 6.9 Hz, 3H), 0.80 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 7.0 Hz, 3H), 0.89, (s, 9H), 0.70−1.25 (m, 9H), 1.38 (s, 9H), 4.25 (s, 1H), 4.68 (ddd, J = 10.6, 10.6, 4.4 Hz, 1H), 6.90, (d, J = 1.9 Hz, 1H), 7.23 (d, J = 1.9 Hz, 1H), 7.38−7.62 (m, 3H), 7.85−8.04 (m, 3H); MS (EI) m/z 514 (28) [M^+], 376 (87) [$M^+ - C_{10}H_{18}$], 358 (100), 343 (33), 328 (11), 302 (49), 287 (24), 259 (14), 57 (99), 41(28). Anal. Calcd for $C_{35}H_{46}O_3$: C, 81.67; H, 9.01. Found: C, 81.84; H 9.27.

(*P*,*S*)-**13**: mp 124−126 °C; $[\alpha]^{20}_D$ +72.2 (*c* 0.65, chloroform); CD λ_{max} ($\Delta\epsilon$) 213 (+362.2), 237 (+67.0), 240 (+69.4), 282 (−57.5); IR (KBr) ν 3420, 3040, 2900, 1655 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.72 (d, J = 6.9 Hz, 3H), 0.81 (d, J = 7.0 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H), 0.92, (s, 9H), 0.94−1.91 (m, 9H), 4.33 (s, 9H), 4.25 (s, 1H), 4.68 (ddd, J = 10.6, 10.6, 4.4 Hz, 1H), 6.90, (d, J = 1.9 Hz, 1H), 7.23 (d, J = 1.9 Hz, 1H), 7.38−7.62 (m, 3H), 7.85−8.04 (m, 3H); MS (EI) m/z 514 (28) [M^+], 376 (87) [$M^+ - C_{10}H_{18}$], 358 (100), 343 (33), 328 (11), 302 (49), 287 (24), 259 (14), 57 (99), 41(28). Anal. Calcd for $C_{35}H_{46}O_3$: C, 81.67; H, 9.01. Found: C, 81.84; H 9.27.

(*M*)-1-(2,4-Di-*tert*-butyl-6-hydroxyphenyl)-2-naphthoic Acid [(*M*)-14]. Water (5.4 mg, 300 μmol) was added at 0 °C to a suspension of potassium *tert*-butyl alcoholate (135 mg, 1.20 mmol) in absolute diethyl ether and stirred for 5 min. A solution of the ester (*M*,*S*)-**13** (77.2 mg, 150 μmol) in diethyl ether (2 mL) was added. The suspension was warmed to room temperature and stirred for 24 h. Aqueous sodium hydroxide solution (1 M, 2 mL) was added to the suspension, and the organic layer was separated. The aqueous layer was acidified with hydrochloric acid (2 M) and extracted with diethyl ether (3 × 3 mL). After drying with $MgSO_4$ and removal of the solvent in vacuo, the acid (*M*)-**14** was obtained as a colorless solid (50.4 mg, 134 μmol, 89%, er 99:1). Mp 139−140 °C; IR (KBr) ν 3620−2550, 3040, 2940, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (s, 9H), 1.41 (s, 9H), 6.84 (d, J = 1.9 Hz, 1H), 7.23 (d, J = 1.9 Hz, 1H), 7.40−7.63 (m, 3H), 7.85 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.7 Hz, 1H), 8.12 (d, J = 8.7 Hz, 1H); MS (EI) m/z 376 (55) [M^+], 358 (69), 343 (50), 328 (22), 302 (73), 287 (50), 259 (19), 57 (100), 41 (28). Anal. Calcd for $C_{20}H_{18}O_2$: C, 79.95; H, 7.50. Found C, 79.74; H 7.61.

(*P*)-1-(2,4-Di-*tert*-butyl-6-hydroxyphenyl)-2-naphthoic Acid [(*P*)-14]. Analogous saponification of (*P*,*S*)-**13** gave (*P*)-**14** (51.4 mg, 137 μmol, 91%, er 99:1), mp 138−140 °C.

(*M*)-1,4-Di-*tert*-butyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one [(*M*)-1f]. DMF (0.3 μL) and oxalyl chloride (8.00 μL, 11.8 mg, 93,0 μmol) were added at 0 °C to a solution of (*M*)-**14** (30.0 mg, 79.7 μmol) in absolute dichloromethane (5 mL). The solution was stirred at 0 °C for 30 min. Triethylamine (17.0 μL, 12.3 mg, 122 μmol) and 4-(dimethylamino)pyridine (DMAP, a few crystals) were added, and stirring at 0 °C was continued for 2 h. After removal of the solvent the residue was dissolved in diethyl ether and purified by preparative TLC (silica 60 $F_{254}S$, 20 cm × 20 cm × 1 mm, petroleum ether/diethyl ether 3:1) to yield (*M*)-**1f** (15.6 mg, 43.8 μmol, 55%, er 96:4) as a light yellow solid. Mp 104−106 °C; $[\alpha]^{22}_D$ +63.5 (*c* 0.50, chloroform); CD (ethanol) λ_{max} ($\Delta\epsilon$) 227 (−382.4), 242 (−285.1), 274 (+64.1), 287 (−0.55), 324 (+97.2). The spectral data of (*M*)-**1f** were fully identically to those of *rac*-**1f**.[2]

(*P*)-1,4-Di-*tert*-butyl-6*H*-benzo[*b*]naphtho[1,2-*d*]pyran-6-one [(*P*)-1f]. From (*P*)-**14**, (*P*)-**1f** (16.3 mg, 45.0 μmol, 57%, er 95:5) was prepared analogously. Mp 105−106 °C; $[\alpha]^{22}_D$ −63.1 (*c* 0.45, chloroform); CD (ethanol) λ_{max} ($\Delta\epsilon$) 227 (+300.8), 241 (+213.6), 243 (+214.3), 275 (−67.5), 288 (−11.7), 325 (−89.5). The spectral data of (*P*)-**1f** were fully identical to those of *rac*-**1f**.[2]

Determination of the Rate Constants by DNMR. Samples were prepared from 20−50 mg of the compounds in high precision 5 mm tubes (Varian 507 PP). At each temperature the sample tubes were allowed to equilibrate thermally for 15 min, and the proton frequency and the impedance of the receiver circuit were carefully compensated before recording a spectrum. Exact temperatures were measured with the

help of NMR-shift thermometers: methanol[26] or semibullvalene[27] for low temperatures and ethylene glycol[28] for high temperatures. Zero filling to 4 times the number of measured data points was performed to give 64 K data points. Particular attention was paid to the phase and baseline corrections, since small deviations from the optimum will result in considerable errors in the rate constants. The rate constants k were calculated from the NMR spectra by the Bruker computer program WINDYNA. Reference half-widths were determined if possible from the signals of nonexchanging molecule protons or otherwise from the rest proton signals of the solvent. The spectra were simulated in the slow exchange regime and then iterated by the program to the experimental spectra of each temperature. The k values were accepted when there was a good optical agreement between the experimental and the iterated spectrum, resulting in a conservatively estimated error of 5%.

Determination of the Rate Constants by HPLC−UV Measurements. The time-dependent decrease of er was measured over two half-lives at several temperatures. The sample was kept at the given temperature (±1 K) using a thermostat. The rates k were calculated by the first-order rate equation (eq 1)

$$k = \frac{\sum t_i \ln(c_0/c_i)}{\sum t_i^2} \quad (1)$$

with the er c_0 at the time $t_0 = 0$ and c_i at t_i, respectively.

Eyring parameters listed in Table 1 were obtained by least-squares fits of $\ln(k/T)$ vs $1/T$ data from eq 2, which results

$$\ln\frac{k}{T} = \frac{-\Delta H^{\ddagger}}{R}\frac{1}{T} + \ln\frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R} \quad (2)$$

from the Eyring and the Gibbs−Helmholtz equations with the Boltzmann constant k_B, the Planck constant h, and the gas constant R. The errors given in Table 1 are statistical errors that result from the regression analysis of the Eyring plot.

Atropisomerization Rate Constants Measured by ^{1}H NMR. Compound **9d** (200 MHz, [D_8]toluene): the experiments showed superimposed proton signals for the ethyl-CH_2 group at C-1 and the methyl group at C-4.

10b (200 MHz, J = 14.5 Hz, CD_2Cl_2): k /s^{-1} (T /K) 5.0 ± 1.0 (186.1), 7.9 ± 0.3 (196.2), 9.2 ± 0.5 (200.4), 14.2 ± 0.5 (211.5), 15.5 ± 0.5 (213.0), 26.0 ± 1.0 (221.7), 29.5 ± 0.5 (223.2), 63.0 ± 1.0 (230.6), 135 ± 5 (239.1), 160 ± 5 (241.5), 280 ± 10 (250.5)

10c (200 MHz, J = 14.6 Hz, [D_8]toluene): k /s^{-1} (T /K) 2.8 ± 0.3 (308), 5.4 ± 0.5 (313), 7.1 ± 0.5 (320), 9.1 ± 0.4 (324), 30 ± 3 (334), 66 ± 2 (350), 73 ± 3 (360).

11a (200 MHz, CD_2Cl_2): the experiments showed fast exchange even at 170 K.

11b (200 MHz, CD_2Cl_2): the experiments showed fast exchange even at 170 K.

11c (200 MHz, J = 6.9 Hz, [D_8]toluene): k /s^{-1} (T /K) 0.75 ± 0.05 (302), 0.90 ± 0.05 (321), 1.70 ± 0.05 (325), 4.25 ± 0.05 (337), 6.25 ± 0.08 (340), 8.00 ± 0.10 (344), 12.4 ± 0.10 (349), 12.7 ± 0.10 (350), 14.0 ± 0.30 (352), 20.5 ± 1.00 (361), 27.0 ± 2.00 (366), 28.5 ± 2.00 (373), 66.0 ± 5.00 (385).

11d (200 MHz, [D_8]toluene): k /s^{-1} (T /K) (a) probe $CH(CH_3)_2$ (J = 6.9 Hz) 1.5 ± 0.2 (349), 3.1 ± 0.1 (362), 5.1 ± 0.3 (369), 9.2 ± 0.2 (376), 20.0 ± 1.0 (387); (b) probe CH_2CH_3 (J = 14.5 Hz) 1.3 ± 0.3 (349), 3.6 ± 0.2 (362), 5.4 ± 0.3 (369), 8.8 ± 0.3 (376), 18.2 ± 0.7 (387).

20 (600 MHz, [D_6]DMSO): k /s^{-1} (T /K) (*eq* → *ax*; probe OMe) 8.20 (363), 24.1 (383), 42.1 (393), 67.4 (403), 107 (413); (*eq* → *ax*; probe 6-H_{ax}) 7.85 (363), 23.5 (383), 40.9 (393), 64.4 (403), 95.0 (413); (*ax* → *eq*; probe OMe) 9.61 (333), 57.1 (363), 129 (383), 238 (393), 310 (403); (*ax* → *eq*; probe 6-H_{eq}) 8.86 (333), 52.2 (363), 124 (383), 213 (393), 306 (403).

Atropisomerization Rate Constants Measured by HPLC−UV. (*P*)-**17** Chiracel OD, flow 1 mL/min, eluent *n*-hexane/2-propanol 95:5, detection at 280 nm, retention times t_R = 40.2 min for (*M*)-**17** and 46.2 min for (*P*)-**17**: k /(10^5 s^{-1}) (T /K) 3.16 ± 0.03 (300), 7.07 ± 0.05 (313), 14.1 ± (0.1) (323).

(*M*)-**1f** Chiracel OD, flow 0.5 mL/min, eluent *n*-hexane/2-propanol (100:1), detection at 280 nm, retention times t_R = 21.1 min for (*M*)-**1f** and 19.2 min for (*P*)-**1f**: k /(10^5 s^{-1}) (T /K) 2.03 (314), 22.2 (335), 119 (354).

(*M*)-**9e**: the column was cooled to the corresponding temperature (±1 K) by a thermostat filled with ethanol. Chiracel OF, flow 0.5 mL/min, eluent petroleum ether/2-propanol (3:1), detection at 280 nm, retention times t_R = 26.7 min for (*M*)-**9e** and 35.8 min for (*P*)-**9e**: k /(10^6 s^{-1}) (T /K) 3.57 (263), 24.4 (273), 374 (298).

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Supporting Information Available: Preparation, ^{1}H NMR, IR, and MS data of **6d**, **6e**, **7b**, **7c**, **8a**, **8b**, **8c**, and **8d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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