

83. Chiral 2-Aryl-2-methyl-2H-1-benzopyrans: Synthesis, Characterization of Enantiomers, and Barriers to Thermal Racemization

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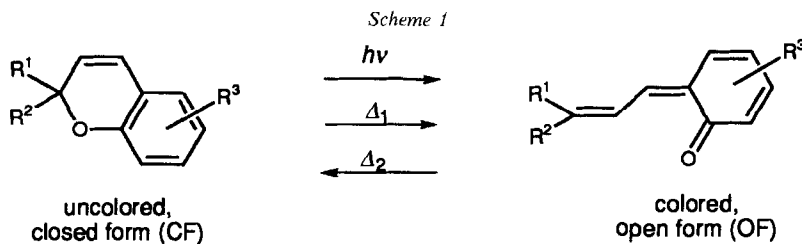
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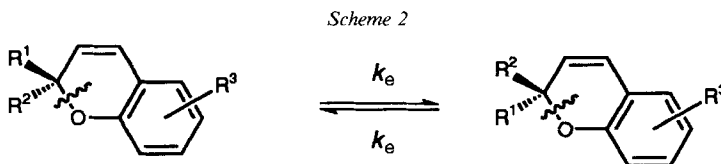
The ease of thermal breaking of the C(sp³)–O bond of the 2-aryl-2-methyl-2H-1-benzopyrans 1–9 was evaluated by measuring the free energy (ΔG_e^\ddagger) of the racemization reaction of optically active compounds. The variation of ΔG_e^\ddagger of the thermal ring opening in terms of structural modifications is discussed. The synthesis of the studied compounds, the preparative separation of enantiomers by liquid chromatography, the determination of enantiomeric purity, the circular dichroism of enriched enantiomers, and the measurement of rate constants of enantiomerization by monitoring the decrease of the polarimetric angle of rotation at suitable temperatures are described.

1. Introduction. – For several years 2H-1-benzopyrans (2H-chromenes) and their benzo derivatives have been of great scientific interest, especially in view of their use in the design of materials exhibiting variable optical transmission [1]. They constitute an important class of photochromic compounds [2], *i.e.*, they show a reversible color change upon light absorption [3]. Under continuous irradiation, the equilibrium (*Scheme 1*) between the uncolored closed form (CF) and the colored open form (OF) depends mainly on the photocoloration yield ($\Phi_{CF \rightarrow OF}$) and the rate constant of thermal bleaching (k_{Δ_2}). These parameters are generally estimated ($\Phi_{CF \rightarrow OF}$) or measured (k_{Δ_2}) for this class of photochromic compounds using flash-photolysis experiments [3b]. However, depending on structural features, solvent, and temperature, thermal coloration (Δ_1) may also be involved (thermochromism) [4].



The ease of thermal breaking of the C(sp³)–O bond can be evaluated by measuring the free energy ΔG_e^\ddagger (or the activation energy) of the racemization reaction of optically active 2H-chromenes (*Scheme 2*). This methodology [5] involves the preparative separa-

tion of enantiomers by enantioselective liquid chromatography, the determination of the enantiomeric purity, and the measurement of the rate constant k_e of enantiomerization by monitoring the decrease of the polarimetric angle of rotation at a suitable temperature and taking into account that $2k_e = k_{\text{rac}}$, the rate constant of the cleavage of the C(sp³)–O bond.



In this paper, we report the synthesis of chiral 2-aryl-2-methyl-2*H*-chromenes **1–9** (Tables 1 and 2), and the characterization of the respective enantiomers. The variation of ΔG_e^\ddagger of thermal opening of the cycle is discussed according to structural modifications.

2. Results. – *Synthesis.* Two different procedures were used to synthesize chiral 2-aryl-2-methyl-2*H*-chromenes. In the first procedure, condensation of the appropriate 2-arylbut-3-yn-2-ol and phenol was performed using a catalytic amount of *p*-toluenesulfonic acid [6] or a large excess of aluminium(III) oxide [7] (Scheme 3, a). According to the alternative procedure, 2*H*-chromenes were obtained by reaction of β -methylcinnamaldehyde with the appropriate titanium(IV) phenolate prepared by treatment of the corresponding phenol with titanium(IV) ethoxide [8] (Scheme 3, b).

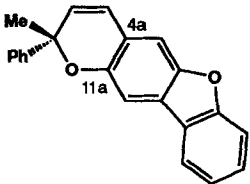
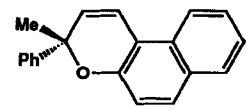
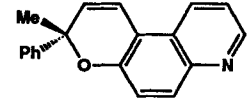
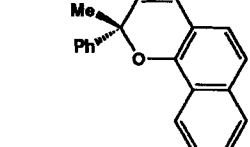
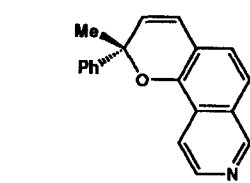
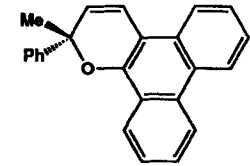
Semi-preparative Enrichment of Enantiomers and Their Characterization. The enantiomer enrichment was performed by liquid chromatography on microcrystalline triacetylcellulose [9] of the racemates at 1.0–4.5 bar. The enantiomers were characterized by liquid chromatography on microcrystalline triacetylcellulose at 90–140 bar, using the specific rotations at two wavelengths and the circular-dichroism spectra ($\Delta\varepsilon = f(\lambda)$), as far as the quantities of enriched enantiomers were sufficient.

Thermal Racemization of Enantiomers. The interconversion of enantiomers according to Scheme 2 was treated as a reversible first-order reaction [10] (Eqn. 1), starting from one enriched enantiomer (1 mg in 1–2 ml of diglyme). In Eqn. 1, α_0 and α_t are the polarimetric angles of rotation at times $t = 0$ and $t \neq 0$, respectively, at one wavelength and constant temperature, the polarimeter cell being protected against external light. The thermal stability was occasionally checked by an independent experiment of the racemic 2*H*-chromene in perdeuterated diglyme at the same temperature and during the same period of time as applied for the kinetic experiment. The ¹H-NMR spectra did not indicate decomposition.

$$\ln \alpha_t = -2k_e t + \ln \alpha_0 \quad (1)$$

The experimental rate constant k_e of enantiomerization was obtained from the slope of a plot of $\ln \alpha_t$ vs. t . If we assume that the enantiomerization proceeds via an intermediate (see Sect. 3), it is easily shown [11] that $k_{\text{rac}} = 2k_e$, where k_{rac} is the rate constant of the cleavage of the C(sp³)–O bond. This statistical factor of 2 was also derived by formal kinetics [12] and was included in the calculation of the half-life $t_{1/2}$ of each

Table 1. Barriers ΔG^\ddagger of Thermal Cleavage of the C(sp³)-O Bond in 2-Methyl-2-phenyl-2H-chromenes in Diglyme. $t_{1/2}$, corresponding half-life.

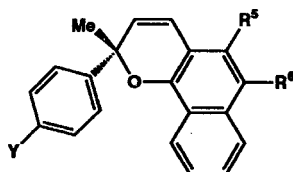
		ΔG_T^\ddagger [kJ/mol]	$t_{1/2}$ [min]	T [°]	π -Bond order of C(11a)-C(4a) ^{a)}
9		132.4 ± 0.8	118	135.0	1.33
1		110.9 ± 0.3	137	69.1	1.49
2		111.1 ± 0.2	141	69.4	1.47
3		111.9 ± 0.2	189	69.4	1.48
4		112.2 ± 0.2	214	69.3	1.49
7		102.6 ± 0.03	6.7	70.0	1.57

^{a)} Calculated according to the PM3 method [19]; for convenience, the numbering of **9** is used also for **1-4** and **7** (systematic numbering in the *Exper. Part*).

2H-chromene molecule (Tables 1 and 2) with respect to bond cleavage (see Eqn. 2). The plots of $\ln \alpha$, vs. t were linear during 2–3 half-life periods. The factor of 2 was also included in the calculation of the barrier ΔG^\ddagger to C(sp³)-O bond cleavage (Tables 1 and 2) by means of the Eyring equation.

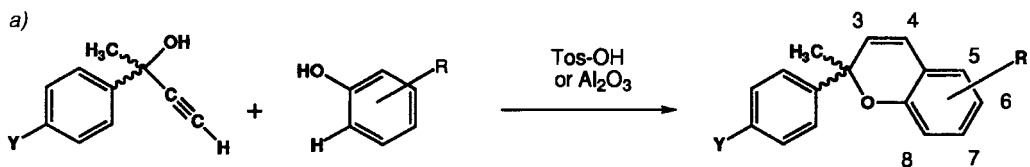
$$t_{1/2} = (\ln 2)/2k_e = (\ln 2)/k_{\text{rac}} \quad (2)$$

Table 2. Barriers ΔG^\ddagger to Thermal Cleavage of the C(sp³)-O-Bond in 2-Aryl-2-methyl-2H-chromenes in Diglyme. $t_{1/2}$, corresponding half-life.

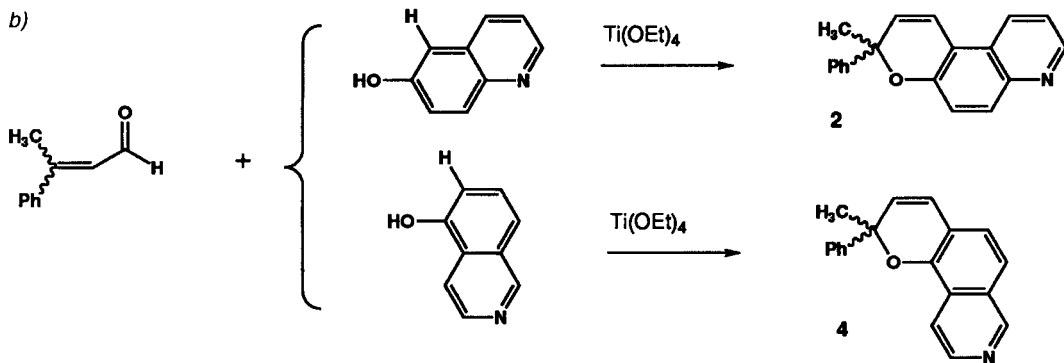


Y	R ⁵	R ⁶	ΔG_T^\ddagger [kJ/mol]	$t_{1/2}$ [min]	T [°C]
3	H	H	111.9 ± 0.2	189	69.4
5	MeO	H	107.3 ± 0.2	38.9	69.2
6		H	103.7 ± 0.2	31.9	59.3
7	H	- benzo -	102.6 ± 0.3	6.7	70.0
8	MeO	- benzo -	98.6 ± 0.2	4.7	59.7

Scheme 3



	Y	R
1	H	5,6-benzo
3	H	7,8-benzo
5	CH ₃ O	7,8-benzo
6		7,8-benzo
7	H	5,6,7,8-dibenzo
8	CH ₃ O	5,6,7,8-dibenzo
9	H	6,7-benzofuro



3. Discussion of the Barriers of C(sp³)–O Bond Cleavage. – Transition State. Besides knowledge of the ground state (*Scheme 2*), information on the transition state is a prerequisite for adequate interpretation of the barriers experimentally determined. In this respect, theoretical calculations represent the only basis of discussion. Several *ab-initio* approaches [13] show that the C(sp³)–O bond in the transition state for 2*H*-pyran is cleaved. Further calculations [14–16] for related molecules are in agreement with this result. No additional barrier of similar or greater height has to be surmounted on the way from the ground state to any intermediate [13] [14] [16]. The two substituents at C(2) in the transition state are situated [13] [14] [16] out of the C(2)–C(3)–C(4) plane (*cf. Fig. 1*) but apparently deviate [14] [16] from the orthogonal arrangement by an estimated angle of 20°, *i.e.*, π = conjugation between the former C(2) and C(3) centers is weak in the transition state.

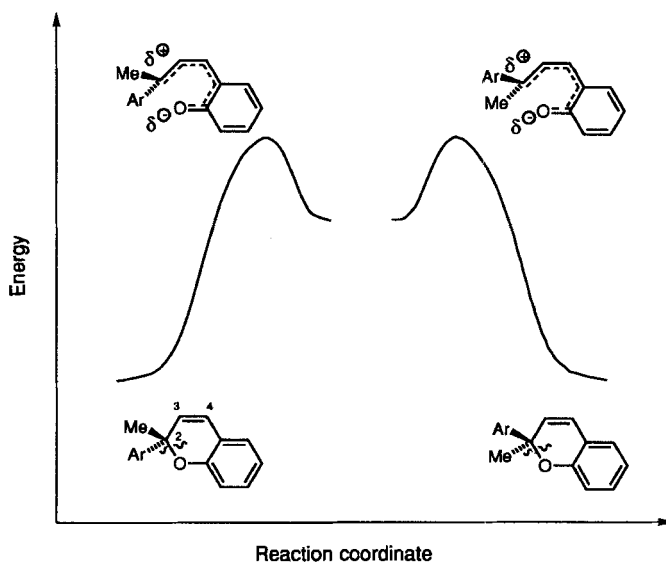


Fig. 1. Assumed partial reaction profile for enantiomerizations

We assume that *biradical* transition states are not involved in our racemization experiments. Solvent effects on the barriers to C(sp³)–O bond cleavage in several 2-alkoxy-2*H*-chromenes [17] provide support for *polar* transition states, as depicted in *Fig. 1*. In the center part of the reaction profile, the molecule has to adopt some conformations suitable for enantiomerization. No information about this region of the profile can be obtained from the kinetics of enantiomerization, as far as no *further* barrier of similar or greater height has to be surmounted. No such barrier was found by calculations [13] [14] [16]. Therefore, the structure of the intermediate(s) of the enantiomerization reaction remains elusive.

Barriers to Bond Cleavage in 2-Aryl-2-methyl-2*H*-chromenes. The barrier heights (ΔG^\ddagger in *Table 1*) are almost identical for 1–4, *i.e.*, for unequal positions of a fused benzo or pyrido ring. However, the presence of a *further* benzo ring such as in 7, decreases the ΔG^\ddagger value by 9 kJ/mol (1 *vs.* 7 and 3 *vs.* 7 in *Table 1* as well as 5 *vs.* 8 in *Table 2*).

Apparently, the transition state for ring opening of **7** or **8** is stabilized by additional conjugation as compared to the transition states of **1** and **3** or **5**. In this respect, it is interesting to notice that the ΔG^\ddagger values can be correlated to the π -bond order of C(1a)–C(4a) (see *Table 1*). The more electron-rich this bond is, the lower ΔG^\ddagger is due to a better assistance of the π -system delocalization intervening in the transition state. This is confirmed by compound **9**, although the ΔG^\ddagger value in this case refers to 135° and can, therefore, not be fully compared to the other values in *Table 1* which were obtained at *ca.* 69° . Indeed, a benzofuro anellation such as in **9** provides less additional conjugation than a benzo or a pyrido anellation such as in **1–4**; hence, the π -bond order of C(1a)–C(4a) is the lowest for chromenes of type **9**. In addition, an O-atom in the *p*-position with respect to the pyran O-atom increases the barrier, as observed for indolinospiropyrans [18]. Finally, the ΔG^\ddagger values decrease in a reasonable way with electron-donating substituents Y at the 3-aryl moiety (Y = MeO or morpholino in *Table 2*). Comparison of **3** vs. **5** and **7** vs. **8** in *Table 2* allows evaluation of the methoxy contribution *ca.* 4 kJ/mol, whereas comparison of **3/6** indicates a morpholino contribution of *ca.* 8 kJ/mol. Apparently, the transition state for thermal ring opening of **5**, **6**, and **8** is stabilized by additional conjugation, relative to the transition state of **3** and **7**. This additional conjugation can be represented (*Fig. 2*) by appropriate resonance formulae for the transition state.

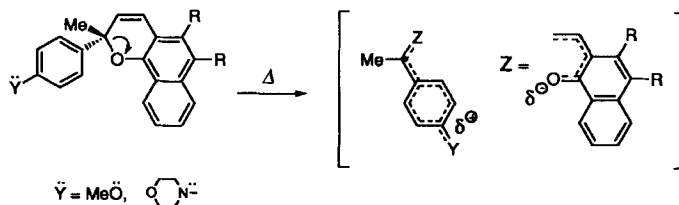


Fig. 2. Thermal ring-opening, proceeding via a transition state which is represented by a possible resonance formula (viewed from another direction, in order to put other molecular fragments into the plane of the paper; the fragment Z is then no longer situated in the plane of the paper). R, R means H, H or benzo.

The present discussion of barriers heights refers to enthalpies of activation ΔH^\ddagger , whereas the experimental results in *Tables 1* and *2* refer to ΔG^\ddagger . Racemization experiments of **7** between 29° and 70° in diglyme resulted in $\Delta H^\ddagger = 99 \pm 3$ kJ/mol and $\Delta S^\ddagger = -15 \pm 7$ J/mol \cdot K. This small absolute ΔS^\ddagger value implies *small* differences between ΔH^\ddagger and ΔG^\ddagger and also a weak dependence of ΔG^\ddagger upon temperature. Therefore, the above semi-quantitative discussion of barriers seems to be justified.

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Experimental Part

General. Anh. toluene was purchased from SDS. DMSO (*Aldrich*) was dried by distillation over CaH₂. Column chromatography (CC): silica gel *Merck 60* (0.063–0.200 mm or 5–200 mm), 20–40 g per g mixture for purification of compounds. Anal. HPLC: steel column 250 × 8 mm, triacetylcellulose (TAC) with particle diameter of 5–10 μm (*Merck*), eluent MeOH, flow rate 0.5–1.5 ml min⁻¹; Δ*p* = 90–140 bar, 22°; for anal. separations of enantiomers (0.3 mg in MeOH) and for the determination of enantiomeric purities. Semi-prep. low-pressure liquid chromatography (LPLC): glass column 300 × 25 mm, TAC with particle diameter of 15–25 μm (*Merck*), eluent MeOH, flow rate 1.5–6.0 ml min⁻¹; Δ*p* = 1.0–4.5 bar, 22°; for enantiomeric enrichments (injected quantities, 9–20 mg of racemates in MeOH). HPLC and LPLC: detection included [19] and *ERC-7210* spectrophotometer and a *Perkin-Elmer-241* polarimeter; more details on the chromatographic equipment have been described previously [9] [20–22]. M.p.s: *Büchi-510* apparatus with capillary tubes or *Analysis-Electrothermal-9100* apparatus. Specific rotation ([α]): *Perkin-Elmer-241* polarimeter; also for monitoring racemizations [23]. UV Spectra: *Beckman-DU-7500*, *ERC-7210*, or *Philips-PU-8620* spectrophotometer; λ_{max}(ε) in nm. Circular-dichroism (CD) spectra: for both enantiomers. *Jasco-J-40A* instrument; at 22°. IR Spectra: in cm⁻¹. ¹H- and ¹³C-NMR Spectra: *Bruker-AC-250*, *Bruker-AM-360*, or *Bruker-ARX-400* spectrometer; in CDCl₃; chemical shifts δ in ppm downfield from SiMe₄, coupling constants *J* in Hz. The CDUV2 computer program was used for UV and CD spectrograms reprocessing [24]. The ZERLEG computer program [24] served for deconvolution [20] of partially overlapping peaks in the HPLC in order to calculate the enantiomeric purities. A computer program was used for the calculations of Δ*G*^{*} [25] from polarimetric racemization data.

1. *Butynols: General Procedure.* A soln. 1-(4-methoxyphenyl)ethanone (2.75 g, 18.3 mmol) 1-[4-(morpholin-4-yl)phenyl]ethanone (3.03 g, 14.8 mmol) in dry DMSO (15 ml) is slowly added to a stirred suspension of lithium acetylide/ethylenediamine complex (2.54 g, 24.8 mmol) in dry DMSO (15 ml). The mixture is stirred under N₂ at 35° (TLC monitoring). The reaction is stopped by addition of ice water (30 ml). After extraction with CHCl₃ (3 × 50 ml), drying (MgSO₄), and evaporation, the residue is purified by column chromatography to afford 3-(4-methoxyphenyl)but-3-yn-3-ol or 2-[4-(morpholin-4-yl)phenyl]but-3-yn-2-ol, respectively.

2-(4-Methoxyphenyl)but-3-yn-3-ol: Reaction time 6 h. After CC (silica gel, hexane/CHCl₃ 3:7), 61% yield. M.p. 37°. IR (KBr): 3800, 3278, 2970, 2955, 2833, 2114, 1608, 1584, 1509. ¹H-NMR (360 MHz, CDCl₃): 1.78 (s, Me(1)); 2.32 (s, OH); 2.67 (s, H–C(4)); 3.82 (s, MeO); 6.90 (m, ³*J* = 8.8, 2 arom. H); 7.59 (m, ³*J* = 8.8, 2 arom. H). ¹³C-NMR (90 MHz, CDCl₃): 32.9 (C(1)); 55.2 (1 MeO); 69.4 (C(2)); 72.8 (1 acet. C); 87.4 (1 acet. C); 113.5 (2 arom. CH); 126.1 (2 arom. CH); 137.1 (1 arom. C); 159.2 (1 arom. C).

2-[4-(Morpholin-4-yl)phenyl]but-3-yn-2-ol. Reaction time 10 h. After CC (silica gel, hexane/AcOEt 2:3), 57% yield. Viscous semisolid. IR (KBr): 3407, 3244, 2874, 2955, 2839, 2105, 1615, 1599, 1514. ¹H-NMR (360 MHz, CDCl₃): 1.77 (s, Me(1)); 2.52 (s, OH); 2.65 (s, H–C(4)); 3.15 (m, ³*J* = 4.8, 4 H, CH₂N); 3.85 (m, ³*J* = 4.8 4 H, CH₂O); 6.98 (m, ³*J* = 8.8, 2 arom. H); 7.55 (m, ³*J* = 8.8, 2 arom. H). ¹³C-NMR (90 MHz, CDCl₃): 32.7 (C(1)); 49.1 (2 CH₂); 66.7 (2 CH₂); 69.3 (C(2)); 72.6 (1 acet. C); 87.4 (1 acet. C); 115.1 (2 arom. CH); 125.8 (2 arom. CH); 136.1 (1 arom. C); 150.8 (1 arom. C).

2. *General Procedures 2H-1-Benzopyrans:* 2.1. The appropriate butynol (5 mmol) and phenol (5 mmol) are dissolved in refluxing anh. toluene (10 ml) under N₂. A catal. amount of TsOH is added, and the soln. is kept under reflux for 2 h. After cooling to r.t., the mixture is poured into 5% aq. NaOH soln. The aq. layer is extracted twice with CH₂Cl₂ and combined org. phase dried (MgSO₄) and evaporated, and the residual oil purified.

Alternatively, the appropriate butynol (1 mmol) and phenol (1 mmol) in toluene containing aluminium(III) oxide (6 mmol, activated, weakly acidic, *Brockmann I*, 150 mesh) are refluxed for 20 min under N₂ (TLC monitoring). An oil remains after evaporation.

2.2. To a soln. of the appropriate phenol (7 mmol) in anh. toluene (35 ml), titanium(IV) ethoxide 1.60 g (7 mmol) in anh. toluene (7 ml) is added at r.t. under N₂. This soln. is refluxed for 30 min and then distilled to completely remove the formed EtOH. After cooling to r.t., a soln. of the appropriate 3-phenylbutanol (7 mmol) in anh. toluene (28 ml) is added dropwise with stirring under N₂. After the addition is completed, the mixture is heated under reflux with stirring for 2 h and quenched by addition of 2M aq. NH₄Cl. The org. layer is washed with 2M aq. NaOH, the aq. layer extracted stepwise with CH₂Cl₂, and the combined org. phase dried (MgSO₄) and evaporated: oily residue.

3-Methyl-3-phenyl-3H-naphtho[2,1-b]pyran (**1**) [26]: According to 2.1 (TsOH). Compound **1** precipitated in hexane and was recrystallized from EtOH: 43% of **1**. M.p. 76°. UV (closed form; EtOH): 214 (21020), 239 (33220), 261 (7600), 288 (3880), 301 (5480), 314 (6100), 345 (6020), 357 (6060). ¹H-NMR (250 MHz, CDCl₃): 1.84 (s, Me); 6.07, 7.16 (2*d*, each ³*J* = 9.9, H–C(1), H–C(2)); 7.18 (*d*, ³*J* = 8.6, 1 arom. H); 7.22–7.32 (*m*, 4 arom. H); 7.45 (*ddd*, ³*J* = 8.5, 7.0, ⁴*J* = 1.4, 1 arom. H); 7.56 (*m*, 2 arom. H); 7.66 (*d*, ³*J* = 8.8, 1 arom. H); 7.72 (*dd*,

$^3J = 8.4$, $^4J = 0.5$, 1 arom. H); 7.92 (*d*, $^3J = 8.5$, 1 arom. H). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): 29.4 (Me); 78.8 (1 C); 114.1 (1 C); 118.4 (1 CH); 119.1 (1 CH); 121.4 (1 CH); 123.6 (1 CH); 125.2 (2 CH); 126.6 (1 CH); 127.4 (1 CH); 128.3 (2 CH); 128.5 (1 CH); 128.6 (1 CH); 129.4 (1 C); 129.7 (1 CH); 130.0 (1 C); 146.1 (C); 151.2 (1 C). Anal. calc. for $\text{C}_{20}\text{H}_{16}\text{O}$: C 88.20, H 5.92; found: C 88.05, H 5.92.

3-Methyl-3-phenyl-3H-pyrano[3,2-*f*]quinoline (2). According to 2.2. CC (silica gel, Et_2O) and recrystallization from toluene or heptane gave 44% of **2**. M.p. 105°. UV (closed form, MeOH): 202 (23740), 248 (35160), 302 (4640), 316 (3500), 352 (3340). $^1\text{H-NMR}$ (250 MHz, CDCl_3): 1.85 (*s*, Me); 6.07, 7.03 (2*d*, each $^3J = 10.0$, H-C(1), H-C(2)); 7.20–7.33 (*m*, 4 arom. H); 7.38 (*d*, $^3J = 9.1$, 1 arom. H); 7.53 (*dd*, $^3J = 8.5$, $^4J = 1.5$, 2 arom. H); 7.92 (*d*, $^3J = 9.1$, 1 arom. H); 8.17 (*d*, $^3J = 8.6$, 1 arom. H); 8.70 (*dd*, $^3J = 4.1$, $^4J = 1.0$, 1 arom. H). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): 29.3 (Me); 79.2 (1 C); 113.7 (1 C); 118.0 (1 CH); 121.2 (1 CH); 121.8 (1 CH); 124.8 (1 C); 125.1 (2 CH); 127.5 (1 CH); 128.3 (2 CH); 129.1 (1 CH); 129.6 (1 CH); 130.9 (1 CH); 144.5 (1 C); 145.5 (1 C); 147.9 (1 CH); 151.1 (1 C). Anal. calc. for $\text{C}_{19}\text{H}_{15}\text{NO}$: C 83.49, H 5.53, N 5.12; found: C 83.44, H 5.56, N 5.07.

2-Methyl-2-phenyl-2H-naphtho[1,2-*b*]pyran (3). According to 2.1 (TsOH). CC (silica gel, pentane/ Et_2O 95:5) gave a yellow oil which crystallized spontaneously. The crystals were washed with pentane or EtOH: 15% of **3**. M.p. 44°. UV (closed form; MeOH): 218 (28780), 258 (25800), 266 (27380), 324 (3280), 336 (3440), 352 (2990). $^1\text{H-NMR}$ (250 MHz, CDCl_3): 1.87 (*s*, Me); 5.98, 6.56 (2*d*, each $^3J = 9.7$, H-C(3), H-C(4)); 7.11 (*d*, $^3J = 8.3$, 1 arom. H); 7.20–7.29 (*m*, 3 arom. H); 7.32 (*d*, $^3J = 8.3$, 1 arom. H); 7.42 (*ddd*, $^3J = \text{masked}$, $^3J = 6.8$, $^4J = 1.6$, 1 arom. H); 7.48 (*ddd*, $^3J = \text{masked}$, $^3J = 6.8$ Hz, $^4J = 1.6$, 1 arom. H); 7.54 (*m*, 2 arom. H); 7.71 (*dd*, $^3J = 7.4$, $^4J = 1.8$, 1 arom. H); 8.33 (*dd*, $^3J = 8.4$, $^4J = 1.5$, 1 arom. H). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): 29.9 (Me); 79.6 (1 C); 115.5 (1 C); 120.4 (1 CH); 122.1 (1 CH); 123.5 (1 CH); 124.7 (1 CH); 124.9 (1 C); 125.0 (2 CH); 125.7 (1 CH); 126.4 (1 CH); 127.4 (1 CH); 127.3 (1 CH); 128.3 (1 CH); 128.4 (2 CH); 134.7 (1 C); 146.3 (1 C); 148.4 (1 C). Anal. calc. for $\text{C}_{20}\text{H}_{16}\text{O}$: C 88.20, H 5.92; found: C 88.20, H 5.94.

2-Methyl-2-phenyl-2H-pyrano[2,3-*f*]isoquinoline (4). According to 2.2. CC (silica gel, Et_2O) and recrystallization from toluene or heptane gave 17% of **4**. M.p. 104°. UV (closed form; MeOH): 214 (25290), 264 (26310), 272 (26560), 350 (3760), 362 (3440). $^1\text{H-NMR}$ (250 MHz, CDCl_3): 1.88 (*s*, Me); 6.09, 6.58 (2*d*, each $^3J = 9.8$, H-C(3), H-C(4)); 7.24 (*m*, 1 arom. H); 7.22 (*d*, $^3J = 8.3$, 1 arom. H); 7.31 (*dt*, $^3J = 7.6$, $^4J = 1.5$, 2 arom. H); 7.44 (*d*, $^3J = 8.3$ Hz, 1 arom. H); 7.52 (*dd*, $^3J = 8.2$, $^4J = 1.5$, 2 arom. H); 8.05 (*d*, $^3J = 5.9$, 1 arom. H); 8.51 (*d*, $^3J = 5.9$, 1 arom. H); 9.11 (*s*, 1 arom. H). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): 29.8 (Me); 80.0 (1 C); 114.8 (1 CH); 119.3 (1 C); 119.9 (1 CH); 122.9 (1 CH); 124.9 (2 CH); 126.0 (1 CH); 127.5 (1 C); 127.7 (1 CH); 128.5 (2 CH); 129.4 (1 C); 130.6 (1 CH); 143.0 (1 CH); 145.5 (1 C); 147.3 (1 C); 152.1 (1 CH). Anal. calc. for $\text{C}_{19}\text{H}_{15}\text{NO}$: C 83.49, H 5.53, N 5.12; found: C 83.38, H 5.48, N 5.06.

2-(4-Methoxyphenyl)-2-methyl-2H-naphtho[1,2-*b*]pyran (5). According to 2.1 (Al_2O_3). CC (silica gel, AcOEt/hexane 1:99) gave 55% of **5**. M.p. 73–74°. UV (closed form; EtOH): 213 (27620), 252 (23950), 260 (25360), 319 (2790), 330 (3100), 357 (2540). $^1\text{H-NMR}$ (360 MHz, CDCl_3): 1.87 (*s*, Me); 3.75 (*s*, MeO); 5.96, 6.58 (*d*, $^3J = 9.7$, H-C(3), H-C(4)); 6.82 (*m*, $^3J = 8.9$, 2 arom. H); 7.13 (*d*, $^3J = 8.3$, 1 arom. H); 7.33 (*d*, $^3J = 8.3$, 1 arom. H); 7.40–7.46 (*m*, 2 arom. H); 7.49 (*m*, $^3J = 8.9$, 2 arom. H); 7.72 (*d*, $^3J = 7.8$, 1 arom. H); 8.31 (*d*, $^3J = 7.8$, 1 arom. H). $^{13}\text{C-NMR}$ (90 MHz, CDCl_3): 24.5 (Me); 50.1 (MeO); 74.8 (1 C); 108.5 (2 CH); 110.4 (1 C); 115.0 (1 CH); 116.8 (1 CH); 118.1 (1 CH); 119.4 (1 CH); 119.7 (1 C); 120.3 (1 CH); 121.1 (2 CH); 121.2 (1 CH); 122.5 (1 CH); 123.2 (2 CH); 129.4 (1 C); 133.0 (1 C); 143.1 (1 C); 153.6 (1 C). Anal. calc. for $\text{C}_{21}\text{H}_{18}\text{O}_2$: C 83.44, H 5.96; found: C 83.42, H 5.95.

2-Methyl-2-(4-(morpholin-4-yl)phenyl)-2H-naphtho[1,2-*b*]pyran (6). According to 2.1 (Al_2O_3). CC (silica gel, AcOEt/pentane 1:19, then 2:23) gave 66% of **6**. M.p. 130–131°. UV (closed form, EtOH): 213 (25870), 255 (23530), 260 (25090), 325 (3620), 338 (3750), 352 (3360). $^1\text{H-NMR}$ (360 MHz, CDCl_3): 1.87 (*s*, Me); 3.10 (*m*, $^3J = 4.9$, 4 H, CH_2N); 3.81 (*m*, $^3J = 4.9$, 4 H, CH_2O); 5.94, 6.56 (2*d*, each $^3J = 9.7$, H-C(3), H-C(4)); 6.83 (*m*, $^3J = 8.8$, 2 arom. H); 7.12 (*d*, $^3J = 8.3$, 1 arom. H); 7.31 (*d*, $^3J = 8.3$, 1 arom. H); 7.40–7.46 (*m*, 2 arom. H); 7.47 (*m*, $^3J = 8.8$, 2 arom. H); 7.72 (*d*, $^3J = 7.7$, 1 arom. H); 8.30 (*d*, $^3J = 7.7$, 1 arom. H). $^{13}\text{C-NMR}$ (90 MHz, CDCl_3): 29.3 (Me); 49.0 (2 CH_2); 66.8 (2 CH_2); 79.1 (1 C); 115.1 (2 CH); 115.4 (1 C); 119.9 (1 CH); 121.9 (1 CH); 123.0 (1 CH); 124.4 (1 CH); 124.7 (1 C); 125.2 (1 CH); 125.9 (2 CH); 126.0 (1 CH); 127.5 (1 CH); 128.2 (1 CH); 134.4 (1 C); 137.2 (1 C); 148.2 (1 C); 150.2 (1 C). Anal. calc. for $\text{C}_{24}\text{H}_{23}\text{NO}_2$: C 80.67, H 6.44, N 3.92; found: C 80.21, H 6.24, N 3.88.

2-Methyl-2-phenyl-2H-phenanthro[9,10-*b*]pyran (7). According to 2.1 (TsOH). CC (silica gel, pentane/ Et_2O 95:5) and recrystallization from EtOH gave 37% of **7**. M.p. 131°. UV (closed form; MeOH): 202 (28670), 216 (25410), 238 (34450), 254 (28890), 264 (23500), 338 (7480), 370 (3120). $^1\text{H-NMR}$ (250 MHz, CDCl_3): 1.91 (*s*, Me); 6.15 (*d*, $^3J = 9.8$, H-C(3) or H-C(4)); 7.20 (*d*, $^3J = \text{H-C(4) or H-C(3)}$); 7.26 (*m*, 3 arom. H); 7.48 (*dt*, $^3J = 7.0$, $^4J = 1.3$, 1 arom. H); 7.53 (*m*, 1 arom. H); 7.58 (*dd*, $^3J = 8.2$, $^4J = 1.3$, 2 arom. H); 7.65 (*m*, 2 arom. H); 7.98 (*dd*, $^3J = 8.6$, $^4J = 1.3$, 1 arom. H); 8.51–8.61 (*m*, 3 arom. H). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3): 29.6 (Me);

79.0 (1 C); 110.7 (1 C); 119.5 (1 CH); 121.9 (1 CH); 122.5 (2 CH); 122.9 (1 CH); 124.2 (1 CH); 124.8 (2 CH); 125.6 (1 C); 126.4 (1 C); 126.7 (1 CH); 126.9 (1 CH); 127.1 (1 CH); 127.2 (1 CH); 127.7 (1 CH); 128.1 (2 CH); 129.1 (1 C); 131.2 (1 C); 145.9 (1 C); 146.7 (1 C). Anal. calc. for $C_{24}H_{18}O$: C 89.41, H 5.6; found: C 89.29, H 5.60.

2-(4-Methoxyphenyl)-2-methyl-2H-phenanthro[9,10-b]pyran (8). According to 2.1 (Al_2O_3). CC (silica gel, $CHCl_3$ /hexane 1:1) gave 50% of **8**. Light-yellow crystals. M.p. 116–117°. UV (closed form, EtOH): 208 (27880), 221 (25620), 240 (32930), 255 (29930), 340 (7650), 372 (3320). 1H -NMR (360 MHz, $CDCl_3$): 1.86 (s, Me); 3.73 (s, MeO); 6.14 (d, $^3J = 9.8$, H–C(3) or H–C(4)); 6.82 (m, $^3J = 8.9$, 2 arom. H); 7.23 (d, $^3J = 9.8$, H–C(4) or H–C(3)); 7.48–7.54 (m, 3 arom. H); 7.59 (t, $^3J = 8.1$, 1 arom. H); 7.65–7.70 (m, 2 arom. H); 8.03 (d, $^3J = 8.1$, 1 arom. H); 8.40–8.55 (m, 1 arom. H); 8.60–8.66 (m, 2 arom. H). ^{13}C -NMR (90 MHz, $CDCl_3$): 28.3 (Me); 55.1 (MeO); 78.7 (1 C); 110.6 (1 C); 113.4 (2 CH); 119.3 (1 CH); 121.8 (1 CH); 122.4 (1 CH); 122.5 (1 CH); 122.9 (1 CH); 124.1 (1 CH); 125.6 (1 C); 126.2 (1 CH); 126.3 (2 CH); 126.5 (1 C); 126.8 (1 CH); 126.9 (1 CH); 127.8 (1 CH); 129.1 (1 C); 131.1 (1 C); 137.8 (1 C); 146.6 (1 C); 158.7 (1 C). Anal. calc. for $C_{25}H_{20}O_2$: C 85.23, H 5.68; found: C 85.07, H 5.65.

2-Methyl-2-phenyl-2H-benzofuro[2,3-g][1]benzopyran (9). According to 2.1 (TsOH). CC (silica gel, pentane) gave a mixture of **9** and the isomeric 4-methyl-4-phenyl-4H-benzofuro[3,2-g][1]benzopyran. Total yield 62%. The isomers were separated by recrystallization from heptane (**9** least soluble). **9**: M.p. 154°. UV (closed form; EtOH): 205 (40000), 226 (30160), 244 (19590), 253 (19580), 268 (10220), 300 (20870), 312 (23440), 342 (9950), 356 (8500). 1H -NMR (250 MHz, $CDCl_3$): 1.78 (s, Me); 6.08, 6.59 (2d, $^3J = 9.7$, H–C(3), H–C(4)); 7.16 (s, 1 arom. H); 7.25 (m, 1 arom. H); 7.27 (t, $^3J =$ masked, $^4J =$ masked, 1 arom. H); 7.32 (m, 2 arom. H); 7.40 (dt, $^3J = 8.2$, $^4J = 1.5$, 1 arom. H); 7.43 (s, 1 arom. H); 7.48 (d, $^3J = 8.0$, 1 arom. H); 7.54 (m, 2 arom. H); 7.85 (d, $^3J = 7.35$ Hz, 1 arom. H). ^{13}C -NMR (100.6 MHz, $CDCl_3$): 29.3 (Me); 78.7 (1 C); 107.6 (1 CH); 108.8 (1 CH); 116.1 (1 CH); 120.6 (1 CH); 121.3 (1 C); 122.5 (1 CH); 123.5 (1 CH); 124.4 (1 C); 124.5 (1 C); 125.2 (2 CH); 127.0 (1 CH); 127.3 (1 CH); 128.2 (2 CH); 130.9 (1 CH); 145.6 (1 C); 149.0 (1 C); 151.1 (1 C); 157.0 (1 C). Anal. calc. for $C_{22}H_{16}O_2$: C 84.59, H 5.16; found: C 84.53, H 5.11.

Semi-preparative Enrichment of Enantiomers. Anal. separations by liquid chromatography on non-racemic sorbents showed that microcrystalline triacetylcellulose [9] as stationary phase and MeOH as eluent (Table 3) were most suitable for a semi-prep. enrichment of enantiomers. Thus, the synthesized racemate (5–10 mg) in MeOH was injected into a low-pressure column (1.0–4.5 bar), the overall scale of separation being 9–10 mg of racemate. After collection of several fractions, the enriched enantiomers were stored at 0–5° and protected against light. Chromene **1** was not completely separated (Table 3) and had to be enriched by a recycling procedure [27]. MeOH was removed under vacuum at 0–5°, yielding crystals in all cases.

Table 3. Retention Factors k' of Racemates on Microcrystalline Triacetylcellulose with MeOH as Eluent^{a)}

	k' (+)	k' (–)	λ [nm]		k' (+)	k' (–)	λ [nm]
1	2.8	2.6	365, 436	6	2.5	1.1	365
2	0.6	1.0	436	7	1.7	4.9	365; 436
3	6.5	1.2	436	8	1.9	^{b)}	365
4	0.8	0.5	436	9	2.9	1.5	436
5	1.7	2.2	365				

^{a)} k' Values refer to 1,3,5-tri-*tert*-butylbenzene as a non-retained standard [9]. Because of unequal columns and, therefore, pressures (90–140 bar), k' values of different 2H-1-benzopyrans are not strictly comparable. λ : Wavelengths of polarimetric detection of (+)- and (–) enantiomers. ^{b)} Broad peak between $k' = 10$ and 20.

Characterization of Enantiomers. Subsequent injection into a high-pressure column (90–140 bar) of microcrystalline triacetylcellulose [9] resulted in retention factors k' (+) and k' (–) (Table 3), determined *via* polarimetric detection. Enantiomeric purities p of (+)- and (–)-**1** (Table 4) were obtained by 1H -NMR in the presence of (+)-(-S)-1-(9-anthryl)-2,2,2-trifluoroethanol. In the case of partial overlap of peaks in the anal. chromatograms (Table 3), a deconvolution procedure [21] was applied to determine the p values given in Table 4.

In the absence of overlap of chromatographic peaks, p was obtained *via* integration of the respective peak areas. Specific rotations (Table 4) and circular-dichroism data (Table 5) served for further characterization of the

Table 4. *Enantiomeric Purities p (± 0.03) of Enriched Enantiomers and Their Specific Rotations (MeOH, ca. 5 mg/ml), corrected for $p = 1^a$*

	p	$[\alpha]^{20}$ [deg ml g ⁻¹ dm ⁻¹]	
		436 nm	578 nm
(+)-1	0.88	+ 200 \pm 40	+ 40 \pm 15
(-)-1	0.98	- 190 \pm 30	- 36 \pm 9
(+)-2	0.92	+ 390 \pm 60	+ 90 \pm 20
(-)-2	0.92	- 550 \pm 70	- 110 \pm 20
(+)-3	0.91	+ 2200 \pm 220	+ 840 \pm 85
(-)-3	0.87	- 1700 \pm 170	- 660 \pm 70
(+)-4	0.94	+ 2700 \pm 300	+ 1000 \pm 110
(-)-4	0.93	- 2400 \pm 250	- 900 \pm 90
(+)-5	0.37	+ 2000 \pm 260	+ 750 \pm 120
(-)-5	0.44	- 1700 \pm 200	- 660 \pm 90
(+)-6	0.77	b)	b)
(-)-6	0.95	b)	b)
(+)-7	0.55	+ 1700 \pm 240	+ 590 \pm 90
(-)-7	0.38	- 1640 \pm 260	- 560 \pm 90
(+)-9	0.90	+ 460 \pm 80	+ 170 \pm 30
(-)-9	0.97	- 470 \pm 70	- 170 \pm 30

^a) Purities p determined by HPLC (cf. Table 3), except for 1 (¹H-NMR in CDCl₃ in the presence of 15 equiv. of (+)-(S)-1-(9-anthryl)-2,2,2-trifluoroethanol).

^b) Quantities of enantiomers insufficient for reliable measurement of $[\alpha]$.

Table 5. *Circular Dichroism (MeOH, 3 to 4 \cdot 10⁻⁴ mol/l) of Enriched Enantiomers. Corrected for an Enantiomeric Purity of 1^a)*

		λ_{\max} [nm] ($\Delta\epsilon_{\max}$ [l mol ⁻¹ cm ⁻¹])				
(+)-1	240 (-32.3)	275 (-1.2)	310 (+2.1)		350 (+2.8)	
(-)-1	240 (+34.3)	275 (+0.9)	310 (-1.7)		350 (-2.6)	
(+)-3	219 (+50.0)	257 (+48.6)	265 (+44.3)	320 (+6.6)	334 (+6.6)	350 (+5.8)
(-)-3	219 (-42.9)	257 (-42.0)	265 (-39.8)	320 (-5.1)	334 (-5.6)	350 (-5.1)
(+)-4	215 (+38.6)	263 (+22.9)	270 (+21.5)		348 (+4.0)	
(-)-4	215 (-37.3)	263 (-21.9)	270 (-21.9)		348 (-4.0)	
(+)-5	225 (+23.5)	260 (+53.1)		335 (+5.3)		350 (+4.7)
(-)-5	225 (-17.4)	260 (-44.5)		335 (-4.3)		350 (-4.0)
(+)-6	240 (-23.7)	266 (+80.0)		330 (+6.7)		350 (+5.8)
(-)-6	240 (+19.5)	266 (-79.9)		330 (-5.7)		350 (-5.4)
(+)-7	239 (-21.4)	254 (+6.5)	277 (+9.1)	290 (+3.0)	335 (+9.3)	
(-)-7	239 (+19.4)	254 (-6.6)	277 (-8.1)	290 (-2.8)	335 (-7.8)	
(+)-9			270 (+5.0)	295 (+2.7)	310 (+3.0)	340 (+6.2)
(-)-9			270 (-5.1)	295 (-2.9)	310 (-3.3)	340 (-5.5)

^a) λ_{\max} : Wavelength of spectral maximum or minimum. $\Delta\epsilon_{\max}$: differential absorption coefficient of maximum or minimum. Signs given, e.g. for (+)-1, refer to specific rotations.

enantiomers. The data for both enantiomers were corrected for an enantiomeric purity of 1 and thus provide an independent check of the samples obtained. The quantities of enriched enantiomers were not sufficient for reliable chiroptical measurements in all cases. The errors, e.g. in Table 4, result mainly from weighting small amounts of samples, but also from the error of p (± 0.03) and sometimes from strong UV absorption bands.

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