Stereochemistry of Planarchiral Compounds, 11[1]

Static and Dynamic Stereochemistry of 10,10′-Dibromo-2,2′-bi(1,6-methano[10]annulenyl)

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Coupling of 2,10-dibromo-1,6-methano[10]annulene with Cu(II) chloride (via the mono-Li derivative) affords a mixture of the *meso* and racemic forms of 10,10′-dibromo-2,2′-bi(1,6-methano[10]-annulenyl) (2) which were separated by chromatography on silica gel. Their configurational assignments followed from ^{1}H- and ^{13}C-NMR spectroscopy and optical resolution. The rotational barrier of *meso*-2 was established as 58 kJ mol^{-1} by temperature-dependent ^{1}H-NMR spectroscopy. After chromatographic resolution of *rac*-2 into the optically active equilibrium mixtures of the rotamers ($[\alpha]_D$ = +525 and −525 in ethanol), they could be separated on silica gel at 0°C (in a ratio of 3.6:1); their CD spectra were recorded at −10°C and the rotational barriers (85 and 88 kJ mol^{-1}, resp.) were established by CD as well as by ^{1}H-NMR kinetics (equilibration of the rotamers). Stereochemical consequences of the presence of two elements of chirality (torsional and annulene chirality) as well as possible reasons for the (relatively) high difference in the rotational barriers for *meso* and racemic forms are discussed.

Stereochemie planarchiraler Verbindungen, 11[1]. – Statische und dynamische Stereochemie von 10,10′-Dibrom-2,2′-bi(1,6-methano-[10]annulenyl)

Bei der Kupplung von 2,10-Dibrom-1,6-methano[10]annulen mit Cu(II)-chlorid (über die Mono-Li-Verbindung) entsteht eine Mischung der *meso*- und Racemat-Form von 10,10′-Dibrom-2,2′-bi(1,6-methano[10]annulenyl) (2), die durch Chromatographie an Kieselgel getrennt wurde. Die Konfigurationszuordnung der Diastereomeren erfolgte durch ^{1}H- und ^{13}C-NMR-Spektroskopie und durch Racematspaltung. Die Rotationsbarriere von *meso*-2 wurde durch temperaturabhängige ^{1}H-NMR-Spektroskopie mit 58 kJ mol^{-1} bestimmt. Nach chromatographischer Enantiomerentrennung von *rac*-2 in die optisch aktiven Gleichgewichtsmischungen der Rotameren ($[\alpha]_D$ = +525 bzw. −525 in Ethanol) konnten diese bei 0°C an Kieselgel (im Verhältnis von 3.6:1) aufgetrennt, ihre CD-Spektren bei −10°C gemessen und die Rotationsbarrieren (85 bzw. 88 kJ mol^{-1}) sowohl durch CD- als auch ^{1}H-NMR-Kinetik (durch Äquilibrierung der Rotameren) bestimmt werden. Die stereochemischen Konsequenzen des Vorliegens von 2 Chiralitätselementen in 2 (Torsions- und Annulen-Chiralität) sowie mögliche Gründe für die (verhältnismäßig) hohe Differenz der Rotationsbarrieren zwischen *meso*- und Racemat-Form werden diskutiert.

Torsional isomerism plays an important role in stereochemical research. Thus, e.g., atropisomerism has been early and extensively studied. Subsequently, this type of chirality which is caused by a torsional barrier around a single bond higher than appr. 95 kJ mol^{-1} has been classified as axial chirality. Also some planarchiral structures (such as cyclophanes) might be regarded as torsional isomers[2].

Interesting stereochemical consequences arise if in addition to torsional chirality further elements of chirality (i.e. stereogenic units)[3] are introduced into suitable molecular structures.

Thus, for example, from tricarbonylchromium complexes of *o,o′*-disubstituted biphenyls – due to their biphenyl and metallocene chirality – several stereoisomers are possible: Symmetrical substitution of a bis-Cr(CO)$_3$ complex results in a racemate and a *meso* form (with an average C_2 and C_s symmetry, resp.)[4]. Even the latter might be resolvable into enantiomers provided the torsional barrier is high enough. From such compounds residual stereoisomers may result suitable for the optical resolution of appropriate arenes[5].

In context with these studies and with our work on chiral [10]- and [14]annulenes[1,2], which represent special types of planarchiral structures, we have now turned our attention to the static and dynamic stereochemistry of 2,2′-bi(1,6-methano[10]annulenyls). These compounds represent a novel type of torsional isomers with "annulene chirality" as the second stereogenic unit.

From the parent compound 2,2′-bi(1,6-methano[10]-annulenyl) (1) two diastereomers are feasible: a racemate and a *meso* form with idealized C_2 and C_s (or S_2) symmetry, resp. (see Scheme 1).

In 1 the rotational barriers (as determined by dynamic ^{1}H-NMR spectroscopy) are low: $\Delta G^{\neq}_{25}$ = 63 kJ mol^{-1} for the racemate (whose configuration was assigned by a qualitative optical resolution on Chiralpak® or Chiralcel® where it revealed two peaks)[6].

Appropriate substitution, however, (e.g. in positions 10 and 10′) should increase the torsional barrier(s) to such an extent that also the chiral (so-called) *meso* form could be resolved into enantiomers. Attempts in this direction seemed promising since with medium-pressure liquid chromatography (MPLC) on microcrystalline triacetylcellulose (especially by the recycling technique)[1,7] a method is now avail-

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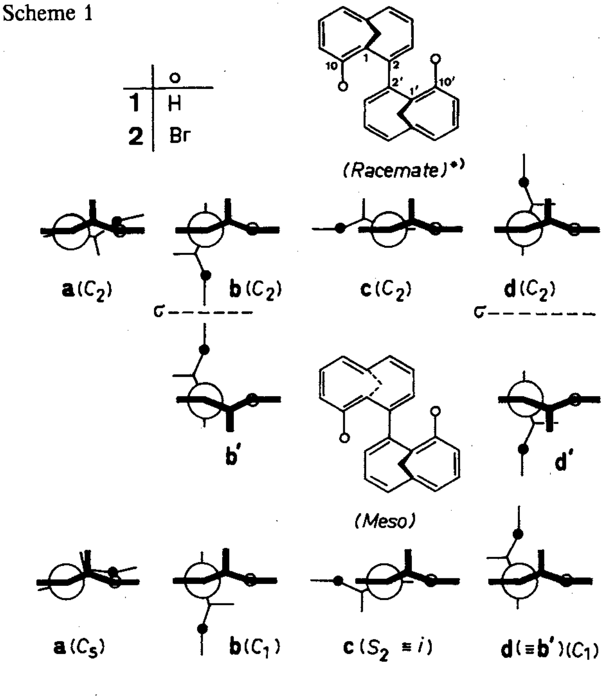
able which might allow the preparative separation even of enantiomers with a relatively low racemization (torsional) barrier.

Scheme 1



*) Of **a** and **c**, resp., only one enantiomer is shown.

The present paper presents results on the stereochemistry of the title compound **2**.

Results and Discussion

The overall stereochemical features of a 10,10′-disubstituted 2,2′-bi(1,6-methano[10]annulenyl) are schematically depicted in Scheme 1, showing four conformers (obtained by torsions of 90° around the 2,2′-bond) of the two diastereomers in a Newman-type representation. Whereas all conformers (**a**−**d**) of the racemate have C_2 symmetry and are therefore chiral, the idealized conformational situation of the *meso* form includes two achiral stereoisomers (**a** and **c**) with a plane or center of symmetry (C_s and S_2, resp.) and chiral (enantiomeric) conformations (e.g. **b** and **d**) with C_1 symmetry. If the rotational barrier around the central 2,2′-bond is low enough (at room temperature) the *average meso* form "behaves" as being achiral.

With the use of stereochemical descriptors [with the subscripts p and a for planar (annulene) and axial (biaryl) chirality, resp.] the general situation may be described as follows (see also Scheme 1):

Racemate **2b**: $(S)_p(S)_a(S)_p$ and its mirror image **2b′**: $(R)_p(R)_a(R)_p$
2d: $(S)_p(R)_a(S)_p$ and its mirror image **2d′**: $(R)_p(S)_a(R)_p$
meso form **2b**: $(S)_p(S)_a(R)_p$ and its mirror image **2d** = **2b′**: $(R)_p(R)_a(S)_p$

As a consequence, two enantiomers of the *meso* form and two enantiomeric pairs of the torsional isomers (**b** and **d**) of the racemate are feasible (with the latter representing residual stereoisomers)[5]. This general concept is valid for all types of biaryls with additional elements of chirality, especially for bi-metallocenes [such as bi("benchrotrenes") and biferrocenyls][4]. More complicated exceptions to this rule arise when the elements of chirality lie within the rotational axis (cf. ref.[8]).

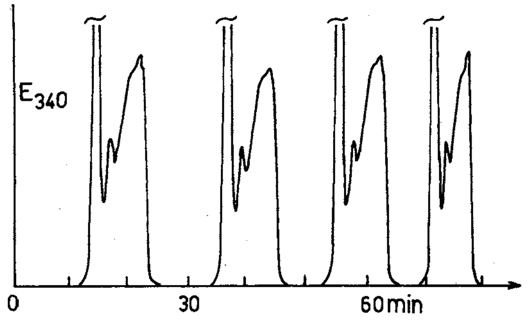


Figure 1. Chromatographic separation of *meso*- and *rac*-**2**

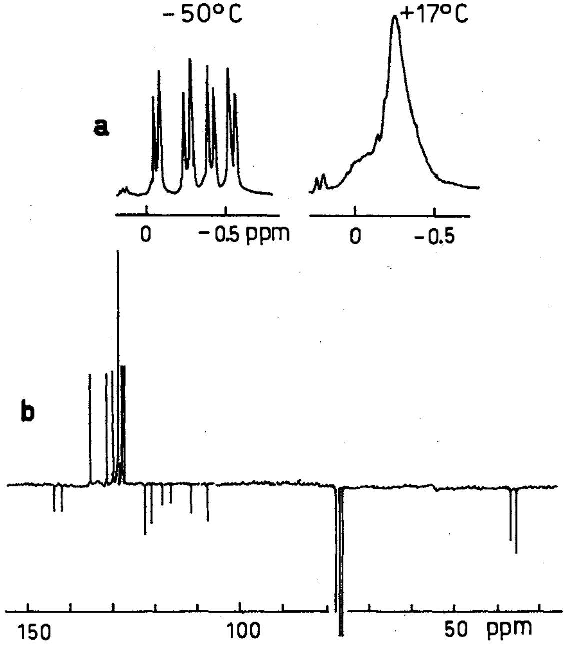


Figure 2. a) ^1H-NMR spectrum of *meso*-**2** at −50 and +20°C. b) $^{13}C\{^1H\}$-NMR spectrum of *meso*-**2** at −40°C

The significant CH_2 regions in the ^1H-NMR and the (^1H) broadband decoupled and *J*-resolved ^{13}C-NMR spectra of *meso*- and *rac*-**2**, which were obtained by chromatographic separation (MPLC) on silica gel (see Figure 1 and Experimental) are shown in Figures 2 and 3. The signals of the ^1H-NMR spectra in the aromatic region are consistent with the assigned structures.

In the ^{13}C-NMR spectrum the *meso* form according to its C_1 symmetry exhibits 11 pairs of lines at −40°C, each pair in an intensity ratio of appr. 1:1 and each line belonging to a distinct carbon atom. In contrast, the racemate (with C_2 symmetry) also exhibits 11 pair of lines, where each pair, due to the different population of the two rotamers (vide infra), shows the same ratio (of appr. 1:3.6) in the intensity

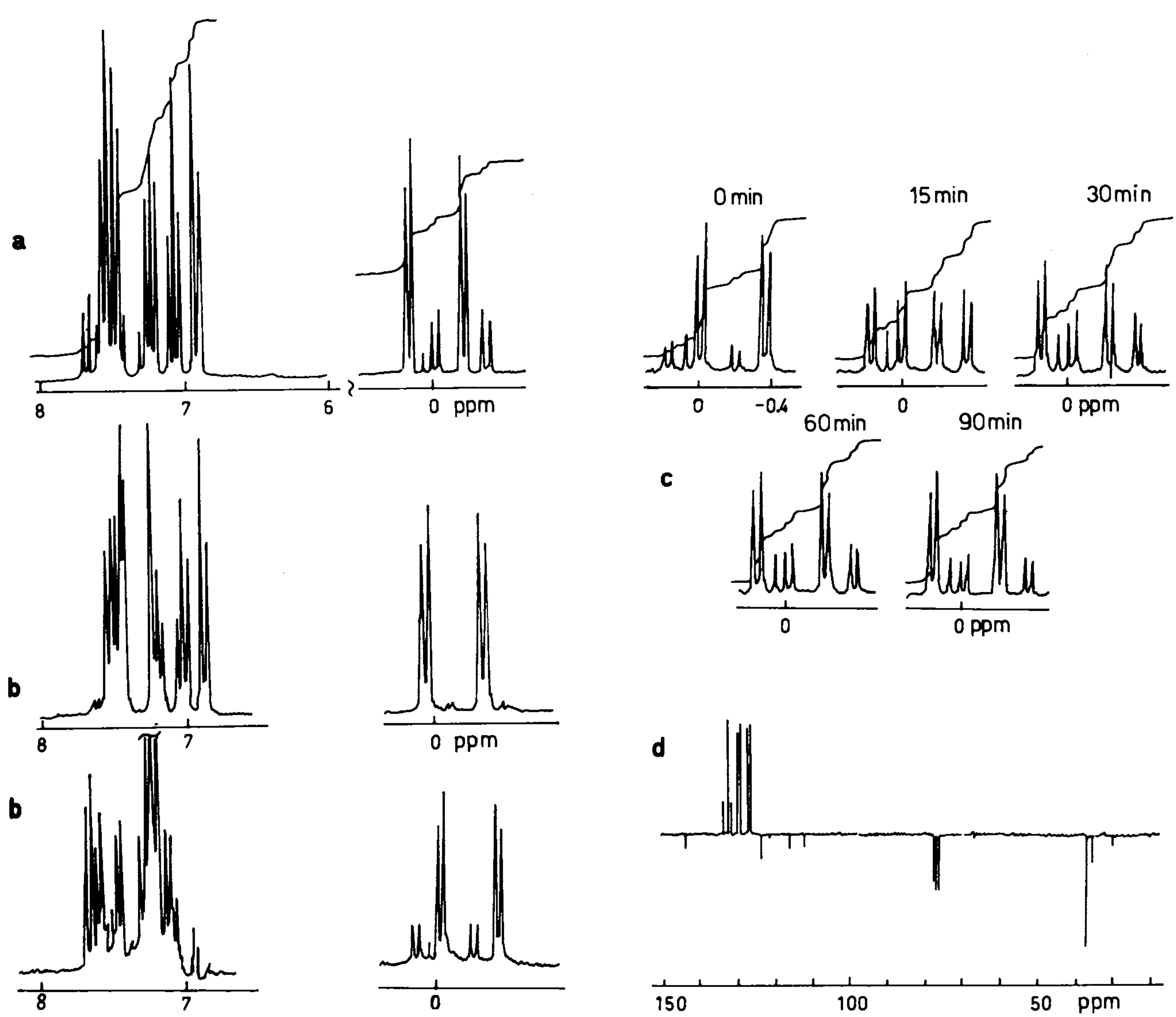


Figure 3. ¹H-NMR spectrum of *rac*-**2**. a) Equilibrium mixture at 20°C. – b) Rotamers at −40°C. – c) Kinetics at 0°C, recorded after 15, 30, 60, and 90 min. – d) $^{13}C\{^1H\}$-NMR spectrum of *rac*-**2** (at 20°C)

of the lines and where each line arises from two symmetrically equivalent carbon atoms (see Figures 2b and 3d).

In order to obtain sharp signals, the spectra of *meso*-**2** had to be recorded at −50 to −40°C thereby avoiding line broadening by exchange processes of the rotamers.

From the coalescence temperature of the CH_2 signals (5 and 20°C, resp.) in the *meso* form (Figure 2a) its rotational barrier was deduced as 58 kJ mol^{-1}. The ¹H-NMR spectrum of the racemate (in the region $\delta = 0$ ppm) revealed the presence of two diastereomeric rotamers in a ratio of appr. 3.6:1 and 2.6:1 at 20 and 100°C, resp., with $\Delta G = 3$ kJ mol^{-1} (Figure 3a). In this case no coalescence could be observed in CD_3CN until 100°C. After their separation on silica gel at 0°C (vide infra) and removing the solvent in high vacuum at −30 to −20°C their ¹H-NMR spectra could be recorded at −40°C. Even then both diastereomers contain more or less significant amounts of the corresponding rotamer (see Figure 3b).

This equilibrium on the other hand provided an access to the rotational barriers (85 and 88 kJ mol^{-1}, resp.) of *rac*-**2** by ¹H-NMR kinetics of the underpopulated rotamer (in $CDCl_3$ at 0°C). After 60 min the equilibrium (with a ratio of 1:3.6) had been attained as shown in Figure 3c.

Both the ¹H- and ¹³C-NMR spectra clearly revealed (vide supra) the racemate to be an equilibrium mixture of torsional isomers (see Scheme 1) with a temperature-dependent ratio of 3.6:1 at 20°C and 2.6:1 at 100°C and ΔG values of 3.2 and 3.0 kJ mol^{-1}, resp., as monitored by the bridge proton signals (vide supra and Figure 3a).

The *meso* form on the other hand consists of two enantiomers ($\Delta G = 0$ kJ mol^{-1}). As mentioned above, the rotational barriers were determined by variable-temperature ¹H-NMR spectroscopy for *meso*-**2** and by ¹H-NMR kinetics at 0°C for the racemate (after separation into its rotamers, vide supra and Figure 3c). The $\Delta G^{\neq}$ values were found to be 58 and 85 or 88 kJ mol^{-1}, resp.

The barrier for *meso*-**2** (58 kJ, corresponding to a half-life of appr. 3 s at −40 °C) obviously is too low for a preparative separation into torsional isomers (= enantiomers) whereas the racemate can be separated by MPLC on silica gel (in hexane-THF) at 0 °C (see Figure 5b). The barrier of 85 kJ was confirmed by CD kinetics (vide infra).

For a complete separation of the racemic mixture **2** into all four possible stereoisomers (**b,b′** and **d,d′**, see Scheme 1) it seemed advantageous to perform in a first step a separation into the stable enantiomers (on triacetylcellulose in ethanol, see Figure 4) — as already employed in the case of torsional isomeric biphenyl-Cr(CO$_3$) complexes[4,9]. Each of the enantiomers is an equilibrium mixture of the torsional isomers **b** and **d**, and **b′** and **d′**, resp., that can subsequently be separated into the rotamers **b** and **d** on the one hand and **b′** and **d′** on the other.

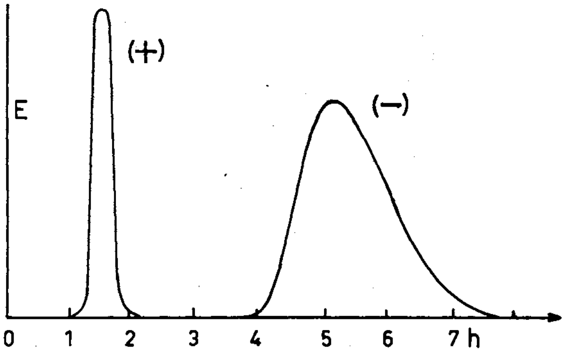


Figure 4. Chromatographic separation of *rac*-**2** on triacetylcellulose in ethanol at 40 °C

Conclusions

A full (360°) torsion around the 2,2′-bond in a biannulenyl such as **1** or **2** encounters two significant steric barriers, namely between positions 3 and 10′ (and 3′ and 10, resp.) on the one hand and between 10 and 10′ on the other hand as shown for the conformers **c** and **a** in Scheme 1. The overall torsional barrier will be determined by the less severe steric interaction — depending on the size of the substituent(s) in position 10 and 10′ (i.e. conformer **c** for the dibromo derivative **2**). An increase of the steric requirement of this substituent should raise the barrier to such an extent as prerequisite for a possible separation of enantiomers (= rotamers) of the so-called *meso* form (**b** and **d** ≡ **b′** in Scheme 1).

Stereochemical consequences of various substituents in positions 10 and 10′ are now under investigation.

The difference of the barriers in the *meso* form and the racemate (in **2** appr. 30 kJ) seems unexpectedly high. It is known, however, from X-ray studies, that the ten-membered perimeter in bridged [10]annulenes is puckered in sort of a W-shape as schematically depicted in Scheme 1[1,10]. Therefore, in the rotation of the racemic form the significant 3−10′ (and 3′−10) interactions take place at the *same* time whereas in the *meso* form these positions pass each other successively. Moreover, the molecule can avoid these interactions to some extent by something like a staggering motion.

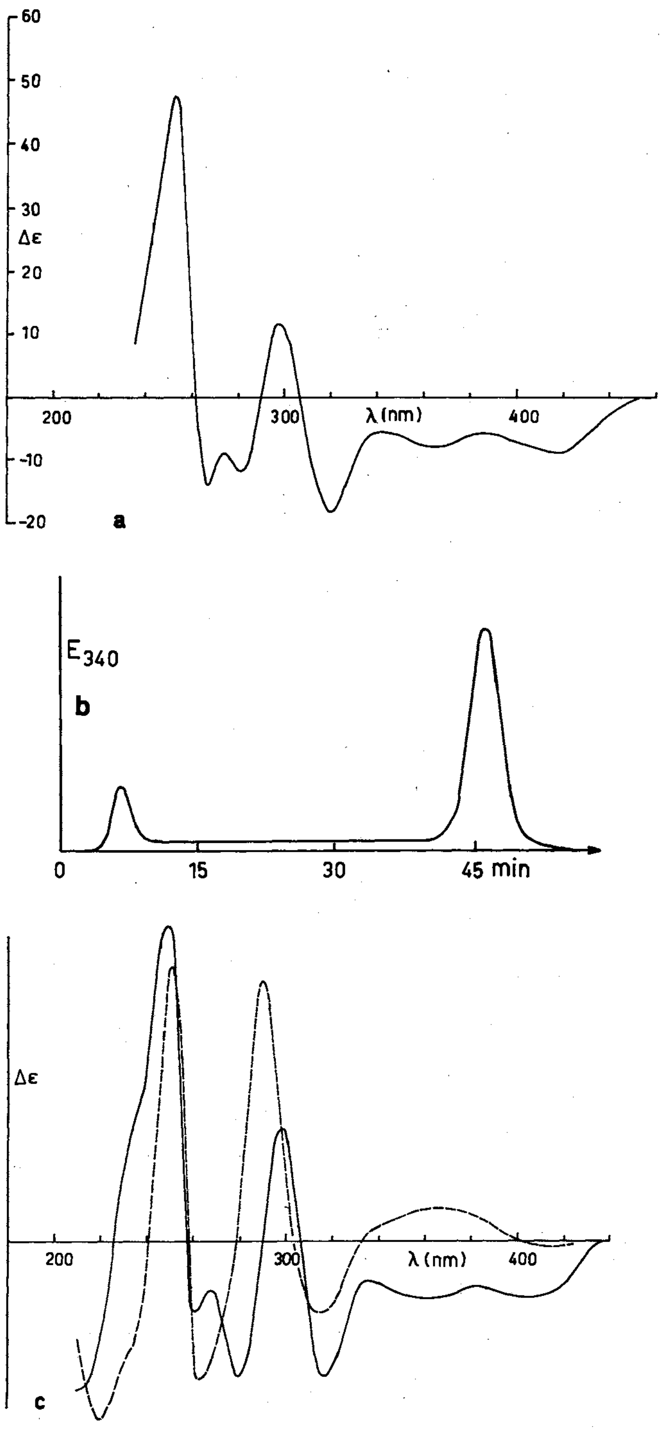


Figure 5. Circular dichroism of (−)-enantiomers of *rac*-**2** in ethanol. a) Equilibrium mixture of rotamers at 0 °C. — b) Separation of a) on silica gel at 0 °C (the elevated base line between the peaks indicates an interconversion of rotamers during the separation). — c) Separated rotamers at −10 °C in ethanol: ——— main, – – – underpopulated isomer

Further investigations (e.g. substitution in position 3 and 3′) and especially forcefield calculations may show whether these assumptions are valid.

As to the absolute chiralities of the enantiomers (cf. Figures 5a and 5c) some preliminary conclusions might be drawn from the CD spectra in comparison with the chirop-

Table 1. Physical data of *meso*- and *rac*-10,10′-dibromo-2,2′-bi(1,6-methano[10]annulenyl) (**2**)

	meso-**2**	*rac*-**2**
M.p. (hexane-CH_2Cl_2)	134–135 °C	221–222 °C
^1H NMR (250 MHz, $CDCl_3$, δ in ppm)	–50 °C: 7.70 (d, 1H; J = 9.5 Hz), 7.53–7.40 (m, 5H), 7.35–7.24 (m, 1H), 7.13–6.85 (m, 4H), 6.41 (d, 1H, J = 10 Hz), –0.08, –0.28, –0.42, –0.55 (dd, 4H, J = 10–10.1 Hz) (see Figure 2a)	0 °C: 7.67 (d, J = 9.2 Hz)[a], 7.6–7.42 (m), 7.3–7.19 (m), 7.07 (t, J = 9 Hz), 6.9 (d, J = 9.3 Hz), 0.15, –0.02, –0.39 (dd, 4H, J = 10–10.3 Hz) (see Figure 3a)
^{13}C NMR ($CDCl_3$)	–40 °C: See Figure 2b	20 °C: See Figure 3d
UV ⟨ethanol, λ_{max} [nm] (ε)⟩	245 (33500), 270 (60200), 336 (13700)	257 (45700), 283 (39500), 367 (15000). Rotamers, after separation at –10 °C: 257 (47500), 281 (39600), 364 (18000), 426 (5000)
MS ($C_{22}H_{16}Br_2$: 437.9619) [m/z]	437.963 ± 0.003	437.963 ± 0.003
CD ⟨ethanol, λ [nm] (Δε)⟩	–	0 °C (equilibrium mixture, Figure 5a): 220 (+), 251 (+48), 267 (–14), 282 (–11), 298 (+11), 321 (–18), 365 (–7), 415 (–8). – For the separated rotamers at –10 °C see Figure 5c

[a] Signal integration in *rac*-**2**: $H_{ar}:H_{bridge} = 3:1$.

tical properties of bridged [10]annulenes of known configurations[1]. These will have to be supported, however, by further studies.

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Experimental

Melting points were determined on a Kofler microscope and are uncorrected. – Medium pressure liquid chromatography (MPLC) was performed on Merck LiChroprep Si-60 (25–40 µm) in *n*-Hexane-THF (0.6%, distilled over $LiAlH_4$) on columns (52 × 400 mm) with an FMI pump (at 2.0–2.8 bar, 20–25 ml/min) and an ISCO UA-5 UV-detector. HPLC: Hewlett-Packard HP 1090-M (on reversed phase KG in various solvents and at various temperatures, e.g. methanol-water, 3:1, at 50 °C) with a diode-array detector. – IR: Perkin-Elmer 237 spectrometer. – MS: Varian MAT CH-7. – Optical rotations: Perkin-Elmer 241 polarimeter. – CD: Dichrograph Mark III (Jobin-Yvon). – All NMR spectra were measured with a Bruker WM-250 spectrometer (in $CDCl_3$) in FT mode using an Aspect-2000 computer.

10,10′-Dibromo-2,2′-bi(1,6-methano[10]annulenyl) (**2**): A solution of 3.0 g (10 mmol) of 2,10-dibromo-1,6-methano[10]annulene[11] in dry ether (80 ml) was treated under Ar at –50 °C with 10.5 ml (10 mmol) of an ethereal Butyllithium solution. After warming the solution to –10 °C the mono-Li derivative was transferred to a precooled (–78 °C) suspension of 1.35 g (10 mmol) of anhydrous Cu(II) chloride in 300 ml of dry ether. The yellow-green mixture was stirred for 2 h at –78 °C and then treated with water (50 ml). The organic layer was separated and the aqueous phase extracted with ether (3 × 50 ml). The combined ether solution was washed with water (3 × 100 ml), dried over Na_2SO_4, evaporated, and the oily orange residue purified by chromatography on alumina (Brockmann, column 3 × 40 cm). Hexane eluted a trace of 2-bromo-1,6-methano[10]annulene and subsequently some starting material. The desired biannulenyl **2** was finally eluted with hexane-CH_2Cl_2 (8:1). Crystallization of the residue from hexane-CH_2Cl_2 gave 1.1 g (50% yield) of a mixture of *meso*- and *rac*-**2** (according to ^1H-NMR spectroscopy in a ratio of 1:3); m.p. 210–214 °C.

$C_{22}H_{16}Br_2$ (440.2)	Calcd. C 60.03	H 3.66	Br 36.30
	Found C 59.87	H 3.61	Br 36.43

The separation of **2** (obtained as just described) into its diastereomers (*meso*- and *rac*-**2**, see Scheme 1) was achieved by MPLC on silica gel in hexane (containing 0.6% of THF) at 20 °C, whereby the *meso* form is less strongly adsorbed. The unusual peak form (Figure 1) can be interpreted as being the result of the interconversion of the two rotamers of the racemate during the separation. After crystallization from CH_2Cl_2, both stereoisomers were pure (as shown by HPLC and ^1H-NMR spectroscopy) with melting points of 134–135 °C (*meso*) and 221–222 °C (racemate). Their configurations were assigned on the basis of ^1H- and especially ^{13}C-NMR spectroscopy (vide supra). In addition, the configuration of *rac*-**2** was also confirmed by optical resolution (vide infra).

For the mass and UV spectra (the latter showing significant differences between *meso*- and *rac*-**2**) see Table 1.

A quantitative separation of the racemate into the two enantiomers was attained on triacetylcellulose in ethanol in one run at 45 °C (Figure 4) where the more strongly adsorbed enantiomer is laevorotatory ($[\alpha]_D = -525$ and $[\alpha]_{546} = -716$, in ethanol). The CD spectrum of this equilibrium mixture is displayed together with the CD spectrum of the corresponding rotamers (obtained by chromatography on silica gel in hexane-THF at 0 °C; see Figure 5b) in Figures 5a and 5c.

As mentioned above, from CD kinetics of the pure underpopulated stereoisomer (at three temperatures, taking the strong Cotton effect at 291 nm as monitor) a barrier of $\Delta G^{\neq} = 85$ kJ mol^{-1} was found, which is consistent with the value derived from NMR kinetics.

CAS Registry Numbers

2 (*meso* form): 112113-26-5 / **2** (*rac* form): 112245-35-9 / **2** ((–) form): 112245-36-0 / 2,10-dibromo-1,6-methano[10]annulene: 5896-04-8

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