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Asymmetric Synthesis of Bi(thio)xanthylidene Overcrowded Alkenes

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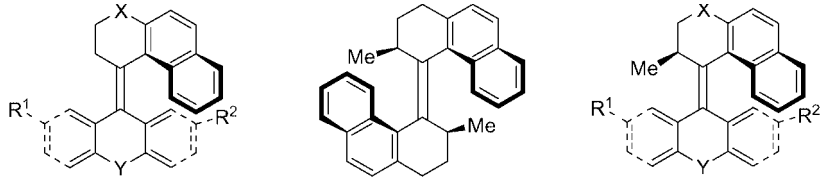
Overcrowded alkenes are a fascinating class of inherent dissymmetric molecules that attract considerable interest for instance as chiroptical molecular switches and unidirectionally rotary motors. A practical synthesis route towards enantiomerically pure overcrowded alkenes is an important goal. We report here the development of an asymmetric synthesis of bi(thio)xanthylidenes. The upper and lower part of the desired alkenes were first coupled to a chiral template. Intramolecular coupling with partial stereocontrol, separation of diastereoisomers and subsequent removal of the templates gave stable enantiomers of bithioxanthylidene. The absolute configuration was determined by X-ray analysis. In the case of bixanthylidene, stereocontrol during the intramolecular coupling reaction was complete, and it was found that the presence of a binaphthol bridging unit prevents the fast racemization process of the bixanthylidene, which it normally exhibited at ambient temperature.

Introduction

Elaborate studies on sterically overcrowded alkenes have revealed their unique photochromic and dynamic properties.[1] Despite the fact that these structures lack a stereogenic center, they may exist as stable, optically active, stereoisomers because of the presence of substituents that cause steric hindrance between upper and lower parts, and enforce a helical distortion to the entire molecule. Inherently dissymmetric, sterically overcrowded, alkenes have gradually evolved into chiroptical molecular switches[2] (Figure 1, **A**) and molecular motors[3] (Figure 1, **B** and **C**) as a result of detailed stereochemical studies. Substituted isomers of chiroptical molecular switches are able to perform reversible (*Z*)–(*E*) isomerizations under the influence of light of appropriate wavelengths and can function as molecular information-storage systems.[2] Photochemical and thermal isomerization pathways of these species were combined in the first-[3a] and second-generation light-driven molecular motors (Figure 1).[3b,3c] Two photochemical and two thermal steps induce a complete 360° rotation of the upper part of the molecule around the central double bond relative to the lower part. The presence of stereogenic centers bearing the methyl substituents, ensures that the rotation takes place in an unidirectional manner. Moreover, the rate of the thermal isomerization steps, governing the speed of rotary motion of the second generation molecular motors, could be adjusted by modification at the X- and Y positions (Figure 1, **C**).[3b–3f]

Applications of these systems include reversible transition between nematic and cholesteric phases of liquid-crystalline material doped with optically active overcrowded alkenes,[4] as well as the photochemical modulation of chirality of thin polymer films modified with these molecules.[5]



A: Chiroptical molecular switch

B: First generation light-driven molecular motor

C: Second generation light-driven molecular motor

Figure 1. Overcrowded alkenes designed as molecular switches and motors.

For all these applications optically active alkenes are required, which are usually obtained by preparative chiral HPLC.[6] To avoid a laborious chiral separation, a practical synthesis route towards enantiomerically pure overcrowded alkenes is a highly desired goal.

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Synthesis methodology towards a related class of inherent dissymmetric compounds, optically active biaryls, has been developed (Figure 2).[7] Control of axial single-bond chirality was achieved by coupling of two aryl moieties to a chiral template. During a subsequent asymmetric intramolecular coupling reaction, the biaryl structure was established with stereocontrol exerted by the chiral template. In a similar way Luh et al. succeeded to prepare optically active bisfluorenylidene with axial double-bond chirality.[8] However, removal of the chiral template resulted in complete loss of optical activity of the bisfluorenylidene because of its low racemization barrier ($\Delta G^{\ddagger}_{rac}$ = 11.5 kcal mol^{-1}).

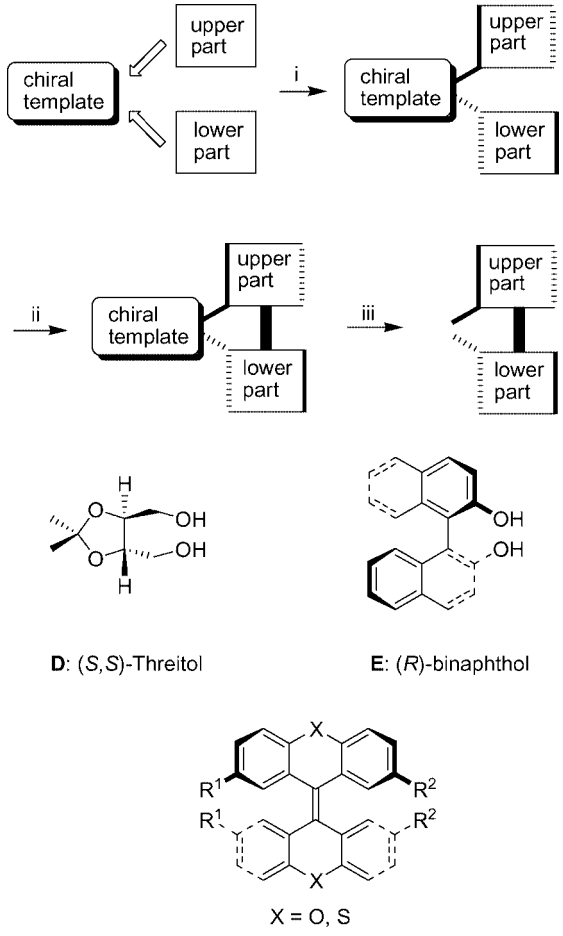

Figure 2. Chiral template-directed asymmetric coupling approach to optically active biaryls and overcrowded alkenes; i) coupling of upper and lower part to chiral template; ii) intramolecular coupling reaction to connect upper and lower part; iii) removal of chiral template to yield optically active product. C_2-symmetric chiral templates with central [**D**: (*S*,*S*)-threitol] and axial [**E**: (*R*)-binaphthol] chirality. Target molecules [**F**: optically active bi(thio)xanthylidenes].

The asymmetric synthesis methodology developed for biaryls inspired us to use a related chiral template strategy to synthesize overcrowded alkenes of which the enantiomers remain stable after removal of the chiral template (Figure 2).[9] C_2-symmetric chiral templates with stereogenic centers (Figure 2, template **D**) as well as axial chirality (Figure 2, template **E**) were employed. We report here the successful asymmetric synthesis of bi(thio)xanthylidenes (Figure 2, **F**). We focussed on the synthesis of enantiomers of bithioxanthylidenes (Figure 2, **F** with X = S) because of their relatively high Gibbs energy of racemization ($\Delta G^{\ddagger}_{rac}$) of about 27.5 kcal mol^{-1}.[1i,10] This energy barrier ensures sufficient stability and prevents fast racemization at room temperature. An important goal is the construction of optically active bixanthylidene (Figure 2, **F** with X = O), as the optically active forms of these overcrowded alkenes have never been synthesized, nor isolated, because they are known to have low racemization and isomerization barriers. For example, a $\Delta G^{\ddagger}_{rac(inv)}$ of 17.7 kcal mol^{-1} and a $\Delta G^{\ddagger}_{iso(E,Z)}$ of 17.5 kcal mol^{-1} has been found for 2,2′-di-*i*Pr-bixanthylidene (Figure 2, **F** with X = O, R^1 = *i*Pr, R^2 = H),[1i,11] whereas various other 2,2′-disubstituted bixanthylidenes (X = O, R^1 = Me, *t*Bu, OMe, R^2 = H)[1,11,12] exhibit values of $\Delta G^{\ddagger}_{iso(E,Z)}$ in the range 17.1–18.4 kcal mol^{-1}. These $\Delta G^{\ddagger}$ values imply that 2,2′-disubstituted bixanthylidenes examined so far can not exist as stable enantiomers at room temperature. Therefore, an important question is whether the attachment of a chiral template will prevent a fast racemization process and will lock the chiral conformation.

Results and Discussion

(*S*,*S*)-Threitol ditosylate (*S*,*S*)-**1**[13] was the first chiral template that was employed (Figure 3). Two 7-methoxy-9-oxo-9*H*-thioxanthene-2-carboxylic acid (**2**) moieties were utilized as upper and lower part.[14] Coupling of the thioxanthone **2** to the chiral template threitol ditosylate (*S*,*S*)-**1** resulted in the formation of (*S*,*S*)-**3** in fair yield. A copper-promoted intramolecular coupling reaction of (*S*,*S*)-**3** furnished the sterically overcrowded alkenes (*S*,*S*,*P*)-**4** (major) and (*S*,*S*,*M*)-**4** (minor) in 20% yield.[15] Prior to the coupling reaction the two ketone moieties were converted into the corresponding dichlorides by reaction with oxalyl dichloride. The bis-*gem*-dichloride intermediate was not isolated, because it is known to be unstable, but underwent in situ intramolecular coupling upon addition of activated Cu bronze.[16] The somewhat low yield is due to considerable formation of oligomers as a result of intermolecular coupling reactions. Working at higher dilution only gave minor improvement. A diastereomeric ratio of (*S*,*S*,*P*)-**4**/(*S*,*S*,*M*)-**4** of 80:20 was determined by ^{1}H NMR spectroscopy implying stereocontrol exerted by the chiral template during the intramolecular coupling reaction. Regioselectivity was complete as intramolecular formation of (*E*) products was excluded and only (*Z*) isomers were found. The successful formation of overcrowded alkenes **4** was confirmed by extensive spectroscopic analysis including X-ray analysis (vide infra). The absorptions of protons H_a, H_b and those of the methoxy substituents considerably shift to higher field when compared with those of (*S*,*S*)-**3** (Figure 3 and Table 1).

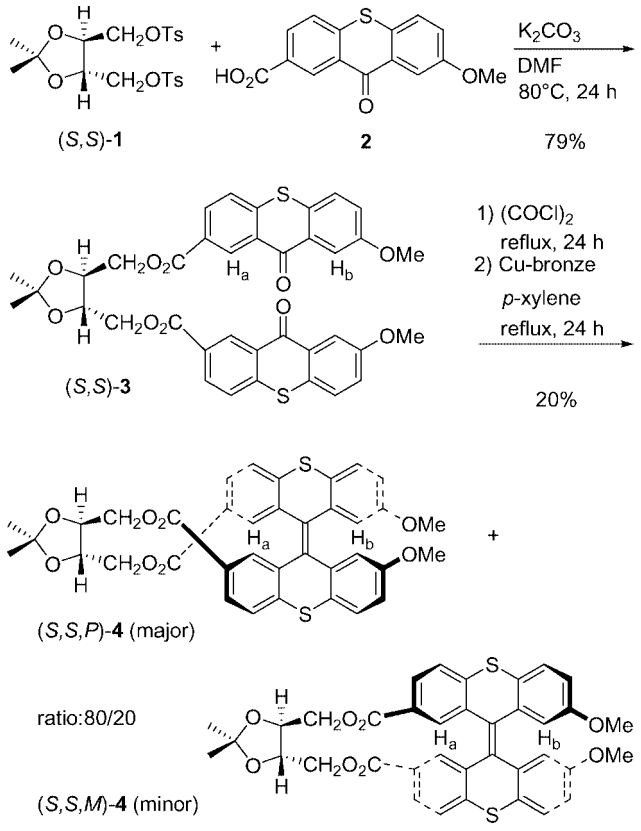

Figure 3. Asymmetric synthesis of optically active overcrowded alkenes (*S*,*S*,*P*)-**4** (major) and (*S*,*S*,*M*)-**4** (minor). (*S*,*S*) Indicates the chirality of the threitol moiety whereas (*P*) (right-handed helix) and (*M*) (left-handed helix) define the helicity at the dimethoxy side of the overcrowded alkene part of the molecule.[17]

Table 1. Selected chemical shifts of (*S*,*S*)-**3** and overcrowded alkenes **4**.[a]

	(*S*,*S*)-**3** [ppm]	(*S*,*S*,*P*)-**4** [ppm]	(*S*,*S*,*M*)-**4** [ppm]
H_a	9.12	7.08	7.03
H_b	7.93	6.35	6.38
MeO	3.89	3.39	3.38

[a] $CDCl_3$.

Recrystallization of the 80:20 mixture of (*S*,*S*,*P*)-**4** (major)/(*S*,*S*,*M*)-**4** (minor) from acetone gave crystals of pure (*S*,*S*,*M*)-**4** (minor product) that were suitable for X-ray analysis.[18] On the basis of the molecular structure and the known configuration of (*S*,*S*)-**1**[13] the absolute configuration of (*S*,*S*,*M*)-**4** could be assigned (Figure 4). Moreover, the analysis of structure (*S*,*S*,*M*)-**4** revealed a "linear" coupling of the template with the alkene part, whereas the major product exhibits a "crossed" coupled structure (Figure 3). The folded structure of the alkene part in (*S*,*S*,*M*)-**4** is confirmed by a folding angle of 50.6° [C(1)–C(2)–C(11)–C(12)] and a twist (ω) of the central double bond of –3.9° [C(36)–C(1)–C(2)–C(11)] [see Supporting Information for complete characterization of (*S*,*S*,*P*)-**4** and (*S*,*S*,*M*)-**4**; see also the footnote on the first page of this article]. The major diastereoisomer (*S*,*S*,*P*)-**4** could not be obtained completely pure. It was however characterized from a mixture [(*S*,*S*,*P*)-**4**/(*S*,*S*,*M*)-**4** 80:20] with the other diastereoisomer (*S*,*S*,*M*)-**4** by ^1H, ^{13}C NMR spectroscopy and HMRS analysis.

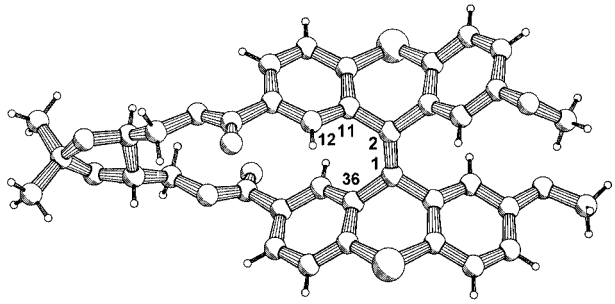

Figure 4. PLUTON drawing of (*S*,*S*,*M*)-**4**.

To increase the yield of the intramolecular coupling reaction and to examine the role of the chiral template we embarked on the use of (*R*)-binaphthol [(*R*)-**5**] and (*S*)-binaphthol [(*S*)-**5**] as chiral templates. The synthesis route to **7** employing (*R*)-**5** is shown in Figure 5 [same procedure was performed with (*S*)-**5**.]. The binaphthol templates, compared to template (*S*,*S*)-**1**, were supposed to enhance the intramolecular coupling and to increase the level of stereocontrol. The diester (*R*)-**6** was prepared from the thioxanthone **2** and (*R*)-**5** in two steps in 94% yield. More importantly, the yield of the subsequent intramolecular *gem*-dichloride coupling reaction,[15] with oxalyl dichloride and activated Cu bronze,[16] increased considerably compared to overcrowded alkenes **4** and diastereoisomers (*R*,*P*)-**7** (major) and (*R*,*M*)-**7** (minor) were obtained in 54% yield. An 81.5:18.5 ratio of (*R*,*P*)-**7**/(*R*,*M*)-**7** was established by ^1H NMR and separation of the isomers was readily achieved by column chromatography. As anticipated the rigid binaphthyl template enforces a favorable orientation of the two thioxanthene moieties for intramolecular coupling. Apart from alkenes **7** only starting material was recovered after the reaction, which implies that no intermolecular coupling took place. Despite the enhanced selectivity for intramolecular coupling, the stereocontrol by the binaphthol (*dr* 81.5:18.5) and threitol chiral templates (*dr* 80:20) were nearly identical. Only formation of (*Z*) isomers was observed akin to stereocontrol by the threitol template (Figure 3). Diastereoisomers (*R*,*P*)-**7** (major) and (*R*,*M*)-**7** (minor) were identified by ^1H, ^{13}C NMR spectroscopy and HRMS (see Experimental Section and Supporting Information). By means of COSY and NOESY NMR all twelve different proton signals of both stereoisomers could be assigned unequivocally. Analogous to overcrowded alkenes **4**, the absorptions of protons H_a and H_b of (*R*,*P*)-**7** (major) and (*R*,*M*)-**7** (minor), which are situated in the fjord region, were found at relatively high field (Table 2). An up-field shift of at least 1.5 ppm was found as compared to (*R*)-**6**, while the absorptions of the protons of the methoxy substituents shifted by more than 0.5 ppm.

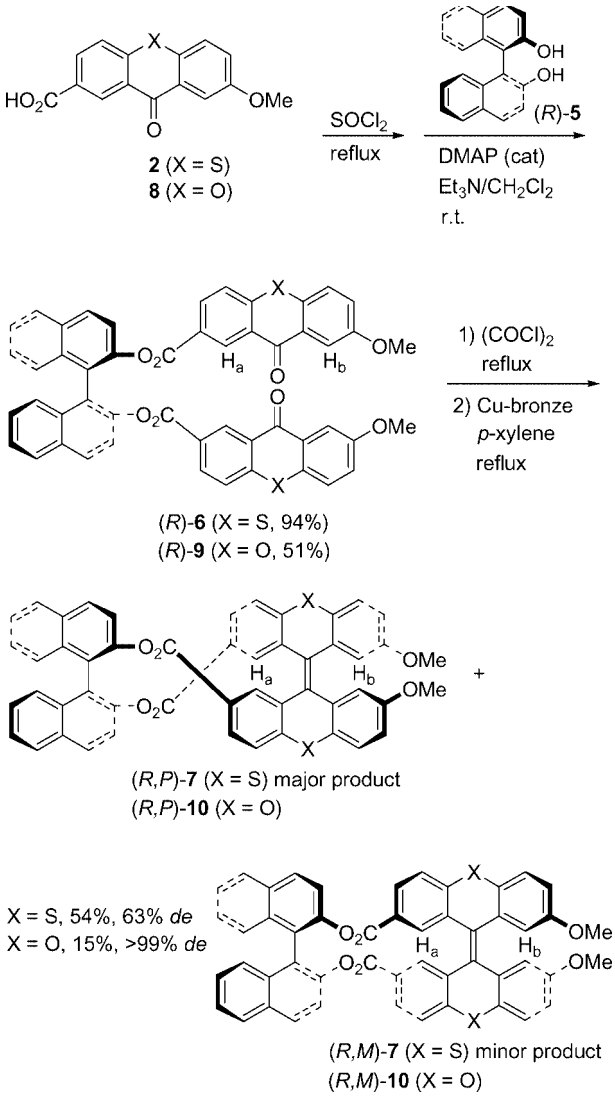

Figure 5. Asymmetric synthesis of optically active overcrowded alkenes **7** and **10** with binaphthol (*R*)-**5** as chiral template. (*R*) Indicates the configuration of the binaphthol moiety, whereas (*P*) (right-handed helix) and (*M*) (left-handed helix) define the helicity at the dimethoxy side of the overcrowded alkene part of the molecule.[17]

Table 2. Chemical shifts (ppm) of protons H_a and H_b of (*R*)-**6**, (*R*)-**9** and overcrowded alkenes **7** and **10**.[a]

	(*R*)-**6** (ppm)	(*R*,*P*)-**7** (ppm)	(*R*,*M*)-**7** (ppm)	(*R*)-**9** (ppm)	(*R*)-**10** (ppm)
H_a	9.02	7.31	7.54	8.77	7.95
H_b	8.01	6.36	6.39	7.67	6.62
MeO	3.91	3.39	3.39	3.91	3.51

[a] $CDCl_3$.

The absolute configuration of the two diastereoisomers (*R*,*P*)-**7** (major) and (*R*,*M*)-**7** (minor) were determined after removal (vide infra) of the binaphthol auxiliary. The configuration of the overcrowded alkenes was assigned by comparison of i) order of elution by chiral HPLC, ii) CD spectra, and iii) optical rotation, with the overcrowded alkene originating from (*S*,*S*,*M*)-**4** (minor) of which the absolute configuration was ascertained by X-ray analysis (vide supra). Both a folded and a twisted structure is present in molecules (*R*,*P*)-**7** (major) and (*R*,*M*)-**7** (minor). The two diastereoisomers differ significantly in structure as is visualized in Figure 5. Although in both isomers the binaphthyl part is twisted and the thioxanthylidene moiety is folded, the formation of the "crossed" coupled product (*R*,*P*)-**7** (major) is favored over the "linear" coupled product (*R*,*M*)-**7** (minor). The major product (*R*,*P*)-**7** exhibits an appealing double helix-type structure, which is visualized by an optimized space-filling model as shown in Figure 6.[19]

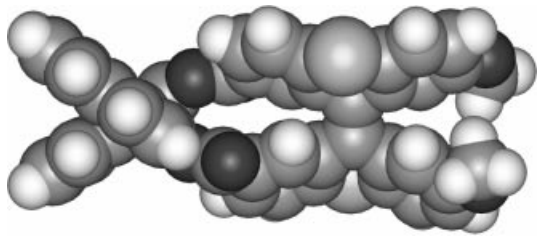

Figure 6. Space filling model of (*R*,*P*)-**7** viewed along the binaphthol single bond and the alkene double bond. Oxygen atoms are red and sulfur atoms are yellow.

Overcrowded alkene (*R*)-**10**, with oxygen atoms in upper and lower part, was synthesized along the same lines as its thio analogues (*R*,*P*)-**7** and (*R*,*M*)-**7** (Figure 5). Two xanthone moieties **8**[20] were coupled to the chiral template (*R*)-binaphthol (*R*)-**5** and the diester (*R*)-**9** was obtained in 51% yield. Conversion of (*R*)-**9** into the bis-*gem*-dichloride by action of oxalyl dichloride, was immediately followed by treatment with activated Cu bronze.[15,16] By this route (*R*)-**10** was obtained in a rather low yield of 15% after purification by column chromatography. In contrast to its thio analogues, extensive formation of oligomers took place through intermolecular coupling reactions. The structure of (*R*)-**10** was established by ^1H, ^{13}C, COSY, and NOESY NMR spectroscopy as well as HRMS determination. Up-field shifts of all aromatic protons were observed as compared to its precursor (*R*)-**9** and again most prominent up-field shifts of 0.82 and 1.05 ppm were displayed by protons H_a and H_b, respectively (Table 2). Moreover, the absorption of the methoxy substituents shifted by 0.40 ppm. All observed up-field shifts are rationalized by shielding effects in the fjord region of the molecule. The NMR analysis of (*R*)-**10** revealed that only one of the two possible diastereoisomers, (*R*,*P*)-**10** and (*R*,*M*)-**10**, was formed since only absorptions of a single isomer were observed. Bixanthylidenes without a bridging template attached are known to have low racemization and isomerization barriers ($\Delta G^{\ddagger}_{rac} \approx 18.0$ kcal mol^{-1}) and consequently racemize rapidly at room temperature.[1i,11,12] To exclude a fast equilibrium at room temperature between diastereoisomers (*R*,*P*)-**10** and (*R*,*M*)-**10**, a sample of (*R*)-**10** in CD_2Cl_2 was examined by ^1H NMR at temperatures as low as –80 °C. At this temperature a barrier of 18.0 kcal mol^{-1} would certainly have led to separation of at least several absorptions as a result of slow thermal interconversion between diastereoisomeric forms [(*R*,*P*)-**10** ⇆ (*R*,*M*)-**10**] on the NMR time scale. As no separation is ob-

served upon cooling, it appears that only one of the two isomers, (*R*,*P*)-**10** or (*R*,*M*)-**10**, has been obtained. Thus, the intramolecular coupling reaction must have proceeded with a diastereomeric ratio of >99%. Moreover, the fast racemization process of bixanthylidene, commonly observed at room temperature, appears to be locked by the attachment of a binaphthol auxiliary. Crystals of (*R*)-**10** suitable for X-ray analysis were not obtained which means that the absolute configuration of the overcrowded alkene part of (*R*)-**10** has not been secured so far. However, optical activity of the alkene moiety was established by CD spectroscopy.

The chiral auxiliaries of overcrowded alkenes (*S*,*S*,*M*)-**4** (minor), (*R*,*P*)-**7** (major), (*R*,*M*)-**7**, (*S*,*M*)-**7** (major), and (*S*,*P*)-**7** (minor) were removed by reduction with $LiAlH_4$ which provided enantiomers of bithioxanthylidene, (*P*,*Z*)-**11** and (*M*,*Z*)-**11**, with *ee* values of 96±1% as was determined by chiral HPLC (Figure 7). The stability of (*P*,*Z*)-**11** and (*M*,*Z*)-**11** was confirmed quantitatively as an activation energy of 26.7 kcal mol^{-1} was determined for the loss of optical activity ($\Delta G^{\ddagger}$ at 70.0 °C, polarimetry). Furthermore, no (*E*) isomers were found. Removal of the binaphthol moiety of (*R*)-**10** at 0 °C led to fast racemization and (*Z*)-(*E*) isomerization of the bixanthylidene moiety. A mixture of (*Z*)- and (*E*) isomers (3:2 ratio) of bixanthylidene **12** (Figure 8) was obtained in 63% yield. The chiral (*Z*) and achiral (*E*) isomers were not separated and were identified by ^{1}H and ^{13}C NMR spectroscopy. Complete loss of optical activity was confirmed by CD spectroscopy.

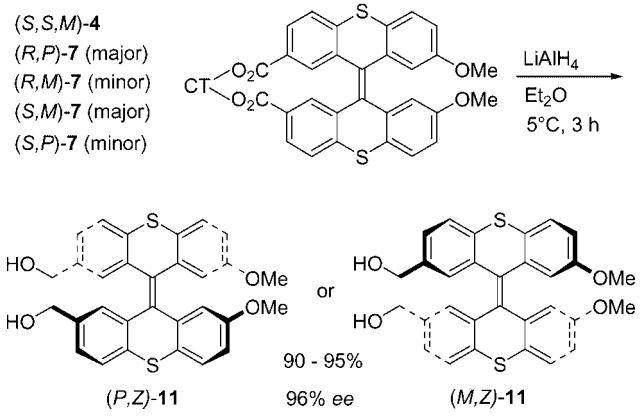

Figure 7. Removal of chiral templates (CT) from overcrowded alkenes **4** and **7**. (*M*) (left-handed helix) and (*P*) (right-handed helix) define the helicity at the dimethoxy side of **11**.[17]

The X-ray analysis of (*S*,*S*,*M*)-**4** (minor) revealed that the overcrowded alkene part has an (*M*) configuration. Removal of the chiral threitol template therefore led to (*M*,*Z*)-**11**. The analytical data of (*P*,*Z*)-**11** and (*M*,*Z*)-**11** (retention times on chiral HPLC, CD data, and optical rotation) obtained from diastereoisomers (*R*,*P*)-**7** (major), (*R*,*M*)-**7** (minor), (*S*,*M*)-**7** (major) and (*S*,*P*)-**7** (minor) were correlated with those of (*M*,*Z*)-**11** obtained from (*S*,*S*,*M*)-**4** (minor) (Table 3). In this manner the absolute configurations of (*R*,*P*)-**7** (major), (*R*,*M*)-**7** (minor), (*S*,*M*)-**7** (major) and (*S*,*P*)-**7** (minor) were determined retrospectively.

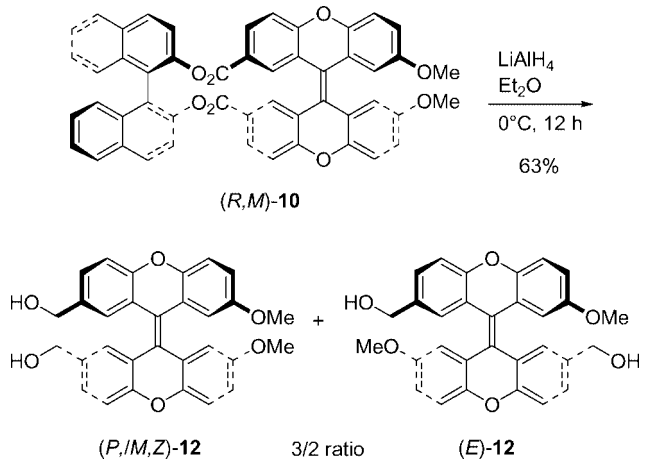

Figure 8. Removal of binaphthol moiety of (*R*)-**10**.

Table 3. Stereochemical correlation and optical data of **4**, **7**, and **11**.

Substrate	$[\alpha]_D^{20}$ [a]	Product	$[\alpha]_D^{20}$ [a]
(*S*,*S*,*M*)-**4**	+203[b]	(*M*,*Z*)-**11**	–92
(*R*,*P*)-**7**	–101	(*P*,*Z*)-**11**	+91
(*R*,*M*)-**7**	+120	(*M*,*Z*)-**11**	–93
(*S*,*M*)-**7**	+100	(*M*,*Z*)-**11**	–92
(*S*,*P*)-**7**	–120	(*P*,*Z*)-**11**	+91

[a] *c* = 1.00, $CHCl_3$. [b] *c* = 0.50, $CHCl_3$.

UV and CD spectra of (*M*,*Z*)-**11** are shown in Figure 9, while characteristic data are given in Table 4 (UV) and Table 5 (CD). CD spectra of enantiomers (*P*,*Z*)-**11** and (*M*,*Z*)-**11** are, as expected, mirror images of each other and seven extrema were found at wavelengths above 215 nm

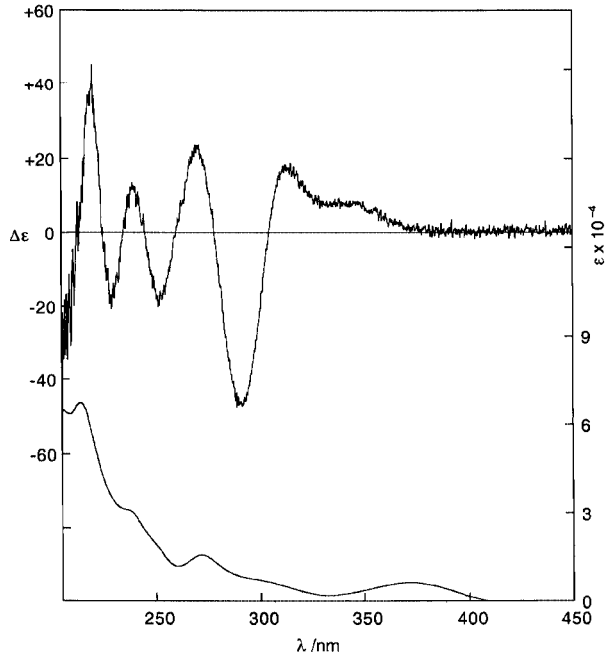

Figure 9. UV and CD spectra of (*M*,*Z*)-**11** (*n*-hexane/2-propanol, 80:20).

Table 4. UV spectra of (*S*,*M*)-**7** (major), (*R*,*M*)-**7** (minor), (*R*)-**10**, (*P*,*Z*)-**11** and **12**.

Compound	λ [nm] ε [1000 cm^2 mol^{-1}]		
(*S*,*M*)-**7**[a]	224 (125000)	278 (25600)	306 (21400)
(*R*,*M*)-**7**[a]	222 (148600)	286 (30400)	378 (7100)
(*R*)-**10**[b]	223 (131100)		392 (7600)
(*P*,*Z*)-**11**[a]	214 (67000)	272 (15800)	372 (6200)
12[a]	228 (43300)	293 (6200)	384 (11600)

[a] *n*-Hexane/2-propanol, 80:20. [b] *n*-Hexane.

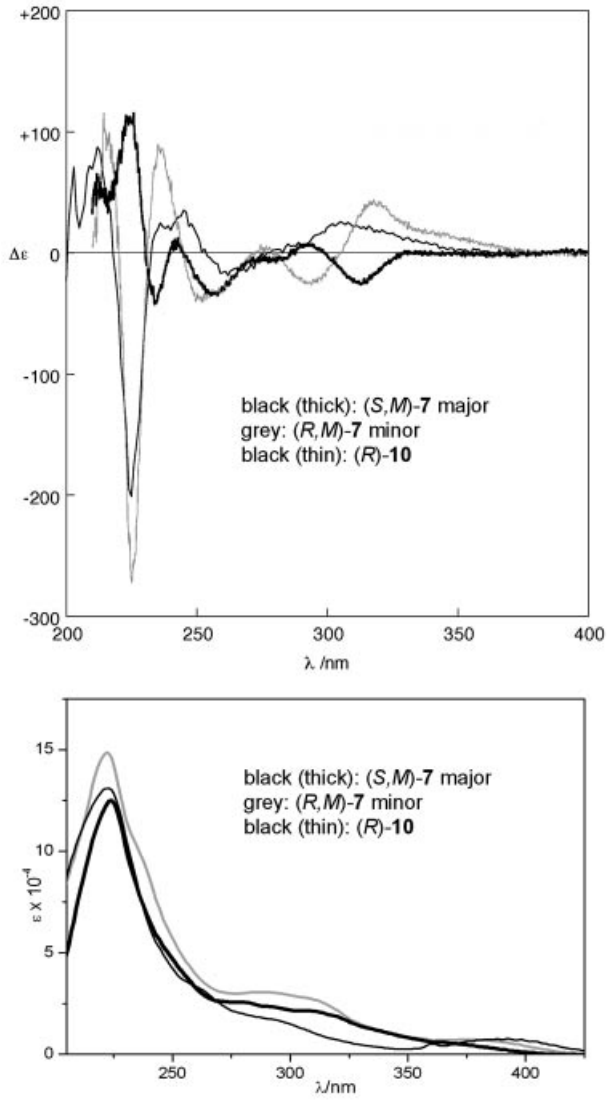

Figure 10. UV and CD spectra of (*S*,*M*)-**7** (major), (*R*,*M*)-**7** (minor) and (*R*)-**10**. Spectra (*S*,*M*)-**7** (major) and (*R*,*M*)-**7** (minor) recorded in *n*-hexane/2-propanol, 80:20. Spectrum (*R*)-**10** recorded in *n*-hexane.

(Table 4). The wavelengths at which the extrema appear and the $\Delta\varepsilon$ values correspond with data of related optically active overcrowded alkenes.[6]

Maxima and minima in the CD spectra of (*S*,*M*)-**7** (major) and (*R*,*M*)-**7** (minor) emerge in the same regions and several bisignate features might indicate exciton coupling[21] (Figure 10 and Table 5). The CD spectrum of (*R*)-**10** was compared with the CD spectra of (*S*,*M*)-**7** and (*R*,*M*)-**7** to find similarities that could possibly lead to an absolute configuration assignment of (*R*)-**10** (Figure 10 and Table 5). However, as can be concluded from Figure 10 unequivocal assignment cannot be made.

Conclusions

The asymmetric synthesis of stable enantiomers of bithioxanthylidene [(*P*,*Z*)-**11** and (*M*,*Z*)-**11**], featuring axial double bond chirality, was realized by using (*S*,*S*)-threitol ditosylate [(*S*,*S*)-**1**], (*R*)-binaphthol [(*R*)-**5**] and (*S*)-binaphthol [(*S*)-**5**] as chiral templates. In the most successful approach, two halves of the envisioned alkene were first coupled to a binaphthol template after which a diastereoselective intramolecular coupling reaction afforded the corresponding alkenes. Removal of the chiral auxiliary group yielded the enantiomers (*P*,*Z*)-**11** and (*M*,*Z*)-**11** with *ee* values of 96%. The employment of (*S*,*S*)-**1** as a chiral template provided a less atractive route to **11** with respect to reaction yields and purification. However, crystals of (*S*,*S*,*M*)-**4** were obtained to allow determination of the absolute configuration of enantiomerically pure (*P*,*Z*)-**11** by X-ray analysis.

Furthermore, the bixanthylidene variant with a binaphthol template (*R*)-**10** was synthesized. Although the alkene part of (*R*)-**10** can have (*P*) or (*M*) helicity, low-temperature ^{1}H NMR studies revealed that only one of the isomers [(*R*,*P*)-**10** and (*R*,*M*)-**10**] was formed during the asymmetric intramolecular coupling reaction implying a diastereomeric ratio of >99%. This finding simultaneously confirmed that the common fast racemization of bixanthylidenes is prevented by the attachment of a binaphthol bridging unit. To the best of our knowledge this is the first time a conformational restricted enantiomerically pure bixanthylidene has been obtained. In conclusion, a new methodology for the construction of optically active overcrowded alkenes, involving an asymmetric coupling route, has been developed.

Experimental Section

General: ^{1}H (300 or 500 MHz) and ^{13}C (50 or 125 MHz) NMR spectra were recorded in $CDCl_3$ or [D_6]DMSO. Chemical shifts are

Table 5. CD spectra of (*S*,*M*)-**7** (major), (*R*,*M*)-**7** (minor), (*R*)-**10** and (*P*,*Z*)-**11**.

Compound	λ [nm] $\Delta\varepsilon$ [1000 cm^2 mol^{-1}]						
(*S*,*M*)-**7**[a]	224 (+110.9)	234 (–39.3)	242 (+8.9)	257 (–33.2)		293 (+6.6)	313 (–24.7)
(*R*,*M*)-**7**[a]	225 (–264.0)	236 (+86.3)		251 (–37.9)	276 (+3.7)	293 (–24.7)	318 (+41.1)
(*R*)-**10**[b]	225 (–195.9)	237 (+22.5)	245 (+33.4)	261 (–17.5)			306 (+25.1)
(*P*,*Z*)-**11**[a]	220 (+37.9)	229 (–17.6)	239 (+11.6)	252 (–18.0)	270 (+22.6)	291 (–46.8)	313 (+17.5)

[a] *n*-Hexane/2-propanol, 80:20. [b] *n*-Hexane.

denoted in δ (ppm) referenced to the residual protic solvents. Column chromatography was performed on silica gel 60 PF_{254} under pressure.

Preparation of (*S*,*S*)-[5-({[(7-Methoxy-9-oxo-9*H*-thioxanthen-2-yl)carbonyl]oxy}methyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl 7-methoxy-9-oxo-9*H*-thioxanthene-2-carboxylate [(*S*,*S*)-3]: Under nitrogen, thioketone **2**[14] (2.00 g, 6.99 mmol), template (*S*,*S*)-**1**[13] (1.10 g, 2.34 mmol), K_2CO_3 (1.06 g, 7.67 mmol), and Bu_4NBr (250 mg, 0.78 mmol) were added to DMF (50 mL). The suspension was heated to 90 °C and stirred for 18 h. After cooling, the solvent was evaporated under reduced pressure and CH_2Cl_2 (20 mL) was added to the residue. The suspension was filtered, and the filtrate concentrated in vacuo to yield a brown residue. Purification by column chromatography on silica gel (CH_2Cl_2/diethyl ether, 20:1, R_f = 0.24) gave pure (*S*,*S*)-**3** (1.29 g, 1.85 mmol, 79%) as a yellow solid. M.p. 196.7–199.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.12 (d, $^4J_{H,H}$ = 2.1 Hz, 2 H, 1-H), 8.10 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 2.1 Hz, 2 H, 3-H), 7.93, (d, $^4J_{H,H}$ = 2.7 Hz, 2 H, 8-H), 7.49 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 4-H), 7.35 (d, $^3J_{H,H}$ = 9.0 Hz, 2 H, 5-H), 7.18 (dd, $^3J_{H,H}$ = 9.0, $^4J_{H,H}$ = 2.7 Hz, 2 H, 6-H), 4.58 (m, 4 H, CH_2O), 4.39 (s, 2 H, OC*H*CCH_2), 3.89 (s, 6 H, OMe), 1.49 (s, 6 H, Me) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 178.61 (s), 165.18 (s), 158.64 (s), 158.64 (s), 142.46 (s), 131.68 (d), 129.97 (s), 128.03 (s), 128.03 (s), 127.28 (d), 127.19 (d), 126.19 (d), 122.86 (d), 110.48 (s), 109.41 (d), 76.26 (d), 64.64 (t), 55.65 (q), 27.13 (q) ppm. HRMS calcd. for $C_{37}H_{30}O_{10}S_2$: 698.1280; found: 698.1283.

(17*S*,21*S*,*M*)-5,33-Dimethoxy-19,19-dimethyl-15,18,20,23-tetraoxa-9,29-dithiaoctacyclo[23.10.2.2^{10,13}.0^{2,11}.0^{3,8}.0^{17,21}.0^{28,36}.0^{30,35}]-nonatriaconta-1,3,5,7,10(39),11,13(38),25,27,30,32,34,36-tridecaene-14,24-dione [(*S*,*S*,*M*)-4 (minor)]: Under nitrogen, a solution of (*S*,*S*)-**3** (744 mg, 1.07 mmol) in oxalyl dichloride (15 mL) was refluxed overnight.[15] Excess of oxalyl dichloride was removed under reduced pressure and the residue was dissolved in freshly distilled *p*-xylene (30 mL, from sodium). Activated Cu bronze[16] (520 mg, 8.18 mmol) was added, and this suspension was refluxed for 24 h. After cooling, the mixture was filtered and the filtrate was concentrated in vacuo to yield a yellow residue. Purification by column chromatography (silica gel, CH_2Cl_2, R_f = 0.30) gave a mixture of two diastereoisomers (*S*,*S*,*P*)-**4** (major)/(*S*,*S*,*M*)-**4** (minor), 80:20 (142 mg, 0.21 mmol, 20%) as a yellow solid. Recrystallization from acetone afforded crystals of diastereomerically pure (*S*,*S*,*M*)-**4** (minor), suitable for X-ray analysis. M.p. 259.2–261.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.65 (dd, $^3J_{H,H}$ = 8.0, $^4J_{H,H}$ = 1.8 Hz, 2 H, 26-,38-H), 7.53 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, 27-,39-H), 7.37 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 7-,31-H), 7.08 (d, $^4J_{H,H}$ = 1.8 Hz, 2 H, 12-,37-H), 6.77 (dd, $^3J_{H,H}$ = 8.6, $^4J_{H,H}$ = 2.3 Hz, 2 H, 6-,32-H), 6.35 (d, $^4J_{H,H}$ = 2.3 Hz, 2 H, 4-,34-H), 4.29 (dd, $^2J_{H,H}$ = 11.4, $^3J_{H,H}$ = 6.4 Hz, 2 H, 16-,22-H), 4.17 (d, $^2J_{H,H}$ = 11.4 Hz, 2 H, 16-,22-H), 3.98 (d, $^3J_{H,H}$ = 6.4 Hz, 2 H, 17-,21-H), 3.38 (s, 6 H, OMe), 1.56 (s, 6 H, Me) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 165.55 (s), 158.24 (s), 141.86 (s), 136.09 (s), 133.11 (s), 133.40 (s), 130.78 (s), 127.52 (d), 127.47 (s), 127.33 (d), 126.40 (d), 125.25 (s), 115.52 (d), 114.02 (d), 108.51 (s), 79.77 (d), 63.83 (t), 55.19 (q), 26.53 (q) ppm. HRMS calcd. for $C_{37}H_{30}O_8S_2$: 666.1382; found: 666.1394. UV (*n*-hexane/2-propanol, 80:20): λ (ε) = 205 nm (77900), 311 nm (17000). CD (*n*-hexane/2-propanol, 80:20): λ ($\Delta\varepsilon$) = 221 nm (–44.2), 250 nm (+17.7), 273 nm (–6.2), 303 nm (+15.7), 341 nm (–2.4), 390 nm (+1.6).

(17*S*,21*S*,*P*)-5,33-Dimethoxy-19,19-dimethyl-15,18,20,23-tetraoxa-9,29-dithiaoctacyclo-[23.10.2.2^{10,13}.0^{2,11}.0^{3,8}.0^{17,21}.0^{28,36}.0^{30,35}]-nonatriaconta-1,3,5,7,10(39),11,13(38),25,27,30,32,34,36-tridecaene-14,24-dione [(*S*,*S*,*P*)-4 (major)]: See afore-mentioned procedure for (*S*,*S*,*M*)-**4** (minor). Despite several attempts the major isomer (*S*,*S*,*P*)-**4** could not be obtained in pure form. However, NMR assignment could be made using the 80:20 mixture with the minor isomer (*S*,*S*,*M*)-**4**. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.62 (dd, $^3J_{H,H}$ = 8.1, $^4J_{H,H}$ = 1.8 Hz, 2 H, 26-,38-H), 7.52 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, 27-,39-H), 7.39 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 7-,31-H), 7.03 (d, $^4J_{H,H}$ = 1.8 Hz, 2 H, 12-,37-H), 6.78 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 2.8 Hz, 2 H, 6-,32-H), 6.38 (d, $^4J_{H,H}$ = 2.8 Hz, 2 H, 4-,34-H), 4.80 (dd, $^2J_{H,H}$ = 11.7, $^3J_{H,H}$ = 3.3 Hz, 2 H, 16-,22-H), 4.29 (dd, $^3J_{H,H}$ = 6.6, $^3J_{H,H}$ = 3.3 Hz, 2 H, 17-,21-H), 4.02 (dd, $^2J_{H,H}$ = 11.7, $^3J_{H,H}$ = 6.6 Hz, 2 H, 16-,22-H), 3.39 (s, 6 H, OMe), 1.49 (s, 6 H, Me) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 165.68 (s), 158.24 (s), 142.21 (s), 135.66 (s), 133.36 (s), 133.27 (s), 131.64 (d), 127.70 (d), 126.95 (s), 126.83 (d), 126.29 (d), 125.26 (s), 115.52 (d), 113.82 (d), 109.38 (s), 74.76 (d), 63.00 (t), 55.19 (q), 27.54 (q) ppm. HRMS calcd. for $C_{37}H_{30}O_8S_2$: 666.1382; found: 666.1394.

(*R*)-1-(2-{[(7-Methoxy-9-oxo-9*H*-thioxanthen-2-yl)carbonyl]oxy}-1-naphthyl)-2-naphthyl 7-Methoxy-9-oxo-9*H*-thioxanthene-2-carboxylate [(*R*)-6]: [same procedure holds for the (*S*)-**6** enantiomer]. Thioxanthone **2**[14] (2.50 g, 8.74 mmol) was refluxed in $SOCl_2$ (25 mL) for 30 min. The excess of $SOCl_2$ was evaporated and the residue was stripped twice with benzene. The residue was dissolved in CH_2Cl_2 (25 mL) and added to a solution of (*R*)-**5** (1.00 g, 3.49 mmol) and DMAP (40 mg) in Et_3N (20 mL) and CH_2Cl_2 (20 mL). This mixture was stirred overnight at room temperature, concentrated in vacuo and the residue was dissolved in CH_2Cl_2 (30 mL). After washing (twice with 2 M aq. HCl) and drying (Na_2SO_4), the solvent was removed in vacuo to yield an orange residue. Purification by column chromatography (Al_2O_3, 6% water, CH_2Cl_2/*n*-hexane, 5:1, R_f = 0.75) gave pure (*R*)-**6** [2.70 g, 3.28 mmol, 94% based on (*R*)-binaphthol-**7**] as a yellow solid. M.p. 206.0–208.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 9.02 [d, $^4J_{H,H}$ = 1.8 Hz, 2 H, 1-H(xan)], 8.01 [d, $^4J_{H,H}$ = 2.7 Hz, 2 H, 8-H(xan)], 7.96 [d, $^3J_{H,H}$ = 9.0 Hz, 2 H (naph)], 7.87 [d, $^3J_{H,H}$ = 9.0 Hz, 2 H, (naph)], 7.76 [dd, $^3J_{H,H}$ = 9.0, $^4J_{H,H}$ = 1.8 Hz, 2 H, 3-H(xan)], 7.56 [d, $^3J_{H,H}$ = 9.0 Hz, 2 H, (naph)], 7.35–7.46 [m, 10 H, (xan and naph)], 7.23 [dd, $^3J_{H,H}$ = 9.0, $^4J_{H,H}$ = 2.7 Hz, 2 H, 6-H(xan)], 3.91 (s, 6 H, OMe) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 178.41 (s), 163.88 (s), 158.51 (s), 146.97 (s), 142.47 (s), 133.32 (s), 131.95 (d), 131.66 (d), 131.61 (s), 129.87 (d), 129.82 (s), 128.08 (d), 127.89 (s), 127.81 (s), 127.17 (d), 127.00 (d), 126.82 (s), 126.13 (d), 126.06 (d), 125.88 (d), 123.68 (s), 122.61 (d), 121.73 (d), 110.32 (d), 55.45 (q) ppm. HRMS calcd. for $C_{50}H_{30}O_8S_2$: 822.1382; found: 822.1399.

(*R*,*P*)-5,46-Dimethoxy-15,36-dioxa-9,42-dithiaundecacyclo-[36.10.2.2^{10,13}.0^{2,11}.0^{3,8}.0^{16,25}.0^{19,24}.0^{26,35}.0^{27,32}.0^{41,49}.0^{43,48}]dopentaconta-1,3,5,7,10(52),11,13(51),16(25),17,19,21,23,26,28,30,32,34,38,40,43,45,47,49-tricosaene-14,37-dione [(*R*,*P*)-7 (major)]: [same procedure holds for (*R*,*M*)-**7** (minor), (*S*,*M*)-**7** (major), and (*S*,*P*)-**7** (minor)]. Under a nitrogen atmosphere, substrate (*R*)-6 (600 mg, 0.73 mmol) was refluxed overnight in oxalyl dichloride (20 mL).[15] The excess of oxalyl dichloride was removed under reduced pressure. The residue was dissolved in freshly distilled *p*-xylene (100 mL, from sodium), activated Cu bronze[16] (1.01 g, 15.90 mmol) was added and the suspension heated at reflux overnight. After cooling, the mixture was filtered and the filtrate was concentrated in vacuo. Purification of the residue by column chromatography (silica gel, CH_2Cl_2/*n*-hexane, 3:1) gave 58 mg ($7.2\cdot10^{-2}$ mmol, 10%, R_f = 0.26) of (*R*,*M*)-**7** (minor) and 254 mg (0.32 mmol, 44%, R_f = 0.19) of (*R*,*P*)-**7** (major) as yellow solids. M.p. 310 °C (dec); (*R*,*P*)-**7** (major) and (*S*,*M*)-**7** (major): ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.96 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 18-,33-H), 7.91 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 20-,31-H), 7.42 (t, $^3J_{H,H}$ =

8.4 Hz, 2 H, 21-,30-H), 7.38 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 7-,44-H), 7.36 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 40-,52-H), 7.31 (d, $^4J_{H,H}$ = 1.5 Hz, 2 H, 12-,50-H), 7.25 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 17-,34-H), 7.25 (t, $^3J_{H,H}$ = 8.4 Hz, 2 H, 22-,29-H), 7.11 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 23-,28-H), 7.01 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 1.5 Hz, 2 H, 39-,51-H), 6.74 (dd, $^3J_{H,H}$ = 8.8, $^4J_{H,H}$ = 2.6 Hz, 2 H, 6-,45-H), 6.36 (d, $^4J_{H,H}$ = 2.6 Hz, 2 H, 4-,47-H), 3.39 (s, 6 H, OMe) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 164.22 (s), 158.11 (s), 147.04 (s), 142.29 (s), 135.71 (s), 135.02 (s), 133.36 (s), 133.36 (s), 131.41 (s), 131.16 (d), 129.23 (d), 128.33 (d), 128.08 (d), 127.04 (d), 126.99 (s), 126.95 (d), 126.73 (d), 126.03 (s), 125.85 (d), 125.62 (d), 123.52 (s), 122.28 (d), 115.20 (d), 113.66 (d), 55.10 (q) ppm. HRMS calcd. for $C_{50}H_{30}O_6S_2$: 790.1484; found: 790.1494.

(*R*,*P*)-5,46-Dimethoxy-15,36-dioxa-9,42-dithiaundecacyclo-[36.10.2.2^{10,13}.0^{2,11}.0^{3,8}.0^{16,25}.0^{19,24}.0^{26,35}.0^{27,32}.0^{41,49}.0^{43,48}]dopenta-conta-1,3,5,7,10(52),11,13(51),16,18,20,22,24,26(35),27,29,31,33,38,40,43,45,47,49-tricosaene-14,37-dione [(*R*,*M*)-7 (minor)]: M.p. 235.0 °C (dec); (*R*,*M*)-**7** (minor) and (*S*,*P*)-**7** (minor): ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.00 (d, $^3J_{H,H}$ = 9.5 Hz, 2 H, 18-,33-H), 7.95 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 20-,31-H), 7.54 (d, $^4J_{H,H}$ = 1.5 Hz, 2 H, 12-,50-H), 7.48 (t, $^3J_{H,H}$ = 8.4 Hz, 2 H, 21-,30-H), 7.46 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 40-,52-H), 7.40 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 7-,44-H), 7.39 (d, $^3J_{H,H}$ = 9.5 Hz, 2 H, 17-,34-H), 7.39 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 1.5 Hz, 2 H, 39-,51-H), 7.24 (t, $^3J_{H,H}$ = 8.4 Hz, 2 H, 22-,29-H), 7.07 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 23-,28-H), 6.79 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 2.9 Hz, 2 H, 6-,45-H), 6.39 (d, $^4J_{H,H}$ = 2.9 Hz, 2 H, 4-,47-H), 3.39 (s, 6 H, OMe) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 165.26 (s), 158.40 (s), 146.92 (s), 141.66 (s), 136.54 (s), 134.16 (s), 133.50 (s), 132.98 (s), 131.70 (s), 131.20 (d), 129.67 (d), 128.03 (d), 127.81 (s), 127.61 (d), 127.49 (d), 127.17 (d), 126.99 (d), 126.59 (d), 125.67 (d), 125.39 (s), 123.25 (s), 122.47 (d), 115.71 (d), 114.52 (d), 55.18 (q) ppm. HRMS calcd. for $C_{50}H_{30}O_6S_2$: 790.1484; found: 790.1494.

(*R*)-1-(2-{[(7-Methoxy-9-oxo-9*H*-xanthen-2-yl)carbonyl]oxy}-1-naphthyl)-2-naphthyl 7-Methoxy-9-oxo-9*H*-xanthene-2-carboxylate [(*R*)-9]: Xanthone **8**[20] (1.00 g, 3.70 mmol) was refluxed in $SOCl_2$ (40 mL) until formation of HCl stopped. The excess of $SOCl_2$ was removed. The remaining solid was stripped twice with benzene (40 mL). The beige solid was dissolved in CH_2Cl_2 (20 mL) and added dropwise to a solution of (*R*)-binaphthol [(*R*)-**5**, 0.50 g, 1.76 mmol] and a catalytic amount of DMAP in CH_2Cl_2 (10 mL) and Et_3N (10 mL). The mixture was stirred overnight at room temperature. The solvents were evaporated and the remaining green solid was dissolved in CH_2Cl_2 (40 mL). The organic layer was washed twice with 1 M HCl (aq) (40 mL) and twice with water (40 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo to yield 1.00 g of crude reaction mixture. Purification by column chromatography [Al_2O_3 (5% water); $CHCl_3$/CH_2Cl_2, 1:1; R_f = 0.56] yielded pure (*R*)-**9** (0.72 g, 0.91 mmol, 51%) as a yellow solid. M.p. 257.1–259.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.77 [d, $^4J_{H,H}$ = 2.2 Hz, 2 H, 1-H(xan)], 7.99 [d, $^3J_{H,H}$ = 8.8 Hz, 2 H, (naph)], 7.95 [dd, $^3J_{H,H}$ = 9.0, $^4J_{H,H}$ = 2.2 Hz, 2 H, 3-H(xan)], 7.90 [d, $^3J_{H,H}$ = 8.1 Hz, 2 H, (naph)], 7.67 [d, $^4J_{H,H}$ = 2.9 Hz, 2 H, 8-H(xan)], 7.58 [d, $^3J_{H,H}$ = 8.8 Hz, 2 H, (naph)], 7.47–7.31 [m, 12 H, (xan and naph)], 3.91 (s, 6 H, OMe). ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 174.56 (s), 162.10 (s), 157.17 (s), 154.83 (s), 149.06 (s), 145.39 (s), 133.63 (d), 131.78 (s), 130.12 (s), 128.45 (d), 128.34 (d), 126.56 (d), 125.52 (d), 124.63 (d), 124.39 (d), 123.61 (d), 123.35 (s), 122.16 (s), 120.55 (s), 120.15 (d), 119.23 (s), 117.93 (d), 116.85 (d), 104.43 (d), 54.44 (q). HRMS calcd. for $C_{50}H_{30}O_{10}$: 790.1836; found: 790.1821.

(*R*)-5,46-Dimethoxy-9,15,36,42-tetraoxyundecacyclo-[36.10.2.2^{10,13}.0^{2,11}.0^{3,8}.0^{16,25}.0^{19,24}.0^{26,35}.0^{27,32}.0^{41,49}.0^{43,48}]dopenta-conta-1,3,5,7,10(52),11,13(51),16,18,20,22,24,26(35),27,29,31,33,38,40,43,45,47,49-tricosaene-14,37-dione [(*R*)-10]: Under nitrogen, substrate (*R*)-**9** (190 mg, 0.24 mmol) was dissolved in oxalyl dichloride (40 mL) and refluxed for 24 h.[15] The excess oxalyl dichloride was removed. The brown residue was dissolved in freshly distilled *p*-xylene (35 mL, from sodium), activated Cu bronze[16] (600 mg, 9.44 mmol) was added and the mixture was refluxed for 24 h. After cooling, the reaction mixture was filtered, and the filtrate was concentrated in vacuo to yield 183 mg of crude product. Purification by column chromatography [Al_2O_3 (5% water); CH_2Cl_2/*n*-hexane, 1:1; R_f = 0.31] yielded pure (*R*)-**10** (27 mg, $3.6\cdot10^{-2}$ mmol, 15%) as a yellow solid. M.p. 330 °C (dec). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 7.98 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 18-,33-H), 7.95 (d, $^4J_{H,H}$ = 1.8 Hz, 2 H, 12-,50-H), 7.94 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, 20-,31-H), 7.57 (dd, $^3J_{H,H}$ = 8.4, $^4J_{H,H}$ = 1.8 Hz, 2 H, 39-,51-H), 7.46 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, 21-,30-H), 7.31 (d, $^3J_{H,H}$ = 8.8 Hz, 2 H, 17-,34-H), 7.24 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, 22-,29-H), 7.21 (d, $^3J_{H,H}$ = 9.2 Hz, 2 H, 7-,44-H), 7.19 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, 40-,52-H), 7.08 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, 23-,28-H), 6.86 (dd, $^3J_{H,H}$ = 9.2, $^4J_{H,H}$ = 2.9 Hz, 2 H, 6-,45-H), 6.62 (d, $^4J_{H,H}$ = 2.9 Hz, 2 H, 4-,47-H), 3.51 (s, 6 H, MeO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 165.17 (s), 158.42 (s), 154.91 (s), 148.86 (s), 147.22 (s), 134.24 (s), 131.64 (s), 130.72 (d), 129.73 (d), 129.59 (d), 127.96 (d), 127.12 (d), 126.55 (d), 125.57 (d), 124.57 (s), 123.96 (s), 123,31 (s), 122.36 (s), 122.28 (d), 120.81 (s), 118.22 (d), 117.46 (d), 116.81 (d), 111.39 (d), 55.36 (q) ppm. HRMS calcd. for $C_{50}H_{30}O_8$: 758.1941; found: 758.1950.

{9-[2-(Hydroxymethyl)-7-methoxy-9*H*-thioxanthen-9-ylidene]-7-methoxy-9*H*-thioxanthen-2-yl}methanol [(*Z*)-11]: General procedure for cleavage of the chiral template from overcrowded alkenes **4** and **7** to yield (*Z*)-**11**. Under nitrogen, $LiAlH_4$ (ca. 0.30 mmol) was suspended in diethyl ether (2.0 mL) at 0 °C. The overcrowded alkene [(*S*,*S*,*M*)-**4** (minor), (*R*,*P*)-**7** (major), (*R*,*M*)-**7** (minor), (*S*,*M*)-**7** (major), or (*S*,*P*)-**7** (minor), ca. $3.5\cdot10^{-2}$ mmol] was added, and the reaction mixture was stirred for 3 h at 5 °C. The diethyl ether was removed under reduced pressure at room temperature and the residue was dissolved in CH_2Cl_2 (10 mL) and 2 M HCl (aq) (10 mL). ***Note:*** *all liquids were cooled to 0 °C before use during workup to avoid any racemization of* (*Z*)-***11***. The organic and water layer were separated and the organic layer was washed (1·10 mL of 2 M aq. HCl), dried (Na_2SO_4), and concentrated in vacuo to yield a yellowish powder. The powder was partly suspended [(*Z*)-**11**] in a mixture of *n*-hexane/CH_2Cl_2, 1:1 (4.0 mL) and stirred for 15 min whereupon binaphthol dissolved. The diol (*Z*)-**11** was collected on a glass filter in 90–95% yield as a slightly yellow powder. M.p. 300.0 °C (dec). ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 7.56 (d, $^3J_{H,H}$ = 7.7 Hz, 2 H, 5-H), 7.53 (d, $^3J_{H,H}$ = 8.6 Hz, 2 H, 4-H), 7.17 (dd, $^3J_{H,H}$ = 8.6, $^4J_{H,H}$ = 1.3 Hz, 2 H, 3-H), 6.85 (dd, $^3J_{H,H}$ = 7.7, $^4J_{H,H}$ = 2.6 Hz, 2 H, 6-H), 6.60 (d, $^4J_{H,H}$ = 1.3 Hz, 2 H, 1-H), 6.24 (d, $^4J_{H,H}$ = 2.6 Hz, 2 H, 8-H), 5.02 (t, $^3J_{H,H}$ = 5.3 Hz, 2 H, OH), 4.11 (d, $^3J_{H,H}$ = 5.3 Hz, 4 H, C*H*$_2$OH), 3.35 (s, 6 H, MeO) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 157.57 (s), 140.19 (s), 135.39 (s), 133.41 (s), 133.14 (s), 133.02 (s), 128.04 (d), 127.49 (d), 126.74 (d), 126.00 (s), 125.51 (d), 114.72 (d), 113.88 (d), 62.17 (t), 54.89 (q) ppm. HRMS calcd. for $C_{30}H_{24}O_4S_2$: 512.1116; found: 512.1102; Determination of $\Delta G^{\ddagger}_{rac.}$ of compound (*Z*)-**11** (polarimetry, dibromoethane, 589 nm): $k_1 = 7.22\cdot10^{-5}$ s^{-1} at 70.0 °C, $\Delta G^{\ddagger}$ = 26.7 kcal mol^{-1}; The *ee* values of (*P*,*Z*)-**11** and (*M*,*Z*)-**11** were determined by chiral HPLC (Daicel, chiralcel OD column, flow rate 1.0 mL min^{-1}, *n*-hexane/2-propanol, 99:1): t_R 98 min for (*P*,*Z*)-**11** and t_R 125 min for (*M*,*Z*)-**11**.

{9-[2-(Hydroxymethyl)-7-methoxy-9*H*-xanthen-9-ylidene]-7-methoxy-9*H*-xanthen-2-yl}methanol [(*P* and *M*,*Z*)-12 and (*E*)-12]: Under

nitrogen, $LiAlH_4$ (15 mg, 0.40 mmol) was suspended in diethyl ether (2.0 mL) at 0 °C. (*R*)-**10** (20 mg, $2.64 \cdot 10^{-2}$ mmol) was added, and the reaction mixture was stirred for 12 h at 0 °C. The diethyl ether was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (5 mL) and 2 M aq. HCl (5 mL). ***Note:*** *all liquids were cooled to 0 °C before use during workup in an attempt to avoid racemization of* (*Z*)-**12**. The organic and water layer were separated and the organic layer was washed [1 × 5 mL of 2 M HCl (aq)], dried (Na_2SO_4), and concentrated in vacuo to yield a yellowish powder. The powder was partly dissolved (binaphthol) and suspended (**12**) in a mixture of *n*-hexane/CH_2Cl_2, 2:1 (2.0 mL) and stirred for 15 min. Diol **12** (8 mg, $1.67 \cdot 10^{-2}$ mmol, 63%) was collected on a glass filter as a slightly yellow powder. ^{1}H NMR revealed a (*Z*)/(*E*) ratio of 59:41. ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C); (*Z*) isomer; δ = 7.30–7.23 (m, 6 H, 3-,4-, and 5-H), 6.98 (s, 2 H, 1-H), 6.89 (dd, $^3J_{H,H}$ = 6.6, $^4J_{H,H}$ = 2.9 Hz, 2 H, 6-H), 6.55 (d, $^4J_{H,H}$ = 2.9 Hz, 2 H, 8-H), 5.03 (t, $^3J_{H,H}$ = 5.5 Hz, 2 H, OH), 4.22 (d, $^3J_{H,H}$ = 5.5 Hz, CH_2OH), 3.45 (s, 6 H); (*E*) isomer; δ = 7.30–7.23 (m, 6 H, 3-,4-, and 5-H), 6.99 (s, 2 H, 1-H), 6.87 (dd, $^3J_{H,H}$ = 6.2, $^4J_{H,H}$ = 2.6 Hz, 2 H, 6-H), 6.50 (d, $^4J_{H,H}$ = 2.6 Hz, 2 H, 8-H), 5.03 (t, $^3J_{H,H}$ = 5.5 Hz, 2 H, OH), 4.25 (d, $^3J_{H,H}$ = 5.5 Hz, 2 H, CH_2OH), 3.40 (s, 6 H, OMe) ppm. ^{13}C NMR (200 MHz, [D_6]DMSO, 25 °C); (*Z*) isomer; δ = 153.05 (s), 152.55 (s), 147.83 (s), 135.36 (s), 126.37 (d), 124.76 (d), 123.27 (s), 122.09 (s), 119.61 (s), 116.84 (d), 115.57 (d), 114.93 (d), 110.40 (d), 61.39 (t), 81.15 (q); (*E*) isomer; δ = 153.20 (s), 152.72 (s), 147.69 (s), 135.36 (s), 125.96 (d), 124.76 (d), 123.39 (s), 122.18 (s), 119.61 (s), 116.84 (d), 115.57 (d), 114.22 (d), 109.62 (d), 61.20 (t), 53.89 (q) ppm. HRMS calcd. for $C_{30}H_{24}O_6$: 480.15726; found: 480.15713.

Supporting Information (see also the footnote on the first page of this article): Two-step procedures for synthesis of xanthones **2** and **8**. Atom numbering scheme and proton assignment of (*S*)-**3**, (*S*,*S*,*M*)-**4** (minor), (*S*,*S*,*P*)-**4** (major), (*R*)-**6**, (*R*,*P*)-**7** (major), (*R*,*M*)-**7** (minor), (*R*)-**9**, (*R*)-**10**, (*Z*)-**11** and (*Z*)- & (*E*)-**12**. ^{1}H NMR spectra of all new compounds. ^{13}C NMR spectra of (*R*,*P*)-**7** (major), (*R*,*M*)-**7** (minor) (*R*)-**10**, (*Z*)-**11** and (*Z*)- & (*E*)-**12**.

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