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Studies toward the Photochemical Synthesis of Functionalized [5]- and [6] Carbohelicenes

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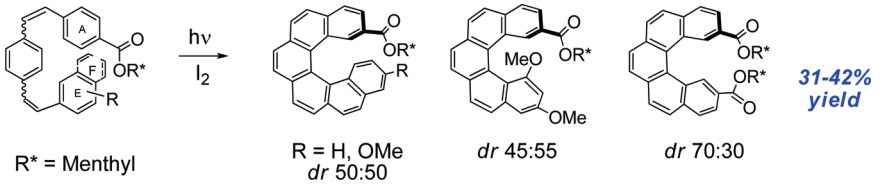

An efficient route to nonsymmetrical helical menthyl esters by means of an oxidative photocyclization reaction of dissymmetric bis-stilbenes is reported. The developed route allows the introduction of functionality on rings A, E, or F, and the influence of the substituent pattern on the photochemical reaction has been examined. Diastereoselectivity is observed when a double chiral induction strategy with dimenthyl helicene esters synthesized in a 70:30 ratio of isomers is used.

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Introduction

The helix is a three-dimensional structure which is discernible in the natural world over a range of scales and contexts. For example, cyclones and snail shells both display this helical structure. In a chemistry context, the conspicuous macromolecular structures of DNA and many proteins are based upon a helical tertiary structure. With two of nature's most fundamental chemistries featuring the helix and its associated chirality, the special nature of the helix in chemistry becomes apparent.

Helicenes are formed from the *ortho* fusion of five or more aromatic rings. The most significant feature of the helicene is the inherent chirality, and this has attracted attention from chemists during recent decades.[1,2] Therefore, significant effort has been devoted to the preparation of helicenes and heterohelicenes as well as the study of their use as ligands and catalysts in asymmetric synthesis,[3] with a chiral diphosphine helicene reported to be an excellent ligand in Pd-catalyzed kinetic resolution involving allylic substitution.[4] On the other hand, highly enantioselective addition of dialkylzinc reagents to aldehydes was described using [5]- and [6]carbohelicenes,[5] bis[5]helicenediol,[6] and tetrathia[7]helicenes[7] as chiral inducers. More recently, Takenaka and co-workers have reported the preparation of helical chiral pyridine *N*-oxides and their efficiency as catalysts for the desymmetrization of *meso*-epoxides.[8]

It is therefore somewhat surprising that despite the stimulating chiral topography, helicenes have been somewhat underused in organic synthesis with respect to the design and synthesis of reagents, catalysts, and ligands for enantioselective transformations. Part of the reason for this may be the difficulty in synthesizing functionalized nonsymmetrical helicenes as single enantiomers as existing syntheses can either be lengthy or offer simple symmetrical systems. Among existing methods,[9] the photodehydrocyclization of suitable stilbene systems remains a direct and convenient strategy to access helicenes.[10]

We have chosen to examine the synthesis of helicenyl esters in this study for three reasons. First, the ester functionality

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(3) For theory concerning helicity and chiral interactions, see: (a) Wang, D. Z. *Tetrahedron* **2005**, *61*, 7125–7133. (b) Wang, D. Z. *Tetrahedron* **2005**, *61*, 7134–7143.
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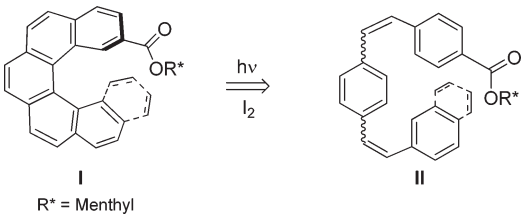
would offer access to a wide range of functionality suitable for exploring the scope of helicenes in asymmetric catalysis contexts. Second, the use of readily available menthyl esters would act as a chiral auxiliary to offer a potentially diastereoselective photocyclization[11,12] or at worst offer the option of resolution by separating diastereomers after photocyclization. Third, as menthyl esters are considerably lipophilic, we felt they may improve the solubility of a notoriously insoluble class of substrate.

Accordingly, we felt that functionalized helicenes **I** (Scheme 1), suitable for later asymmetric synthetic studies, could be rapidly accessed through a tandem double-oxidative photocyclization of suitable 1,4-bis-stilbenes **II** (Scheme 1). This report details our efforts to synthesize functionalized helicenes through a convergent tandem photocyclization route.

SCHEME 1. Functionalized [5]- and [6]Helicenes by Oxidative Photocyclization of Bis-stilbenes



Results and Discussion

Since $E \leftrightarrow Z$ isomerization occurs during the irradiation process, no specific (*E*,*E*), (*E*,*Z*), or (*Z*,*Z*) configuration of the bis-stilbene is required for the photocyclization reaction. Therefore, we planned to prepare bis-stilbenes **II** with (*E*,*E*) geometry by means of two distinct Wittig olefination couplings. Accordingly, we have explored a five-step process based on a consecutive Wittig-olefination strategy.

Monosubstituted [6]Helicene 8a. Phosphonium bromide salt **2**,[13] formed in excellent yield from commercially available 4-methylbenzyl bromide **1** and triphenylphosphine,[14] was subjected to a Wittig reaction with 2-naphthaldehyde to give a crude 1:1 mixture of (*E*)- and (*Z*)-stilbenes. After purification by chromatography, iodine-mediated isomerization allowed isolation of (*E*)-stilbene **3a**[15] in 79% yield. Treatment of **3a** with NBS and a substoichiometric amount of dibenzoyl peroxide[16] afforded the benzyl bromide **4a**,[17] which was in turn converted into the corresponding phosphonium salt **5a** in 79%. The second Wittig reaction was then accomplished by treating **5a** and chiral aldehyde (+)-**6**[18] in THF with *t*-BuOK. This procedure led to a 1:1 mixture of bis-stilbenes (*E*,*Z*) and (*E*,*E*). Due to the low solubility of the (*E*,*E*)-isomer, the crude mixture was not purified by chromatography and was directly subjected to iodine mediated isomerization. Recrystallization of the resulting crude product furnished pure (*E*,*E*)-bis-stilbene **7a** in 63% yield. Irradiation of a solution of **7a** in benzene ($c = 4.10^{-4}$ M) in the presence of 2 equiv of oxidant (I_2) and an excess of propylene oxide as HI scavenger[10] furnished our first target, 2-substituted [6]helicene **8a**, as a 1:1 mixture of diastereoisomers (Scheme 2). All attempts to separate the two isomers by crystallization or chromatography (silica gel or neutral alumina) failed, and the diastereomeric mixture of helicenes **8a** was isolated in 42% yield after purification on neutral alumina. Various photocyclization conditions (solvent, dilution, reaction time) were tested to optimize the reaction (Table 1). Bis-stilbene **7a** was partially soluble in toluene and totally soluble in benzene (entries 1−3). The reaction afforded a mixture of several products from which only the helicene was able to be identified with the yield improved by increasing the reaction concentration from 0.16 to 0.4 mM

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(18) Chiral aldehyde (+)-**6** and its isomer (−)-**6** were prepared in 96% yield from commercially available 4-formylbenzoic acid and (+)- or (−)-menthol using a DCC/DMAP coupling reaction.

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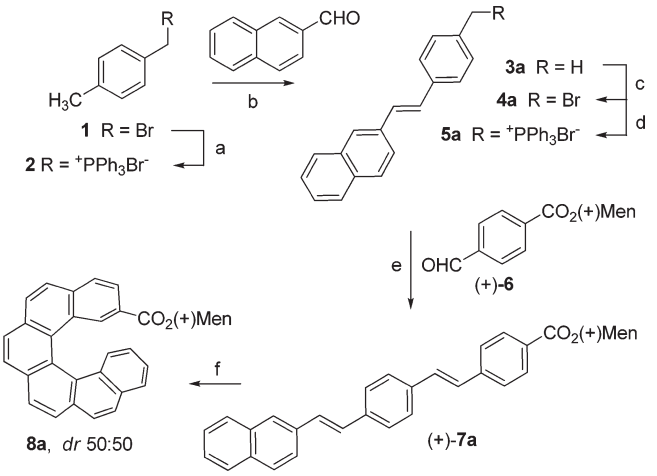
SCHEME 2. Synthesis of Monosubstituted [6]Helicene 8a[a]



[a]Reagents and conditions: (a) PPh_3 (1.1 equiv), toluene, reflux, 15 h, 98%; (b) (i) 2-naphthaldehyde (1.0 equiv), 2 (1.05 equiv), THF, 0 °C, then t-BuOK (1.1 equiv), 0 °C to rt, 15 h, (ii) I_2 (5 mol %), toluene, reflux, 15 h, 79%; (c) NBS (1.1 equiv), dibenzoyl peroxide (3.3 wt %), CCl_4, reflux, 72 h, 68%; (d) PPh_3 (1.1 equiv), toluene, reflux, 15 h, 79%; (e) (i) (+)-6 (1.0 equiv), 5a (1.05 equiv), THF, 0 °C, then t-BuOK (1.1 equiv), 0 °C to rt, 15 h, (ii) I_2 (5 mol. %), toluene, reflux, 15 h, 63%; (f) hν, I_2 (2.0 equiv), propylene oxide (100 equiv), benzene (c = 4.10^{-4} M), rt, 3 h, 42%.

TABLE 1. Oxidative Photocyclization of 7a[a]

entry	solvent	concn (10^{-4}M)	time, h	**7a**, %
1	hexane	1.6	2	0[b]
2	PhMe	1.6	2	20[c]
3	C_6H_6	1.6	2	30
4	C_6H_6	4	2	42
5	C_6H_6	4	6	40
6	C_6H_6	10	5	10[d]

[a]Reaction conditions: *hν* (400 W), I_2 (2.0 equiv), solvent (concentration *c*), propylene oxide (100 equiv), time, rt. [b]Substrate not soluble, starting material recovered. [c]Substrate not completely soluble, some starting material recovered. [d]Crude product containing significant levels of byproduct

(entry 4). However, a further increase in reaction concentration led to a drop in yield from 40% to 10% with the concomitant formation of unidentified byproduct (entry 6).

It has to be pointed out that no selectivity was observed during the photocyclization of menthyl ester **7a**. This result was consistent with the lack of induction observed earlier by Cochez et al. during the photocyclization of a similar monostilbene substrate.[11d]

We then turned our attention to di- and trisubstitution and envisaged the synthesis of hexa- and pentahelicenes **8b**−**d** for two reasons (Figure 1): (a) OMe and CF_3 substituents may increase substrate solubility and (b) the possible interaction of these substituents and the menthyl ester moiety during cyclization may improve stereoselectivity during the photocyclization.

Disubstituted [6]Helicene 8b. The strategy developed to prepare helicene **8a** was extended to the synthesis of its 14-methoxy analogue **8b** (Scheme 3). Wittig reaction involving phosphonium salt **2** and 6-methoxy-2-naphthaldehyde followed by iodine-catalyzed isomerization afforded (*E*)-stilbene **3b** in 70% yield. Stilbene **3b** was in turn converted in two steps to the phosphonium bromide salt **5b** (40% yield), which was then subjected to a second Wittig olefination

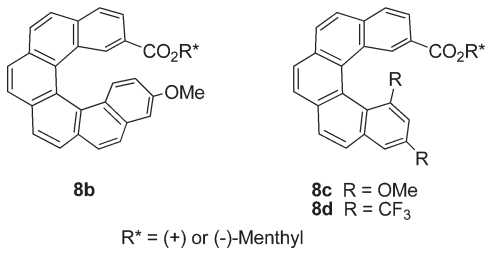
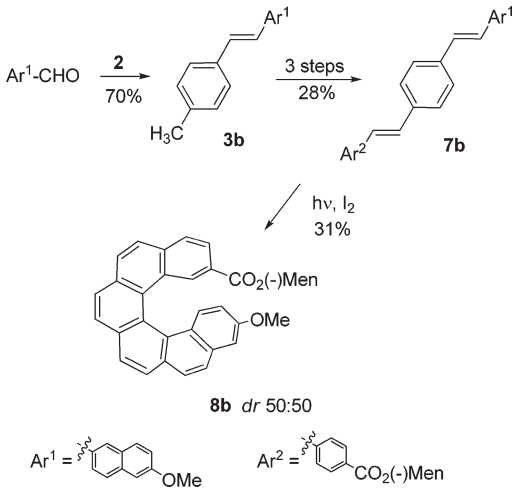


FIGURE 1. New substituted [5]- and [6]helicene targets.

SCHEME 3. Synthesis of a 14-Methoxy Analogue of Helicene 8a



reaction using aldehyde (−)-**6** to give the pure bis-stilbene **7b** (70% yield). As observed with its congener **7a**, photocyclization of dialkene **7b** led to helicene **8b** as a 50:50 mixture of diastereoisomers in moderate yield. Interestingly, despite the presence of the OMe substituent, bis-stilbene **7b** displayed poorer solubility than **7a** and more diluted conditions ($c = 2.10^{-4}$ M) were required. However, an encouraging partial separation of diastereoisomers was observed during the chromatography on neutral alumina; initial fractions containing a 1:4 mixture, the middle fractions a 2:3 mixture, and the latter fractions a 3:2 mixture of diastereoisomers.

Trisubstituted [5]Helicenes 8c and 8d. In order to prepare the dimethoxy-substituted substrate **7c**, a change in the order of constructing the bis-stilbene was required. In contrast to the route discussed in Scheme 2, the intermediary phosphonium salt was formed upon the menthol ester unit.[19] Stilbene **9**, isolated in 89% yield, was subjected to radical bromination conditions to afford bromo derivative **10** in 61% yield. Its phosphonium bromide salt **11** was then reacted with 3,5-dimethoxybenzaldehyde to provide after iodine-mediated isomerization, the (*E*,*E*)-bis-stilbene **7c** in 73% yield (Scheme 4).

Irradiation of a solution of **7c** in benzene gave the helicene **8c** in 35% yield. Gratifyingly, a weak chiral induction was observed with this dimethoxy-substituted substrate, and **8c** was obtained as a 45:55 mixture of diastereoisomers. Unfortunately, those isomers remained inseparable by

(19) Attempts at performing a benzylic bromination reaction using 3,5-dimethoxytoluene led to inseparable mixtures of aromatic bromination products.

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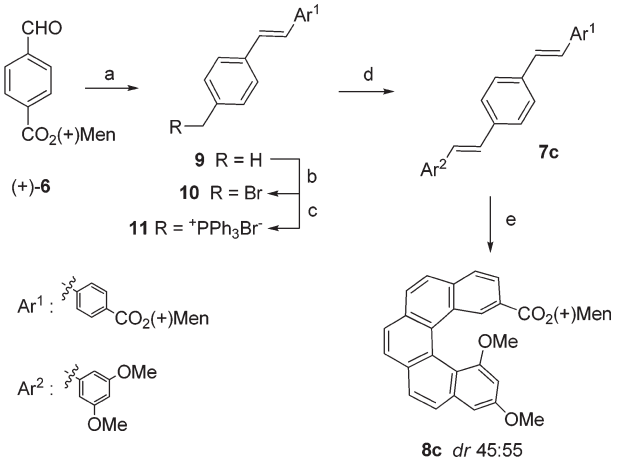
SCHEME 4. Route to Dimethoxy[5]helicene 8c[a]



[a]Reagents and conditions: (a) (i) (+)-6 (1.0 equiv), 2 (1.05 equiv), THF, 0 °C, then t-BuOK (1.1 equiv), 0 °C to rt, 15 h, (ii) I_2 (5 mol %), toluene, reflux, 15 h, 89%; (b) NBS (1.1 equiv), dibenzoyl peroxide (3.3 wt %), CCl_4, reflux, 48 h, 61%; (c) PPh_3 (1.1 equiv), toluene, reflux, 15 h, 73%; (d) (i) 3,5-dimethoxybenzaldehyde (1.0 equiv), 11 (1.05 equiv), THF, 0 °C, then t-BuOK (1.1 equiv), 0 °C to rt, 15 h, (ii) I_2 (5 mol. %), toluene, reflux, 15 h, 73%; (e) hν, I_2 (2.0 equiv), propylene oxide (100 equiv), benzene (c=3.5.10^{-4} M), rt, 3 h, 35%.

recrystallization or attempted chromatographic separation using a number of different stationary phases.

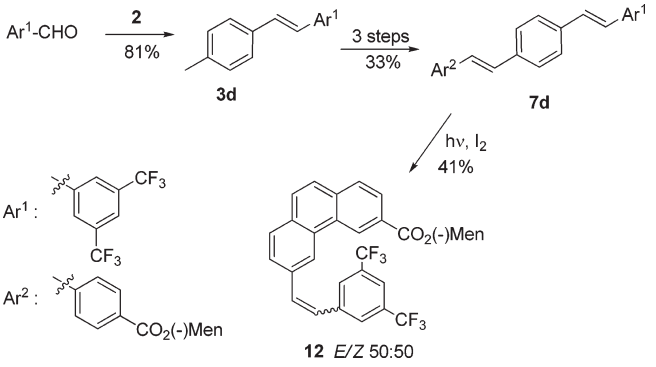
For the synthesis of the ditrifluoromethyl-substituted derivative, the application of the initial strategy to 3,5-ditrifluoromethylbenzaldehyde successfully afforded the bis-stilbene **7d** in 27% yield over four steps (Scheme 5).

Submission of **7d** to photocyclization conditions produced a complicated crude mixture from which no traces of helicenes **8d** were observed after purification on neutral alumina.[20] Instead, the major product monostilbene **12** was isolated in 41% yield as a 1:1 mixture of *E*- and *Z*-geometrical isomers which were not separable by chromatography on silica gel or neutral alumina with the structures assigned by ^{1}H NMR analysis on the basis of the coupling constants measured for four distinct alkene protons (7.54 ppm: J = 16.2 Hz, 7.36 ppm: J = 16.2 Hz, 7.10 ppm: J = 12.2 Hz, 6.75 ppm: J = 12.2 Hz).

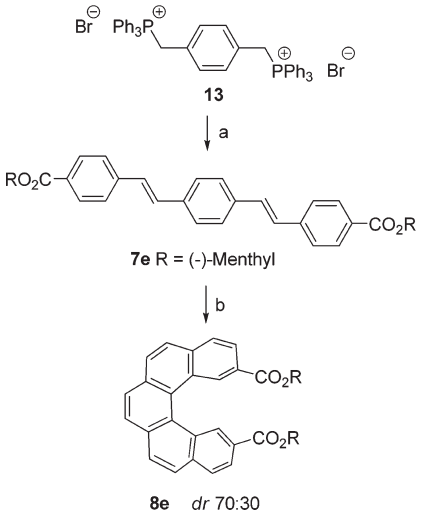
A possible explanation for the exclusive monophotocyclization would be the electron-withdrawing effect of CF_3 substituent with the displacement of the electron density from the styrene moiety to the CF_3 substituents disfavoring the second photocyclization occurring.[21]

[5]Helicenes by Double-Stereochemical Induction. As no satisfactory diastereoselectivity was observed during the photocyclization step, we decided to explore the possibility of a double-induction effect by introducing two identical chiral auxiliaries on the photocyclization substrate. For that, we prepared the di-(−)-menthyl diester **7e** in 89% yield by means of a double Wittig reaction using the aldehyde (−)-**6** and the bis-phosphonium bromide salt **13** (Scheme 6). Bis-stilbene **7e** proved to be more soluble than the other

SCHEME 5. Synthesis and Photocyclization of Bis(trifluoromethyl) Bis-stilbene 7d



SCHEME 6. Stereoselective Synthesis of Disubstituted [5]Helicene 8e by Double Induction[a]



[a]Reagents and conditions: (a) (i) (−)-6 (1 equiv), 13 (0.5 equiv), THF, 0 °C, then t-BuOK (2.1 equiv), 0 °C to rt, 15 h, (ii) I_2 (5 mol %), toluene, reflux, 15 h, 89%; (b) hν, I_2 (2.0 equiv), propylene oxide (100 equiv), hexane (c=4.10^{-4} M), rt, 3 h, 35%.

substrates, and the photocyclization reaction was accomplished in hexane (c = 4.10^{-4} M) using the previously developed conditions. Contrary to what was reported by Cochez et al. during the monophotocyclization of a dimenthyl diester substrate,[11c] an asymmetric induction was observed with bis-stilbene **7e**. [5]Helicene **8e** was isolated in 35% yield as a 70:30 mixture of helical diastereoisomers.[22]

Conclusions

In conclusion, we have developed routes to poly functionalized [5]- and [6]helicenyl esters using a photocyclization key step, allowing formation of the helical core in yields of 31−42%. Symmetrical diester helicene **8e** was readily prepared using a one-pot double-Wittig coupling reaction (31% yield for the two steps), while a strategy based on two consecutive Wittig reaction afforded dissymmetric helicenes **8a**−**c** in six steps and 7−31% overall yields.

(20) Despite the total consumption of the starting material, some unreacted iodine remained in the solution after irradiation (pink color), proving that the double photocyclization did not work completely.

(21) The 50:50 ratio of (*E*)- and (*Z*)-monostilbenes obtained from the unique (*E*,*E*)-bis-stilbene **7d** is due to the isomerization of (*E*)-alkene into the (*Z*)-isomer during irradiation, which allows the molecule to adopt a suitable conformation for cyclization.

(22) Extensive efforts have been made to effect separation by normal-phase HPLC. Unfortunately, we have not been able to isolate a single diastereomer to allow optical rotation studies.

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During this work, we have demonstrated that the influence of substitution of the aromatic system on the photocyclization reaction is key for the successful outcome of this double-photocyclization strategy. Furthermore, the solubility of bis-stilbenes is dependent on the substitution pattern, and therefore, scale-up is also limited. Electron-withdrawing groups upon the bis-stilbene substrates disfavor the photocyclization reaction. However, suitable poly substitution is important to induce selectivity during the photocyclization step. Thus, an interesting diastereoselective reaction was observed using a double-chiral-induction strategy to provide dimenthyl diester **8d** as a 70:30.

Attempts to resolve the synthesized helicenes and their study as potential catalysts are currently under investigation in our laboratories.

Experimental Section

(+)-Menthyl 4-[2-[4-(2-(2-Naphthyl)-(*E*)-ethenyl)phenyl]-(*E*)-ethenyl]benzoate (7a). To a suspension of aldehyde (+)-**6** (625 mg, 2.17 mmol) and phosphonium salt **5a** (1.33 g, 2.27 mmol) in dry THF (30 mL) cooled to 0 °C was added potassium *tert*-butoxide (268 mg, 2.39 mmol) portionwise over a period of 10 min. The orange suspension was allowed to warm to room temperature, and the mixture was stirred at this temperature overnight. Water (30 mL) was added, and the aqueous phase was extracted with dichloromethane (3 × 20 mL). The combined organic fractions were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude yellow solid was suspended in toluene (30 mL), and a catalytic amount of iodine (5 mol %) was added. After being refluxed overnight, the solution was cooled to room temperature to give a yellow precipitate that was filtered off and recrystallized from acetone to afford the pure ester **7a** (700 mg, 63%) as yellow crystals: mp = 244−246 °C (from acetone); $[\alpha]^{20}_D$ = +33.0 (*c* 0.122, $CHCl_3$); FTIR 1710, 1595, 1559, 1540, 1506, 1419, 1274; ^{1}H NMR (300 MHz, $CDCl_3$) 8.02 (d, *J* = 8.2 Hz, 2H), 7.88−7.70 (m, 5H), 7.59−7.51 (m, 5H), 7.49−7.39 (m, 2H), 7.31 (d, *J* = 17.2 Hz, 1H), 7.23 (s, 1H), 7.21 (d, *J* = 16.3 Hz, 2H), 7.12 (d, *J* = 17.2 Hz, 1H), 4.92 (td, *J* = 10.8, 4.5 Hz, 1H), 2.12 (dm, *J* = 12.2 Hz, 1H), 1.90 (sept-d, *J* = 6.9, 2.5 Hz, 1H), 1.78−1.66 (m, 2H), 1.60−1.48 (m, 2H), 1.25−1.02 (m, 2H), 0.95−0.80 (m, 1H), 0.92 (d, *J* = 6.3 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.0, 141.8, 137.5, 136.3, 134.9, 133.9, 133.3, 130.8, 130.2, 129.8, 129.2, 128.6, 128.5, 128.2, 127.9, 127.7, 127.3, 127.1, 126.9, 126.5, 126.4, 126.1, 123.6, 75.0, 47.5, 41.2, 34.5, 31.6, 26.7, 23.9, 22.2, 20.9, 16.7; HRMS (EI) *m*/*z* calcd for $C_{37}H_{38}O_2$ [$M^{\bullet+}$] 514.2866, found 514.2869.

(−)-Menthyl 4-[2-[4-(2-(6-Methoxy-2-naphthyl)-(*E*)-ethenyl) phenyl]-(*E*)-ethenyl]benzoate (7b). The same procedure as for **7a** using aldehyde (−)-**6** and phosphonium salt **5b** was followed. After isomerization of the crude material, successive recrystallizations from dichloromethane and acetone afforded the pure (*E*,*E*) isomer **7b** (850 mg, 70%) as bright yellow crystals: mp = 295−297 °C (from acetone); $[\alpha]^{20}_D$ = −38.8 (*c* 0.052, $CHCl_3$); FTIR 3055, 2988, 1714, 1602, 1422, 1266; ^{1}H NMR (300 MHz, $CDCl_3$) 8.03 (d, *J* = 8.4 Hz, 2H), 7.81 (s, 1H), 7.77−7.71 (m, 3H), 7.60−7.54 (m, 6H), 7.33−7.12 (m, 6H), 4.94 (td, *J* = 10.5, 4.5 Hz, 1H), 3.94 (s, 3H), 2.14 (dm, *J* = 11.3 Hz, 1H), 1.98 (m, 1H), 1.85−1.65 (m, 2H), 1.62−1.50 (m, 2H), 1.20−1.02 (m, 2H), 0.95−0.90 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR too insoluble to register a correct spectra; HRMS (EI) *m*/*z* calcd for $C_{38}H_{40}O_3$ [M^+] 544.2972, found 544.2990.

(+)-Menthyl 4-[2-[4-(2-(3,5-Dimethoxyphenyl)-(*E*)-ethenyl) phenyl]-(*E*)-ethenyl]benzoate (7c). To a suspension of 3,5-dimethoxybenzaldehyde (50 mg, 0.30 mmol) and phosphonium salt **11** (280 mg, 0.39 mmol) in dry THF (10 mL) cooled to 0 °C was added potassium *tert*-butoxide (47 mg, 0.42 mmol) portionwise over a period of 10 min. The orange suspension was allowed to warm to room temperature, and the mixture was stirred at this temperature overnight. Water (5 mL) was added, and the aqueous phase was extracted with dichloromethane (3 × 5 mL). The combined organic fractions were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude yellow solid was suspended in toluene (5 mL), and a catalytic amount of iodine (5 mol %) was added. The mixture was refluxed overnight and then concentrated in vacuo. Purification by flash chromatography (diethyl ether/petroleum ether 5:95) afforded **7c** as the pure (*E*,*E*) isomer (115 mg, 73%): yellow solid; R_f = 0.20 (diethyl ether/petroleum ether 1:9); mp = 67−69 °C (from toluene); $[\alpha]^{20}_D$ = +28.7 (*c* 0.942, $CHCl_3$); IR 3053, 2975, 2920, 1705, 1600, 1450, 1400, 1262; ^{1}H NMR (300 MHz, $CDCl_3$) 8.04 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.53 (s, 4H), 7.22 (d, *J* = 16.5 Hz, 1H), 7.14 (d, *J* = 16.5 Hz, 1H), 7.08 (s, 2H), 6.69 (d, *J* = 1.8 Hz, 2H), 6.41 (t, *J* = 1.8 Hz, 1H), 4.94 (td, *J* = 10.7, 4.2 Hz, 1H), 3.84 (s, 6H), 2.14 (dm, *J* = 11.8 Hz, 1H), 1.98 (sept-d, *J* = 6.8, 2.2 Hz, 1H), 1.80−1.69 (m, 2H), 1.64−1.50 (m, 2H), 1.27−1.10 (m, 2H), 0.97−0.90 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.0, 161.1, 141.7, 139.4, 137.2, 136.3, 130.7, 130.2, 129.7, 128.8, 127.7, 127.3, 127.1, 126.4, 104.7, 100.2, 74.9, 55.5, 47.4, 41.1, 34.5, 31.6, 26.6, 23.8, 22.2, 20.9, 16.7; HRMS (EI) *m*/*z* calcd for $C_{35}H_{40}O_4$[M^+] 524.2921, found 524.2929.

(−)-Menthyl 4-[2-[4-(2-(3,5-Bis(trifluoromethyl)phenyl)-(*E*)-ethenyl)phenyl]-(*E*)-ethenyl]benzoate (7d). The same procedure as for **7a** using aldehyde (−)-**6** and phosphonium salt **5d** was followed. After isomerization of the crude material, purification by flash chromatography (diethyl ether/petroleum ether 5:95) afforded **7d** as a the pure (*E*,*E*)-isomer (204 mg, 63% yield): yellow solid; R_f = 0.40 (diethyl ether/petroleum ether 5:95); mp = 177−179 °C (from toluene); $[\alpha]^{20}_D$ = −28.7 (*c* 1.152, $CHCl_3$); FTIR 2957, 2871, 1706, 1606, 1457, 1420, 1380, 1278; ^{1}H NMR (300 MHz, $CDCl_3$) 8.06 (d, *J* = 8.2 Hz, 2H), 7.92 (s, 2H), 7.75 (s, 1H), 7.61−7.55 (m, 6H), 7.24 (d, *J* = 16.3 Hz, 1H), 7.23 (d, *J* = 16.3 Hz, 1H), 7.17 (d, *J* = 16.3 Hz, 1H), 7.14 (d, *J* = 16.3 Hz, 1H), 4.96 (td, *J* = 10.9, 4.3 Hz, 1H), 2.16 (dm, *J* = 12.3 Hz, 1H), 2.0 (sept-d, *J* = 6.9, 2.9 Hz, 1H), 1.80−1.70 (m, 2H), 1.65−1.51 (m, 2H), 1.27−1.07 (m, 2H), 1.0−0.90 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 6H), 0.83 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.0, 141.5, 139.5, 137.4, 135.9, 132.4, 132.1, 132.0, 130.4, 130.2, 130.0, 129.7, 128.4, 127.5, 127.4, 126.5, 126.3, 125.7, 125.3, 120.9, 75.0, 47.5, 41.2, 34.5, 31.6, 26.7, 23.8, 22.2, 20.9, 16.7; HRMS (EI) *m*/*z* calcd for $C_{35}H_{34}O_2F_6$ [M^+] 600.2458, found 600.2454.

(−)-Menthyl 4-[2-[4-(2-(4-(−)-Menthyloxycarbonylphenyl)-(*E*)-ethenyl)phenyl]-(*E*)-ethenyl]benzoate (7e). To a suspension of aldehyde (−)-**6** (1.0 g, 3.47 mmol) and *p*-xylenebis(triphenylphosphonium bromide) **13** (1.37 g, 1.73 mmol) in dry THF (10 mL) cooled to 0 °C was added potassium *tert*-butoxide (428 mg, 3.82 mmol) portionwise over a period of 10 min. The orange suspension was allowed to warm to room temperature, and the mixture was stirred overnight. Water (15 mL) was added, and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic fractions were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude yellow solid was suspended in toluene (10 mL), and a catalytic amount of iodine was added. After refluxing overnight and evaporation of the solvent, the crude solid was purified by flash chromatography (diethyl ether/petroleum ether 1:1) to afford the pure diester **7e** (1.0 mg, 89%) as a yellow solid: R_f = 0.30 (diethyl ether/petroleum ether 1:1); mp = 130−132 °C (from CH_2Cl_2); $[\alpha]^{20}_D$ = −52.5 (*c* 1.01, $CHCl_3$); FTIR 1706, 1605, 1507, 1279. ^{1}H NMR (300 MHz, $CDCl_3$) 7.96 (d, *J* = 8.2 Hz, 4H), 7.48 (d, *J* = 8.2 Hz, 4H), 7.46 (s, 4H), 7.13 (d, *J* = 16.0 Hz, 2H), 7.06 (d, *J* = 16.0 Hz, 2H), 4.86 (td, *J* = 10.8, 4.1 Hz, 2H), 2.06 (dm, *J* = 12.3 Hz, 2H), 1.90 (sept-d, *J* = 6.6, 2.7 Hz, 2H), 1.70−1.60 (m, 4H), 1.55−1.42 (m, 4H), 1.14−0.95 (m, 4H), 0.90−0.80 (m, 2H), 0.85 (d, *J* = 6.8 Hz, 12H), 0.84 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (75.5 MHz,

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$CDCl_3$) 166.0, 141.6, 136.8, 130.6, 130.2, 129.8, 127.9, 127.3, 126.4, 74.9, 47.1, 41.1, 34.5, 31.6, 26.7, 23.8, 22.2, 20.9, 16.7; HRMS (EI) m/z calcd for $C_{44}H_{54}O_4$ [M^+] 646.4017, found 646.4018.

Photocyclization Procedure. Photocyclizations were performed on 0.10−0.20 mmol scale (c = (2−4) × 10^{-4} M) in a 500 mL photoreactor. The photocyclization substrate **7a**−**e** (1 equiv) and iodine (2 equiv) were dissolved in 500 mL of benzene (for **7a**−**d**) or hexane (**7e**). Propylene oxide (100 equiv) was added, and the mixture was placed in the photoreactor equipped with an immersion high-pressure mercury lamp (400 W). The solution was irradiated for 2−3 h (until total disappearance of the pink color), and solvent was evaporated under reduced pressure. The crude red oil was purified by column chromatography on neutral alumina.

2-(+)-Menthyloxycarbonyl[6]helicene (8a) was obtained as a 50:50 diastereomeric mixture of *M* and *P* helicenes after chromatography on neutral alumina (diethyl ether/petroleum ether 2:8): $c = 4.10^{-4}$ M in benzene; pale yellow oil (42 mg, 42% yield); R_f = 0.40 (diethyl ether/petroleum ether 5:95); FTIR 3049, 2955, 2926, 2869, 1705, 1620, 1455, 1255; ^{1}H NMR (300 MHz, $CDCl_3$) 8.41 (d, J = 0.8 Hz, 0.5H), 8.34 (d, J = 0.8 Hz, 0.5H), 8.10−7.80 (m, 10H), 7.80 (dd, J = 8.0, 1.0 Hz, 0.5H), 7.77 (dd, J = 8.0, 1.0 Hz, 0.5H), 7.57 (bd, J = 8.3 Hz, 0.5H), 7.55 (bd, J = 8.3 Hz, 0.5H), 7.21 (ddd, J = 8.0, 7.0, 1.1 Hz, 0.5H), 7.20 (ddd, J = 8.0, 7.0, 1.1 Hz, 0.5H), 6.67 (ddd, J = 8.3, 7.0, 1.0 Hz, 1H), 4.73 (td, J = 10.9, 4.3 Hz, 0.5H), 4.61 (td, J = 10.9, 4.3 Hz, 0.5H), 1.97−0.77 (m, 9H), 1.06 (d, J = 6.6 Hz, 1.5H), 0.99 (d, J = 7.0 Hz, 1.5H), 0.87 (d, J = 6.6 Hz, 1.5H), 0.72 (d, J = 7.0 Hz, 1.5H), 0.71 (d, J = 7.0 Hz, 1.5H), 0.55 (d, J = 7.0 Hz, 1.5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.1, 165.9, 134.3, 134.2, 133.4, 133.3, 132.4, 132.3, 131.7, 131.6, 131.5, 131.4, 130.4, 130.2, 129.6, 129.5, 129.3, 129.2, 128.8, 128.7, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 126.9, 126.7, 126.2, 126.1, 125.8, 125.7, 125.6, 125.5, 124.8, 124.7, 124.1, 74.4, 74.3, 47.0, 46.9, 40.9, 40.7, 34.7, 34.3, 31.5, 25.9, 25.8, 23.6, 23.1, 22.5, 22.2, 21.4, 20.6, 16.5, 16.0; HRMS (ESI) m/z calcd for $C_{37}H_{35}O_2$ [M + H] $^+$ 511.2632, found 511.2629.

2-(−)-Menthyloxycarbonyl-14-methoxy[6]helicene (8b) was obtained as a 50:50 diastereomeric mixture of *M* and *P* helicenes after chromatography on neutral alumina (diethyl ether/petroleum ether 2:8): $c = 2.10^{-4}$ M in benzene; pale yellow oil (17 mg, 31% yield); R_f = 0.20 (diethyl ether/petroleum ether 5:95); FTIR 3054, 2926, 2871, 1703, 1620, 1422, 1265; ^{1}H NMR (300 MHz, $CDCl_3$) 8.45 (s, 0.5H), 8.38 (s, 0.5H), 8.05−7.83 (m, 10H), 7.48 (d, J = 9.2 Hz, 0.5H), 7.43 (d, J = 9.2 Hz, 0.5H), 7.13 (d, J = 2.8 Hz, 0.5H), 7.11 (d, J = 2.8 Hz, 0.5H), 6.33 (dd, J = 9.2, 2.8 Hz, 0.5H), 6.31 (dd, J = 9.2, 2.8 Hz, 0.5H), 4.74 (td, J = 10.6, 4.2 Hz, 0.5H), 4.60 (td, J = 10.6, 4.2 Hz, 0.5H), 1.98−0.70 (m, 9H), 1.06 (d, J = 6.5 Hz, 1.5H), 1.0 (d, J = 7.0 Hz, 1.5H), 0.86 (d, J = 6.5 Hz, 1.5H), 0.71 (d, J = 7.0 Hz, 1.5H), 0.70 (d, J = 7.0 Hz, 1.5H), 0.52 (d, J = 7.0 Hz, 1.5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.2, 166.0, 157.3, 134.4, 134.2, 134.0, 133.8, 133.6, 133.5, 131.5, 131.4, 130.6, 130.4, 130.3, 129.5, 129.4, 129.3, 129.1, 128.8, 128.7, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3, 127.2, 127.1, 126.9, 126.8, 126.7, 125.9, 125.7, 124.5, 124.3, 123.8, 116.0, 115.9, 107.4, 107.0, 74.4, 74.3, 55.3, 55.2, 47.0, 46.8, 40.9, 40.7, 34.8, 34.4, 31.5, 31.4, 26.3, 26.0, 23.8, 23.2, 22.5, 22.2, 21.5, 20.6, 16.5, 16.1; HRMS (EI) m/z calcd for $C_{38}H_{36}O_3$ [M^+] 540.2659, found 540.2662

2-(+)-Menthyloxycarbonyl-12,14-dimethoxy[5]helicene (8c) was obtained as a 45:55 diastereomeric mixture of *M* and *P* helicenes after chromatography on neutral alumina (diethyl ether/petroleum ether 4:6): $c = 3.5.10^{-4}$ M in benzene; pale yellow oil (32 mg, 35% yield); R_f = 0.25 (diethyl ether/petroleum ether 1:9); FTIR 3050, 2957, 2925, 1700, 1625, 1455, 1405, 1265; ^{1}H NMR (300 MHz, $CDCl_3$) 9.02 (bs, 0.55H), 8.91 (bs, 0.45H), 8.11 (dd, J = 8.3, 1.6 Hz, 0.45H), 8.07 (dd, J = 8.3, 1.6 Hz, 0.55H), 8.01−7.83 (m, 7H), 7.02 (bd, J = 2.4 Hz, 1H), 6.49 (d, J = 2.4 Hz, 0.55H), 6.47 (d, J = 2.4 Hz, 0.45H), 4.91 (td, J = 10.9, 4.4 Hz, 0.45H), 4.77 (td, J = 10.9, 4.4 Hz, 0.55H), 4.03 (s, 1.65H), 4.02 (s, 1.35H), 3.0 (s, 1.35H), 2.99 (s, 1.65H), 2.15 (dm, J = 11.9 Hz, 0.55H), 1.90−1.39 (m, 7.45H), 1.22−0.80 (m, 1H), 1.02 (d, J = 6.5 Hz, 1.65H), 0.98 (d, J = 7.0 Hz, 1.35H), 0.88 (d, J = 6.5 Hz, 1.35H), 0.82 (d, J = 7.0 Hz, 1.35H), 0.68 (d, J = 7.0 Hz, 1.55H), 0.57 (d, J = 7.0 Hz, 1.55H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.9, 166.6, 159.0, 158.9, 157.6, 157.5, 135.6, 135.5, 133.0, 132.8, 132.5, 132.0, 131.2, 128.9, 128.8, 128.6, 128.0, 127.7, 127.6, 127.4, 127.2, 127.1, 127.0, 126.7, 126.6, 126.4, 126.3, 125.6, 125.5, 123.7, 117.5, 99.4, 99.3, 98.9, 98.8, 74.5, 74.3, 55.4, 54.2, 54.1, 47.1, 46.8, 41.0, 40.7, 34.5, 31.6, 26.3, 23.7, 23.2, 22.3, 22.2, 21.0, 20.6, 16.5, 16.2; HRMS (EI) m/z calcd for $C_{35}H_{36}O_4$ [M^+] 520.2608, found 520.2608.

2 13-Di-(−)-menthyloxycarbonyl[5]helicene (8e) was obtained as a 70:30 mixture of *M* and *P* helicenes after chromatography on neutral alumina (diethyl ether/petroleum ether 2:8): $c = 4.10^{-4}$ M in hexane; pale yellow oil (45 mg, 35% yield); R_f = 0.40 (diethyl ether/petroleum ether 5:95); FTIR 3050, 2948, 2927, 2864, 1710, 1450, 1264; ^{1}H NMR (300 MHz, $CDCl_3$) 9.27 (s, 1.4H), 9.15 (s, 0.6H), 8.16 (dd, J = 8.4, 1.4 Hz, 0.6H), 8.13 (dd, J = 8.4, 1.4 Hz, 1.4H), 8.03−7.89 (m, 8H), 4.76 (td, J = 10.6, 4.3 Hz, 0.6H), 4.71 (td, J = 10.6, 4.3 Hz, 1.4H), 2.04−1.87 (m, 2H), 1.72−1.53 (m, 4H), 1.52−1.39 (m, 6H), 1.28−1.15 (m, 2H), 1.11−0.95 (m, 2H), 0.93−0.73 (m, 2H), 0.99 (d, J = 6.5 Hz, 2.1H), 0.84 (d, J = 7.0 Hz, 0.9H), 0.80 (d, J = 6.5 Hz, 0.9H), 0.66 (d, J = 7.0 Hz, 0.9H), 0.63 (d, J = 7.0 Hz, 2.1H), 0.57 (d, J = 7.0 Hz, 2.1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.1, 135.2, 132.8, 132.6, 130.8, 130.4, 130.3, 129.9, 128.8, 128.6, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.1, 127.0, 126.9, 126.5, 74.9, 74.8, 47.2, 46.8, 41.0, 40.8, 34.4, 31.1, 26.2, 25.9, 23.5, 23.1, 22.2, 22.1, 21.4, 20.7, 16.3, 15.8; HRMS (EI) m/z calcd for $C_{44}H_{50}O_4$ [M^+] 642.3704, found 642.3707.

3-(−)-Menthyloxycarbonyl-6-[2-(3,5-difluorophenyl)ethenyl]phenanthrene (12) was obtained as an unseparable 50:50 mixture of the *E* and *Z* alkenes after chromatography on neutral alumina (diethyl ether/petroleum ether 2:8): $c = 2.10^{-4}$ M in benzene; pale yellow oil (25 mg, 41% yield); R_f = 0.50 (diethyl ether/petroleum ether 5:95); FTIR 3055, 2987, 2929, 1705, 1605, 1422, 1265; ^{1}H NMR (300 MHz, $CDCl_3$) 9.47 (bs, 0.5H), 9.28 (bs, 0.5H), 8.87 (bs, 0.5H), 8.68 (bs, 0.5H), 8.23 (dd, J = 8.3, 1.5 Hz, 0.5H), 8.21 (dd, J = 8.3, 1.5 Hz, 0.5H), 8.03 (s, 1H), 7.95−7.69 (m, 6H), 7.54 (d, J = 16.2 Hz, 0.5H), 7.38 (m, 1H), 7.36 (d, J = 16.2 Hz, 0.5H), 7.10 (d, J = 12.2 Hz, 0.5H), 6.75 (d, J = 12.2 Hz, 0.5H), 5.08 (m, 1H), 2.22 (m, 1H), 2.04 (m, 1H), 1.81−1.75 (m, 2H), 1.63 (m, 1H), 1.29−1.21 (m, 3H), 1.01−0.83 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 166.5, 166.4, 139.5, 139.3, 135.2, 135.1, 134.9, 134.6, 133.9, 133.0, 132.7, 132.5, 132.4, 132.1, 132.0, 131.9, 131.6, 131.1, 131.0, 129.8, 129.7, 129.5, 129.1, 129.0, 128.9, 128.8, 127.8, 127.1, 126.9, 126.6, 126.5, 125.3, 125.1, 125.0, 123.8, 122.5, 121.7, 121.5, 121.1, 120.9, 75.4, 75.3, 47.6, 47.5, 41.2, 34.5, 31.7, 26.9, 24.0, 23.9, 22.7, 22.2, 20.9, 20.6, 16.8; HRMS (EI) m/z calcd for $C_{35}H_{32}O_2F_6$ [M^+] 598.2301, found 598.2284.

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Supporting Information Available: General experimental methods, characterization data, and copies of ^{1}H and ^{13}C NMR spectra for all synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.