Diastereoselective Intramolecular *meta* Photocycloaddition of Side-Chain-Substituted 5-(2-Methoxyphenyl)pent-1-enes

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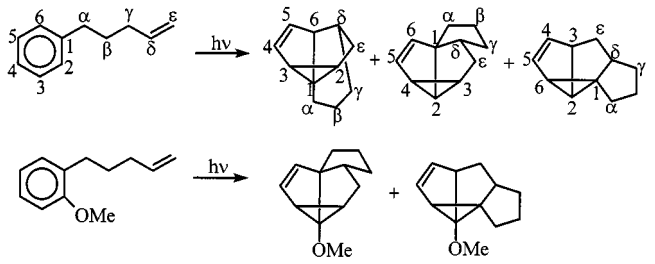
Irradiation of a series of 5-(2-methoxyphenyl)pent-1-enes substituted with a hydroxy or trimethylsilyloxy group at the α-, β-, or γ-position of the side-chain yields in all cases *meta* photocycloadducts, in which the configuration at the substituted carbon atom is mainly *endo*. This indicates that the diastereoselectivity originates from minimization of steric interactions between the side-chain substituent and the *ortho*-methoxy group at the arene unit. Hydrogen bonding does not seem to be involved. The introduction of the side-chain substituents also influences the regioselectivity of the addition: The linear to angular adduct ratios are significantly increased compared to the case of the parent compound.

Introduction

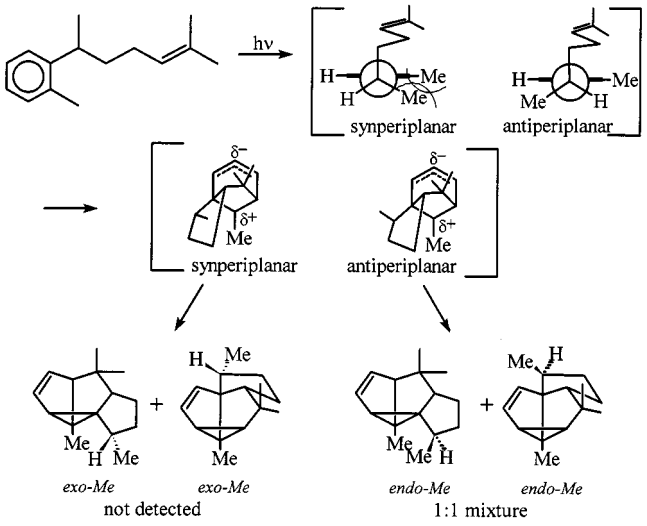
The intramolecular version of the *meta* photocycloaddition of arenes to alkenes has been shown to be very useful in the construction of fused polycycles.[1] In particular, Wender's group has used the reaction for the synthesis of polyquinanes,[2] while Keese and co-workers have used it to prepare fenestranes.[3] The synthetic potential of the reaction is demonstrated by the photochemical behaviour of 5-phenylpent-1-ene and of 5-(2-methoxyphenyl)pent-1-ene (Scheme 1).



Scheme 1. Intramolecular *meta* photocycloaddition of 5-phenylpent-1-ene and 5-(2-methoxyphenyl)pent-1-ene

Upon irradiation of the parent compound, three of the four possible adducts are formed, viz. one 2,6-adduct and two 1,3-adducts. The *o*-methoxy derivative yields only 1,3-adducts. This shows that the introduction of suitable substituents on the arene moiety of the bichromophore permits control over the mode of addition.[4] Moreover, Gilbert and co-workers have shown that within the 1,3-addition mode, regioselectivity (i.e. the ratio of linear to angular 1,3-adducts) can be achieved by the introduction of either a specific (viz. chlorine) substituent on the alkene part of the bichromophore,[5] or by the introduction of heteroatoms at the 4-position of the bichromophore.[6]

When an *ortho*-methyl substituent is present on the arene nucleus and an α-substituent is attached to the side-chain (the benzylic position), the stereochemistry of this benzylic carbon atom is fixed in the adducts so that diastereoselectivity results (Scheme 2).



Scheme 2. *endo*-Configurational preference of the side-chain substituent in the adduct, due to steric interactions

It has been proposed that this diastereoselection originates from non-bonded repulsive interactions between the substituents.[7,8] As shown in Scheme 2, the synperiplanar approach is subject to steric restrictions, while in the antiperiplanar approach the substituents are conveniently oriented away from each other. The products that arise following the latter mode of attack are called *endo* adducts. Conceivably, the diastereoselectivity might be reversed if the interaction between the substituents is attractive, as for example in compounds with an α-hydroxy substituent on the side-chain and an *ortho*-methoxy group at the arene.[9] Indeed, it was recently reported that two 5-(2-methoxyphenyl)pent-1-ene derivatives with a γ-hydroxy group yielded adducts with the hydroxy group in the so-called *exo* orientation.[10] The diastereoselectivity observed was as-

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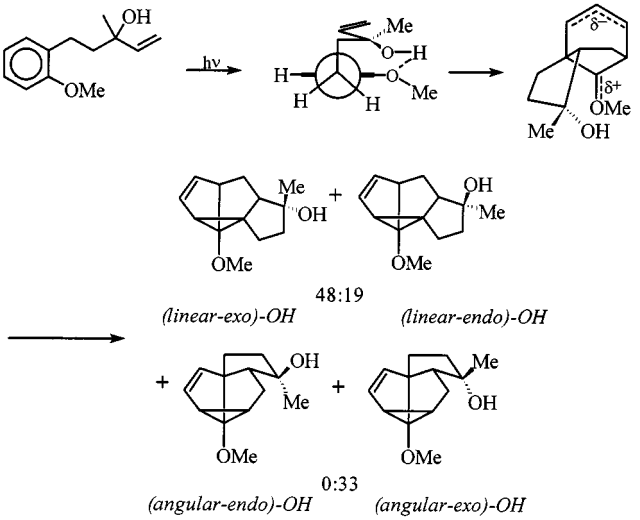
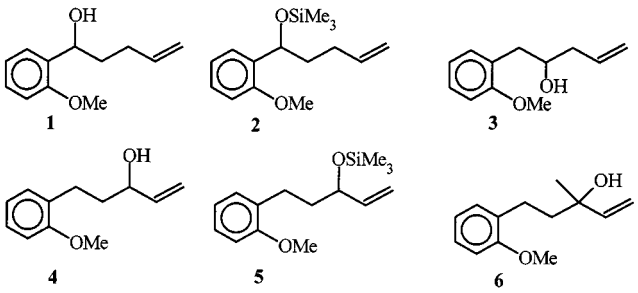
cribed to a hydrogen bond between the 3-hydroxy group and the 2-methoxy substituent (Scheme 3).



Scheme 3. *exo*-Configurational preference of the hydroxy substituent in the adduct, attributed to hydrogen-bond formation

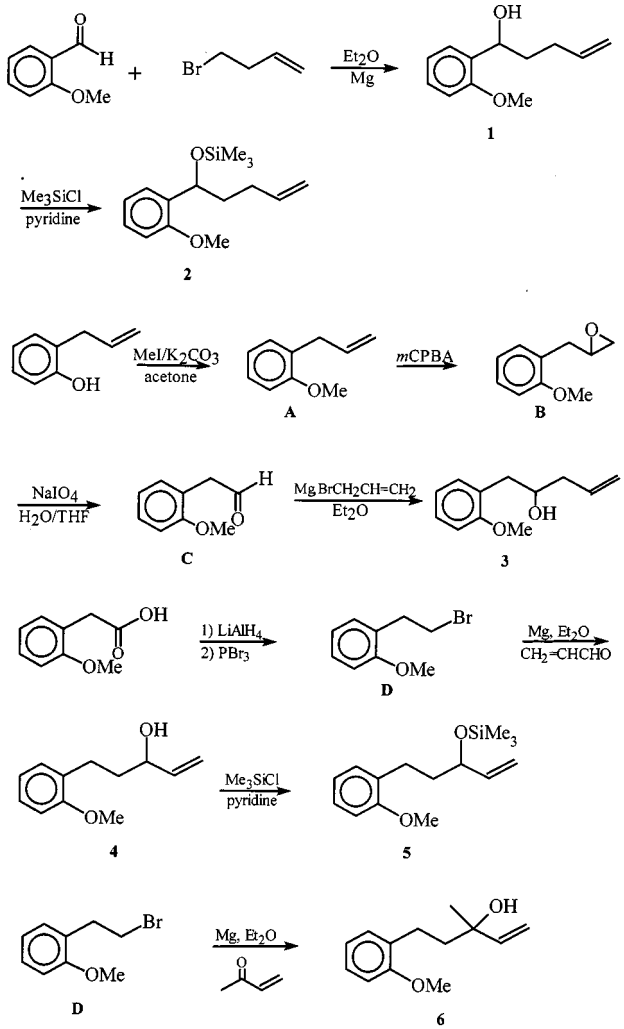
A problem with this explanation, however, is that the bichromophore has two substituents at the γ-carbon atom of the side-chain. As a hydroxy group is smaller than a methyl group,[11,12] the steric model depicted in Scheme 2 might also explain these results. Minimization of steric interactions would lead to a preference for adducts with the methyl group in the *endo* position and thus with the hydroxy group in the *exo* position.

In this paper, we wish to report our findings concerning the diastereoselectivities achieved in the irradiation products of a series of 5-(2-methoxyphenyl)pent-1-enes bearing hydroxy or trimethylsilyloxy groups at the α-, β-, or γ-position of the side-chain (compounds **1**−**5**). These compounds are well-suited for probing the importance of hydrogen-bond formation during the photocycloaddition, since they have only one side-chain substituent. For the sake of comparison, the γ-hydroxy-γ-methyl compound **6**, the photochemical behaviour of which has already been described,[10a] was also included in these studies.



Results

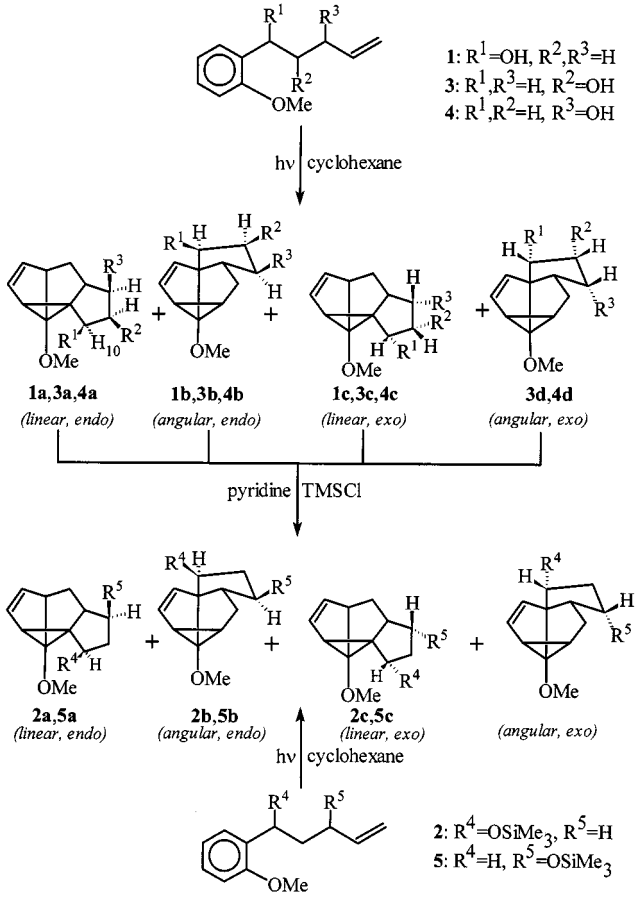
Starting materials **1**−**6** were synthesized as outlined in Scheme 4 (for details, see Experimental Section). Ir-



Scheme 4. Synthesis of starting materials **1**−**6**

radiation (λ_{exc} = 254 nm) of the α-hydroxy derivative **1** in cyclohexane for 10.5 h yielded three 1,3-adducts **1a**, **1b**, and **1c** in a 3:1:1 ratio, in a total yield of 50% (Scheme 5).

The position (*endo* or *exo*) of the hydroxy group was determined by ^{1}H-NMR NOESY, and was shown to be *endo* in the main linear adduct **1a**, *endo* in the sole angular adduct **1b**, and *exo* in the minor linear adduct **1c**. The chemical shift of the proton geminal to the substituent (OH or OTMS) is a good indicator of the configuration at the relevant carbon atom. In the linear adduct with OH *endo* (**1a**), 10-H (cf. Scheme 5) resonates at δ = 4.1. In the linear adduct with *exo*-OH (**1c**), the geminal proton resonates at δ = 4.5. Models of the adducts show that in the linear adduct with *exo*-OH, 10-H is directed away from the methoxy group, whereas in the *endo*-OH compound this proton resides near the methoxy substituent. This electron-rich environment shields the proton, which results in an upfield shift compared to that in the *exo*-OH compound. This observation holds true for all the *meta* adducts described in this paper. The *endo* selectivity in the case of **1** was confirmed by converting the hydroxy group of the adducts **1a**−**c** into a trimethylsilyloxy group. The products were



Scheme 5. Products of the irradiation of **1**, **2**, **3**, **4**, **5** and the conversion of **1a**−**c** into **2a**−**c**, and of **4a**−**d** into **5a**−**d**

found to be identical to the *meta* adducts obtained upon irradiation of the trimethylsilyl derivative **2**, which yielded **2a**, **2b**, and **2c** in a ratio of 3:1:0.7.

The β-hydroxy compound **3** yielded two major adducts **3a** and **3b**, as well as two minor adducts **3c** and **3d**, after 10.5 h of irradiation in cyclohexane (**3a**/**3b**/**3c**/**3d** = 4:2:1:0.1) (Scheme 5). In both major adducts, the hydroxy groups are in the *endo* position. In the minor products, the hydroxy groups are *exo*. Interestingly, this preference for *endo* is opposite to the preference observed with compounds that lack the *ortho*-methoxy substituent at the aromatic nucleus. Upon irradiation of 5-phenylpent-1-en-4-ol, for example, a 5:2 ratio in favour of the *exo*-OH was found for the linear adducts, while of the possible angular adducts only that with *exo*-OH was detected.[13]

Irradiation of the γ-hydroxy compound **4** also yielded mainly adducts with *endo*-OH. The linear adducts (**4a** and **4c**) showed an 8:3 preference for *endo*-OH, while for the angular adducts (**4b** and **4d**) this ratio was 3:1. Again, this was checked by converting the hydroxy groups in the adducts into trimethylsilyloxy groups, and comparing the product ratios with those obtained following the irradiation of **5** (Scheme 5).

Repetition of the experiment described by Zhang and Guo with the γ-hydroxy-γ-methyl compound **6**[10a] confirmed their results (see Table 1). However, we found 8% of the total amount of adduct to be the angular adduct **6d** with *endo*-OH, a product not reported by these authors. The ratio of *exo*-OH/*endo*-OH in the linear adducts **6a** and **6c** was 3:1. The isolation and identification of the angular *endo*-OH adduct **6d** further provides an *exo*/*endo* ratio for hydroxy in the angular adducts, which also turned out to be 3:1. The results of the irradiations of compounds **1**−**6** are summarized in Table 1.

Discussion

endo/*exo* Selectivity

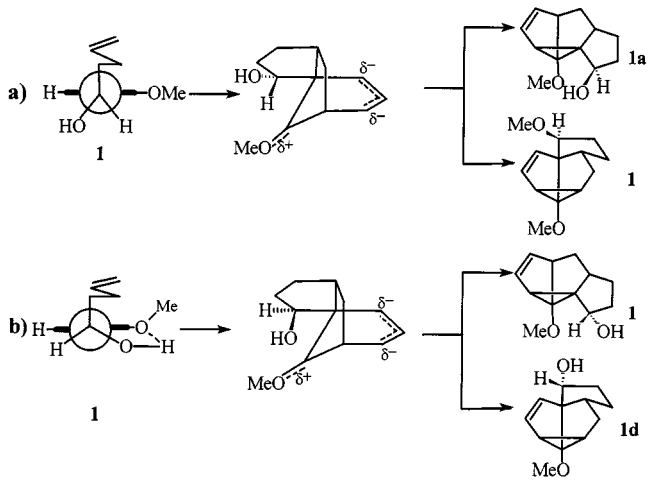
As discussed in the introduction, two effects may determine the induction of diastereoselectivity in the adducts of compounds **1**, **3**, and **4**: a steric, repulsive interaction or a hydrogen bonding, attractive interaction between the substituents. With compounds **2** and **5**, the latter effect cannot occur. As illustrated in Scheme 6 for compound **1**, in cases where the steric effect is dominant, mainly adducts with the side-chain substituent in the *endo* position will be formed.

In cases where the hydrogen-bond formation effect prevails, the (hydroxy) substituent will appear mainly in the *exo* position in the adduct. For all compounds examined in this study with one substituent on the side-chain and an *ortho*-methoxy group at the arene (**1**−**5**), preponderantly the adducts are formed which have the side-chain substituent in the *endo* position. The *exo*/*endo* ratio varies from 0.17 to 0.39 (Table 1). These results are in accordance with the hypothesis that minimization of steric interactions between the substituents is the decisive factor. Thus, the steric model is operative for bichromophoric compounds **1** and **2**, for **3**,

Table 1. Yields of products of the irradiations of **1**−**6** (GC ratios, normalized to 100%)

Compound	lin-*endo*	ang-*endo*	lin-*exo*	ang-*exo*	*exo*/*endo*	lin/ang
1 (α-OH)	59	19	22	−	0.28	4.3
2 (α-OTMS)	63	22	14	−	0.17	3.5
3 (β-OH)	56	27	15	2	0.21	2.5
4 (γ-OH)	42	32	16	10	0.35	1.4
5 (γ-OTMS)	49	23	28	−	0.39	3.5
6 (γ-OH,γ-Me)[a]	15(19)	8(−)	49(48)	28(33)	3.4	1.8(2.0)

[a] *endo* refers to the orientation of the hydroxy group (cf. Scheme 3); the values reported in ref.[10a] are given in parentheses.



Scheme 6. Predictions based on the steric model of Scheme 2 (**a**) compared to the hydrogen-bond formation model of Scheme 3 (**b**) in the intramolecular *meta* photocycloaddition of **1**

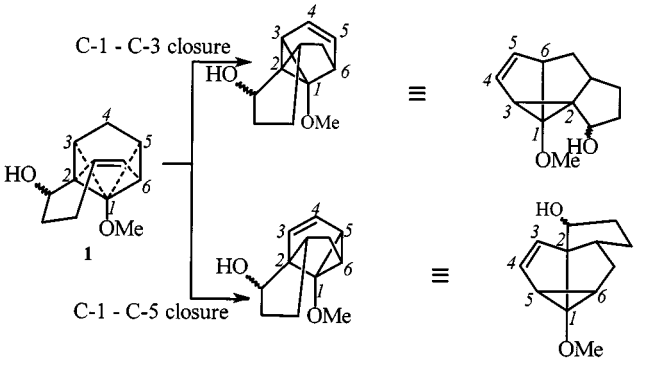
and for **4** and **5**, and hydrogen bonding does not determine the course of the addition. In agreement with a steric effect being the determining factor, increase of the steric requirements of the α-substituent [changing the hydroxy group (as in **1**) into a trimethylsilyloxy group (as in **2**)] leads to an increase in the *endo*/*exo* ratio. The *A* values of these two groups are 0.60 and 0.75, respectively.[11] However, the *endo*/*exo* ratio does not increase on going from **4** to **5**.

For compound **6**, with two substituents on the side-chain, the methyl group appears mainly in the *endo* position and the hydroxy group mainly in the *exo* position in both the linear and the angular adducts (Table 1). This diastereoselectivity can also be explained in terms of the steric model. The methyl group is larger (certainly in the solvent used, viz. cyclohexane) than the hydroxy group. In cyclohexane, the *A* values for a methyl and a hydroxy group are 1.74 and 0.60, respectively,[11] and their E_s values are −1.24 and −0.55.[12] In conclusion, in all cases minimization of steric interaction between the side-chain substituent and the *ortho*-methoxy group on the arene moiety seems to be the principal factor in determining the configuration of the side-chain carbon atom in the adduct.

Linear/Angular Selectivity

For all compounds examined, the linear/angular adduct ratio (see Table 1) was larger than that for the parent compound 5-(2-methoxyphenyl)pent-1-ene, which yielded linear and angular adducts in a 0.8 to 1 ratio.[4a] This indicates that the side-chain substituents influence the direction of closure of the three-membered ring (C-1 to C-3 closure preferred over C-1 to C-5 closure in Scheme 7).

In studies of intermolecular *meta*-photocycloaddition reactions, it has been noted that with electron-donating substituents at one of the carbon atoms at which addition takes place, the closure of the three-membered ring occurs mainly *away* from this carbon atom.[14] If this (i.e. C-1 to C-5 closure) also holds true for the intramolecular *meta* photocycloaddition, mainly angular adducts should be formed, as shown in Scheme 7 for compound **1**. This is in contrast to the observation that all compounds examined here show a preference for the formation of linear adducts upon photolysis. It can be argued that in the intramolecular case the nature of the transition structure favours closure of the three-membered ring *towards* the addition site (i.e. C-1 to C-3 closure), since C-2 wishes to attain sp^3-hybridization as soon as possible to accommodate the steric congestion around it. If this is the case, mainly linear adducts can be expected to be formed, which is indeed observed. The effect is more important in *exo* than in *endo* product formation, because in the latter case the hydroxy group is in closer proximity to the methoxy group (Scheme 7). Another explanation could be direction by a field effect of the side-chain substituent. The oxygen atom of the hydroxy or trimethylsilyloxy group will be preferentially located away from the methoxy group, and thus directed towards the allylic position (C-3, Scheme 7), where a negative charge develops during the polarization of the aromatic nucleus in the S_1 state. The lone pairs of the oxygen atom will then push C-3 towards closure of the three-membered ring, thereby producing a linear adduct. This effect will be most dominant in *endo* adducts. The possibility that substituents can exert a field effect on the direction of the three-membered ring-closure has previously been postulated in relation to the intermolecular reaction of benzene with (*E*)-1,2-dichloroethene[15] and in the intramolecular reactions of 1- and 2-chloro-5-phenylpent-1-enes.[5]



Scheme 7. Direction of ring-closure of the three-membered ring of **1** leading to linear and angular adducts

Whatever the cause of the effect, it seems to be quite general, since several other bichromophores with both an *ortho* and a side-chain substituent also yield adducts in linear/angular ratios consistently larger than unity. For example, with 5-(2,5-dimethylphenyl)-3-methylpent-1-ene the ratio is 1.9.[16] 6-(*tert*-Butyldimethylsilyloxy)-6-(2-methoxyphenyl)hex-2-ene, a compound that bears a rather close resemblance to compound **2**, also exhibits a preference for the formation of linear (*endo*) adducts.[17] It might be argued that the large linear/angular ratio could be the result of the occurrence of a vinylcyclopropane−cyclopentene rearrangement. For all compounds **1**−**6**, however, the ratios remained constant throughout the photolysis. Moreover, the vinylcyclopropane−cyclopentene rearrangement usually

increases the proportion of angular adduct during the course of the reaction, and thus decreases the linear/angular ratio.[2a]

Conclusions

The photoproducts of **2** are identical to the products obtained after conversion of the hydroxy groups in the adducts formed upon photolysis of **1** into trimethylsilyloxy groups. Only the ratios are somewhat different (Table 1). This is also the case for the photoproducts of **5** and **4**. These results indicate that the antiperiplanarity model[7][8] of Scheme 2 also holds for hydroxy substituents. Hydrogen bonding in the transition structure between a hydroxy group on the side-chain and the methoxy group at the arene (Scheme 6) does not seem to play a role in determining the diastereoselectivity of the reaction. The explanation offered by Zhang and co-workers[10] for the diastereoselectivity in **6** is therefore likely to be incorrect. The results can better be explained by considering the steric effect exerted by the larger of the two side-chain substituents. The fifth compound studied with one substituent on the side-chain (**3**) also yielded mainly adducts with the hydroxy groups in the *endo* position. Again, this can be rationalized with reference to the antiperiplanarity model shown in Scheme 6. Interestingly, the hydroxy group in the adducts is mainly found in the *exo* position (2.4:1) when the β-hydroxy compound lacks an *ortho*-arene substituent, as in the case of 3-hydroxy-5-phenylpent-1-ene.[13] This also seems to be the result of steric hindrance, since in the corresponding disubstituted compound (β-OH, β-Me) the largest (Me) group preferentially adopts the *exo* position (3:1).[13]

In conclusion, introduction of an *ortho*-methoxy substituent at the arene *reverses* the *endo/exo* preference in the adducts. The preference is dictated by steric factors, and hydrogen bonding does not seem to be important. This opens a promising route for the introduction of chirality in the reaction. The *endo* to *exo* preference allows selective conversion of enantiomerically pure side-chain-substituted compounds to *meta* adducts. This type of approach has been shown to be successful in the total synthesis of (−)-retigeranic acid by Wender and Singh,[2b] and in the synthesis of (1*S*,5*R*)-*exo*-(6*S*)-hydroxy-8,8-(ethylenedioxy)bicyclo[3.2.1]octane by Sugimura et al.[18]

An additional advantage of introducing substituents at the connecting chain in the bichromophore is that regioselectivity is induced in the 1,3-mode of *meta* photocycloaddition. Further research is needed to elucidate the fine interplay of electronic and steric factors that determine the ratio of formation of linear and angular adducts.

Experimental Section

General Aspects: Starting materials were obtained from Aldrich Chemicals (Belgium) or Acros Chemicals (The Netherlands) and were used without further purification. Solvents were distilled where necessary. Diethyl ether was distilled from NaH, and THF from $LiAlH_4$. DMF, DMSO, and pyridine were dried overnight with molecular sieves, acetone with K_2CO_3. All solvents used in the irradiation experiments were distilled and checked for UV purity. − Column-chromatographic separations were performed using Merck silica gel (230−400 mesh). For preparative HPLC separations, an LKB Bromma 2150 pump equipped with an LKB Bromma 2151 variable-wavelength detector and a Zorbax Sil column (DuPont), 2.1 × 25 cm, was used. Preparative GC was performed with a Varian Aerograph model 90p with H_2 as carrier gas and an SE-30 column. Analytical GC was carried out with a Varian 3400 using a WCOT fused-silica column (Cp-Sil-5 CB, 25 m) or with a Hewlett-Packard instrument with a WCOT fused-silica column (CP-Sil-19 CB, 50 m). − UV absorption spectra were measured with a Varian DMS 200 spectrophotometer. − NMR spectra were recorded with JEOL FX-200 or Bruker WM300 spectrometers, with Me_4Si as internal standard. − Irradiations were carried out in a Rayonet Photochemical Reactor RPR 200, fitted with eight 254-nm lamps, placed in a room cooled to 4°C (for preparative irradiations), or in a "merry-go-round" fitted with a low-pressure Hanau TNN 15/32 mercury lamp in quartz tubes equipped with stirring rods (for analytical irradiations). − Mass spectra were obtained with a Finnigan MAT 900 spectrometer [EI or CI (NH_3)]. − Fluorescence spectra were recorded with a SPEX equipped with a SPEX Fluorolog lamp, a SPEX Torin TA300 photomultiplier, and a SPEX DM1B Spectroscopy Laboratory Coordinator computer.

Syntheses of Starting Materials (see Scheme 4): 5-Hydroxy-5-(2-methoxyphenyl)pent-1-ene (**1**) was synthesized in 22% yield by a Grignard reaction of 4-bromobut-1-ene with anisaldehyde. The corresponding trimethylsilyloxy compound **2** was prepared from **1** according to the established procedure using pyridine and Me_3Si-Cl.[19] Synthesis of the β-hydroxy compound **3** required a more elaborate sequence. *o*-Allylphenol was first methylated with MeI and K_2CO_3 in acetone.[20] Treatment of **A** with *m*-chloroperbenzoic acid afforded epoxide **B**, which was cleaved with sodium periodate to form aldehyde **C**.[21] A Grignard reaction of **C** with allyl bromide gave the desired compound in an overall yield of 20% based on *o*-allylanisole. The two γ-substituted compounds **4** and **5** were obtained by first converting *o*-methoxyphenylacetic acid in two steps (30%) into 1-bromo-2-(2-methoxyphenyl)ethane (**D**). This bromide was then subjected to a Grignard reaction with acrolein, which gave **4** in 11% yield. The corresponding trimethylsilyloxy derivative **5** was prepared from **4** using the pyridine/TMSCl protocol (46%). Compound **6** was synthesized by means of a procedure different from that in the literature.[10a] Bromide **D**, an intermediate in the syntheses of **4** and **5**, was subjected to a Grignard reaction with methyl vinyl ketone, which furnished **6** in 20% yield.

5-Hydroxy-5-(*o*-methoxyphenyl)pent-1-ene (1): A solution of 4-bromobut-1-ene (5.0 g, 37 mmol) in 10 mL of dry diethyl ether was added dropwise to 0.9 g (37 mmol) of magnesium turnings in 10 mL of ether and the reaction was initiated by gentle heating. After all the bromide had been added, the mixture was refluxed for a further 1 h. It was then cooled to 0°C, whereupon a solution of 5.0 g (37 mmol) of *o*-anisaldehyde in 10 mL of diethyl ether was added, and the resulting mixture was refluxed for another 1 h. After cooling once more, water and saturated ammonium chloride solution were added. The mixture was stirred until a clear, two-phase system was obtained. The layers were then separated, and the aqueous layer was extracted three times with diethyl ether. The combined organic layers were washed with sodium bisulfite solution to remove unreacted aldehyde, then dried ($MgSO_4$), and the solvent was evaporated. Purification of the resulting yellow oil by column chromatography (light petroleum/diethyl ether, 5:1) afforded 2.6 g of product (13.5 mmol, 22%). − ^{1}H NMR (200 MHz,

$CDCl_3$, TMS): δ = 7.3−6.8 (m, 4 H, arom.), 6.0−5.7 (m, 1 H, 2-H), 5.1−4.7 (m, 3 H, 1-H and 5-H), 3.8 (s, 3 H, OCH_3), 2.3−2.0 (m, 2 H, 3-H), 2.0−1.8 (m, 2 H, 4-H), 1.2 (br. s, 1 H, OH). − ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 156.5 (arom.), 138.5 (C-2), 132.3 (arom.), 128.2 (arom.), 126.9 (arom.), 120.7 (arom.), 114.5 (arom.), 110.5 (C-1), 70.5 (C-5), 55.2 (OCH_3), 36.4 (C-4), 30.3 (C-3). − MS; *m/z* found 192.1122; calcd. 192.1150.

5-Trimethylsilyloxy-5-(*o*-methoxyphenyl)pent-1-ene (2): To a suspension of 0.5 g (2.6 mmol) of **1** in 10 mL of pyridine, 0.4 g (3.7 mmol) of trimethylsilyl chloride was added dropwise. After stirring for 1 h, the excess pyridine was evaporated, and the residue was diluted with diethyl ether. The pyridinium salt was filtered off, and the filtrate was concentrated to dryness. Yield: 0.41 g (1.6 mmol, 62%). − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.4−6.6 (2 d, 2 t, 4 H, arom.), 5.9−5.6 (m, 1 H, 2-H), 5.1−4.9 (m, 2 H, 1-H), 4.8 (t, 1 H, 5-H), 3.7 (s, 3 H, OCH_3), 2.2−1.9 (m, 2 H, 3-H), 1.8−1.5 (m, 2 H, 4-H), −0.07 (s, 9 H, $-SiMe_3$). − ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 155.3 (arom.), 138.7 (C-2), 133.7 (arom.), 128.1 (arom.), 127.5 (arom.), 120.4 (arom.), 114.0 (arom.), 109.8 (C-1), 67.7 (C-5), 55.0 (OCH_3), 37.9 (C-4), 30.0 (C-3), 0.0 ($SiMe_3$).

4-Hydroxy-5-(*o*-methoxyphenyl)pent-1-ene (3): To a solution of 5.0 g (34 mmol) of *o*-allylanisole (**A**) in 200 mL chloroform (cooled in an ice-bath) was added 6.0 g (35 mmol) of *m*CPBA. The mixture was stirred overnight, then washed with 10% NaOH solution and with water, and dried ($MgSO_4$). Evaporation of the solvent yielded 5.2 g of the epoxide **B** (95% pure according to GC), which was then treated with a solution of 12 g (56 mmol) of $NaIO_4$ (excess) in ca. 100 mL of water/THF (1:1) and the resulting mixture was heated under stirring.[21] The layers were separated and the organic layer was concentrated. Column chromatography (hexane/diethyl ether, 7:1) afforded ca. 1 g of aldehyde **C** (65% pure by GC). − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 9.7 (t, 1 H, aldehyde, *J* = 2.0 Hz), 7.3−6.8 (m, 4 H, arom.), 3.8 (s, 3 H, OCH_3), 3.6 (d, 2 H, benzylic, *J* = 1.7 Hz). − Aldehyde **C** was then added to a Grignard reagent prepared from 0.2 g (8 mmol) of magnesium and 1.0 g (8 mmol) of allyl bromide. The mixture was refluxed, allowed to cool, and washed with water and saturated NH_4Cl solution. The aqueous layer was extracted three times with diethyl ether. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The product mixture was found to contain 64% (GC analysis) of the desired product, which was purified by means of preparative GC. This yielded 0.17 g of **3** (0.9 mmol, 20%) (> 99% pure). − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.2−6.8 (m, 4 H, arom.), 6.0−5.8 (m, 1 H, 2-H), 5.2−5.1 (dd, 2 H, 1-H), 4.0−3.8 (m, 1 H, 4-H), 3.8 (s, 3 H, OCH_3), 2.8 (dd, 2 H, 5-H), 2.3 (m, 2 H, 3-H).

2-(*o*-Methoxyphenyl)ethanol: To a suspension of 4.3 g (113 mmol) $LiAlH_4$ in 150 mL of dry diethyl ether at 0°C was added 15.0 g (90 mmol) of *o*-methoxyphenylacetic acid. The mixture was refluxed for 1 h and then cooled in an ice bath. Water (100 mL) was slowly added, followed by 135 mL of 10% sulfuric acid. The ether layer was separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic fractions were washed with water (twice) and with brine, and dried ($MgSO_4$). Evaporation of the solvent yielded 14.0 g (92 mmol, 99%) of a yellow oil. − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.2−6.8 (m, 4 H, arom.), 3.75 (t, 2 H, 1-H, *J* = 6.5 Hz), 3.74 (s, 3 H, OCH_3), 2.9 (t, 2 H, 2-H, *J* = 5.3 Hz), 2.7 (s, 1 H, OH). − ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 157.4 (arom.), 130.6 (arom.), 127.4 (arom.), 126.8 (arom.), 120.3 (arom.), 110.2 (arom.), 62.3 (C-1), 55.0 (OCH_3), 33.8 (C-2).

1-Bromo-2-(*o*-methoxyphenyl)ethane (D): To 14.0 g (92 mmol) of 2-(*o*-methoxyphenyl)ethanol, cooled in an ice bath, 8.15 g (30 mmol) of phosphorus tribromide was slowly added. After stirring for 2.5 h, saturated aqueous sodium carbonate solution was added. The aqueous phase was extracted three times with diethyl ether. The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo. Column chromatography of the residue (hexane/diethyl ether, 2:1) afforded 5.7 g (42 mmol, 30%) of the bromide **D**. − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.4−6.9 (m, 4 H, arom.), 3.9 (s, 3 H, OCH_3), 3.6 (t, 2 H, 1-H, *J* = 6.2 Hz), 3.2 (t, 2 H, 2-H, *J* = 7.8 Hz).

3-Hydroxy-5-(*o*-methoxyphenyl)pent-1-ene (4): To 0.59 g (25 mmol) of Mg in 10 mL of dry diethyl ether, 2.0 g (15 mmol) of 1-bromo-2-(*o*-methoxyphenyl)ethane (**D**) was added dropwise, and the reaction was initiated with ultrasound. After all the bromide had been added, the mixture was cooled to 0°C and a solution of 2.4 g (43 mmol) of acrolein in diethyl ether was added dropwise. The resulting mixture was refluxed for 1 h. After cooling once more, water and saturated aqueous NH_4Cl solution were added. The layers were allowed to separate, and the aqueous layer was extracted three times with diethyl ether. After drying ($MgSO_4$) and concentrating of the combined organic layers, column chromatography of the residue (ICN alumina N-Super I, light petroleum/diethyl ether, 5:1, followed by neat diethyl ether) yielded 0.20 g (1 mmol, 7%) of the product. It was necessary to use alumina as the column material, since silica appeared to be too acidic; a significant amount of diene was formed using a silica column). − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.2−6.8 (m, 4 H, arom.), 6.0−5.8 (m, 1 H, 2-H), 5.1 (m, 2 H, 1-H), 4.0 (dt, 1 H, 3-H), 3.8 (s, 3 H, OCH_3), 2.7 (t, 2 H, 5-H, *J* = 6.2 Hz), 2.2 (br. s, 1 H, OH), 1.9−1.7 (m, 2 H, 4-H). − ^{13}C NMR (50 MHz, $CDCl_3$, TMS): δ = 156.9 (arom.), 140.8 (C-2), 129.6, 129.3, 126.9, 120.2 (arom.), 113.8 (C-1), 109.9 (arom.), 71.7 (C-3), 54.8 (OCH_3), 36.9 (C-5), 25.6 (C-4).

5-(*o*-Methoxyphenyl)-3-(trimethylsilyloxy)pent-1-ene (5): To 0.53 g (2.8 mmol) of **4** in 10 mL of pyridine was added 0.4 g (3.7 mmol) of trimethylsilyl chloride. After stirring for 1 h, the excess pyridine was evaporated, and the residue was diluted with diethyl ether. The pyridinium salt was filtered off, and the filtrate was concentrated to dryness. The residual oil was purified by column chromatography (hexane/diethyl ether, 4:1). This gave the desired compound in 46% yield (1.3 mmol, 0.34 g). − ^1H NMR (200 MHz, $CDCl_3$, TMS): δ = 7.2−6.8 (m, 4 H, arom.), 6.0−5.7 (m, 1 H, 2-H), 5.2−4.9 (m, 2 H, 1-H), 4.1 (dt, 1 H, 3-H), 3.8 (s, 3 H, OCH_3), 2.7 (t, 2 H, 5-H), 1.9−1.7 (m, 2 H, 4-H), 0.1 (s, 9 H, $SiMe_3$).

3-Hydroxy-5-(*o*-methoxyphenyl)-3-methylpent-1-ene (6): To 0.51 g (21 mmol) of Mg in 10 mL of dry diethyl ether was added a solution of 2.7 g (20 mmol) of 1-bromo-2-(*o*-methoxyphenyl)ethane (**D**) in 10 mL ether, and the reaction was initiated with ultrasound. The resulting mixture was refluxed for 30 min, and then cooled in an ice bath. Methyl vinyl ketone (0.9 g, 13 mmol) was added (***CAUTION:*** Violent reaction!), the reaction mixture was refluxed for 1 h, and was then allowed to cool to room temperature. Water and saturated aqueous NH_4Cl solution were added, and the mixture was stirred until a clear two-layer system was obtained. The aqueous layer was extracted with diethyl ether, the combined organic fractions were

Table 2. Irradiation conditions of bichromophores **1**−**6**

Compound	**1**	**2**	**3**	**4**	**5**	**6**
Amount [g]	1.0	0.41	0.17	0.20	0.33	0.47
Irrad. time [h]	10.5	9	10.5	3	5	9
Conversion (%)	65	80	67	72	62	60

Table 3. ^{1}H-NMR data of photoadducts obtained upon irradiation of **1**−**6**

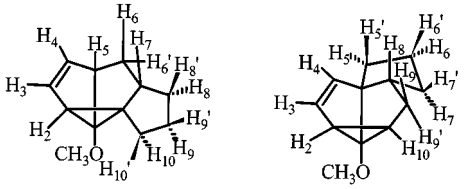


Table 3a. Linear adducts

	OCH_3	2-H	3-H	4-H	5-H	6-H	6′-H	7-H	8-H	8′-H	9-H	9′-H	10-H	10′-H
1a	3.37	2.4	5.7	5.5	3.25	1.8−1.6		1.85	1.4	2.13	2.05−1.9		4.1	−
1c[a]	3.3		6.15	6.04									−	4.5
2a	3.37	2.3	5.7	5.5	3.23	1.71	1.8	1.8	1.3	2.05	2.2	2.0	4.1	−
2c[a]	3.23	2.33	5.83	5.64	3.1								−	4.5
3a	3.41	2.12	5.67	5.52	3.28	2.06		2.06	2.1−1.2		4.37	−	2.1−1.2	
3c[b]	3.37		5.65	5.53	3.22						−	4.44	2.1−1.2	
4a	3.37	2.15	5.72	5.50	3.25	1.74		1.9	4.0	−	2.0−1.8		2.1−2.0	
4c	3.38	2.16	5.73	5.65	3.22	1.68			−	4.25				
5a	3.36	2.11	5.70	5.47	3.24	1.66		1.84	3.94	−	2.0−1.5		2.0−1.5	
5c	3.39	2.25	5.61	5.49	3.24	2.19	1.45	2.0	−	4.2	1.9−1.7		1.63−1.55	
6a	3.36	2.14	5.70	5.46	3.23	1.75	1.70	1.8	−	−	2.10−1.95		1.80−1.65	
6c	3.39	2.05	5.63	5.51	3.33	2.15	1.85	1.6	−	−	1.9		1.65	

[a] These compound were found in the same fraction as **1a** and **2a**; full assignment was therefore not possible. − [b] This compound was found in the same fraction as **3b**; full assignment was therefore not possible.

Table 3b. Angular adducts

	OCH_3	2-H	3-H	4-H	5-H	5′-H	6-H	6′-H	7-H	7′-H	8-H	9-H	9′-H	10-H
1b	3.33	2.2	5.73	5.63	4.50	−	1.61	2.37	1.74	2.12	1.49	2.37−2.28		2.1
2b	3.33	2.33	5.71	5.52	4.42	−	3 × m: 2.4−2.1, 1.8−1.4, 1.2							
3b	3.38	2.25	5.56	5.45	2.12	1.75	4.29	−	2.05	1.60	2.15	2.15−2.0		1.64
3d	3.38	2.1	5.90	5.63	1.40	2.02	−	4.42	1.75	2.0	1.95	1.65	2.60	2.5
4b[c]	3.32	2.15	5.57	5.50					4.15	−				2.0
5b[d]	3.31	2.08	5.5	5.5					−	4.09				
6b	3.35	2.2	5.55	5.55	1.50	1.50	1.97	2.05	−	−	1.90	1.75	2.22	1.92
6d[e]	3.4	2.05	5.73	5.63					−	−				

[c] This compound was found in the same fraction as **4a**; full assignment was therefore not possible. − [d] This compound was found in the same fraction as **5c**; full assignment was therefore not possible. − [e] This compound was formed in very low yield and could not be isolated in a pure state; full assignment was not possible.

dried ($MgSO_4$), and the solvent was evaporated. Column chromatography (light petroleum/diethyl ether, 5:1) yielded 0.48 g (2.5 mmol, 20%) of **6**. − ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.2−6.8 (m, 4 H, arom.), 5.8 (dd, 1 H, 2-H), 5.1 (dt, 2 H, 1-H), 3.8 (s, 3 H, OCH_3), 2.7−2.6 (m, 2 H, 5-H), 2.0 (s, 1 H, OH), 1.9−1.7 (m, 2 H, 4-H), 1.3 (s, 3 H, CH_3). − ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 157.2 (arom.), 144.9 (C-2), 130.7, 129.7, 126.9, 120.4 (arom.), 111.6 (C-1), 110.2 (arom.), 73.2 (C-3), 55.1 (OCH_3), 42.2 (C-5), 27.7 (C-4), 24.8 (CH_3).

Irradiations: The irradiations (λ_{exc} = 254 nm) of compounds **1**−**6** were performed using 1% (w/v) solutions in cyclohexane (UV-pure) (Table 2). The progress of the transformations was followed by GC. Products were separated by means of preparative GC, except in the case of **1**, where preparative HPLC was used. Prior to the separations, the mixtures were passed through a short silica column to remove any polymeric material formed during the irradiation.

MS Data: 4b: *m/z*: calcd. 192.1150; found 192.1134. − **5a**: *m/z*: calcd. 264.1545; found 264.1546. − **5b**: *m/z*: calcd. 264.1545; found 264.1537. − **5c**: *m/z*: calcd. 264.1545; found 264.1505.

NMR Data: See Table 3.

[1] J. Cornelisse, *Chem. Rev.* **1993**, *93*, 615−669.

[2] [2a] P. A. Wender, L. Siggel, J. M. Nuss, *Organic Photochemistry*, vol 10 (Ed.: A. Padwa), Marcel Dekker, New York, **1989**, p. 357−473. − [2b] P. A. Wender, S. K. Singh, *Tetrahedron Lett.* **1990**, *31*, 2517−2520. − [2c] P. A. Wender, M. A. de Long, *Tetrahedron Lett.* **1990**, *31*, 5429−5432. − [2d] D. De Keukeleire, S.-L. He, *J. Chem. Soc., Chem. Commun.* **1992**, 419−420. − [2e] C. Baralotto, M. Chanon, M. Julliard, *J. Org. Chem.* **1996**, *61*, 3576−3577.

[3] [3a] J. Mani, J.-H. Cho, R. R. Astik, E. Stamm, P. Bigler, V. Meyer, R. Keese, *Helv. Chim. Acta* **1984**, *67*, 1930−1941. − [3b] J. Mani, R. Keese, *Tetrahedron* **1985**, *41*, 5697−5701. − [3c] J. Mani, S. Schüttel, C. Zhang, P. Bigler, C. Müller, R. Keese, *Helv. Chim. Acta* **1989**, *72*, 487−495. − [3d] C. Zhang, D. Bourgin, R. Keese, *Tetrahedron* **1991**, *47*, 3059−3074. − [3e] P. A. Wender, T. M. Dore, M. A. de Long, *Tetrahedron Lett.* **1996**, *37*, 7687−7690.

[4] [4a] G. C. R. Ellis-Davies, A. Gilbert, P. Heath, J. C. Lane, J. V. Warrington, D. L. Westover, *J. Chem. Soc., Perkin Trans. 2* **1984**, 1833−1841. − [4b] H. A. Neijenesch, E. J. Ridderikhoff, C. A. Ramsteijn, J. Cornelisse, *J. Photochem. Photobiol. A: Chem.* **1989**, *48*, 317−336. − [4c] H. A. Neijenesch, R. J. P. J. de Ruiter, E. J. Ridderikhoff, J. O. van den Ende, L. J. Laarhoven, L. J. W. van Putten, J. Cornelisse, *J. Photochem. Photobiol. A: Chem.* **1991**, *60*, 325−343.

[5] K. Cosstick, A. Gilbert, *J. Chem. Soc., Perkin Trans. 1* **1989**, 1541−1542.
[6] [6a] D. C. Blakemore, A. Gilbert, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2265−2270. − [6b] D. C. Blakemore, A. Gilbert, *Tetrahedron Lett*. **1994**, *35*, 5267−5270.
[7] P. A. Wender, R. J. Ternansky, *Tetrahedron Lett*. **1985**, *26*, 2625−2628.
[8] *cf*. P. A. Wender, R. Ternansky, M. de Long, S. Singh, A. Olivero, K. Rice, *Pure Appl. Chem*. **1990**, *62*, 1597−1602.
[9] For an example of such an effect in an intramolecular [2+2] photocycloaddition, see: M. T. Cimmins, A. L. Choy, *J. Am. Chem. Soc.* **1997**, *119*, 10237−10238.
[10] [10a] C. Zhang, X.-C. Guo, *Synth. Commun.* **1994**, *24*, 3157−3165. − [10b] C. Zhang, X.-C. Guo, X.-M. Shen, Y.-F. Xu, *Synth. Commun*. **1995**, *25*, 775−781.
[11] E. L. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley & Sons, New York, **1994**, p. 695−697.
[12] R. Gallo, *Prog. Phys. Org. Chem*. **1983**, *14*, 115−163.
[13] H. M. Barentsen, A. B. Sieval, J. Cornelisse, *Tetrahedron* **1995**, *51*, 7495−7520.
[14] E. M. Osselton, C. P. Eyken, A. W. H. Jans, J. Cornelisse, *Tetrahedron Lett*. **1985**, *26*, 1577−1580.
[15] [15a] J. Cornelisse, A. Gilbert, P. W. Rodwell, *Tetrahedron Lett*. **1986**, *27*, 5003−5006. − [15b] A. Gilbert, P. Heath, P. W. Rodwell, *J. Chem. Soc., Perkin Trans. 1* **1989**, 1867−1873.
[16] P. A. Wender, S. K. Singh, *Tetrahedron Lett*. **1985**, *26*, 5987−5990.
[17] P. A. Wender, K. Fisher, *Tetrahedron Lett*. **1986**, *27*, 1857−1860; in this paper, the lin/ang ratio is reported to be 1:2.3 in the text, but 2:1 in the experimental. In ref.[2a], a ratio of 2:1 is reported, which we take to be the actual value.
[18] T. Sugimura, N. Nishiyama, A. Tai, T. Hakushi, *Tetrahedron: Asymmetry* **1994**, *5*, 1163−1166.
[19] W. Gerrard, K. D. Kilburn, *J. Chem. Soc.* **1956**, 1536−1539.
[20] G. N. Vyas, N. M. Shah, *Org. Synth. Coll. Vol.* **1963**, *4*, 836−838.
[21] M. Goldbach, E. Jäkel, M. P. Schneider, *J. Chem. Soc., Chem. Commun.* **1987**, 1434−1435.

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