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Stereocontrolled intramolecular *meta*-arene–alkene photocycloaddition reactions using chiral tethers: efficiency of the tether derived from 2,4-pentanediol

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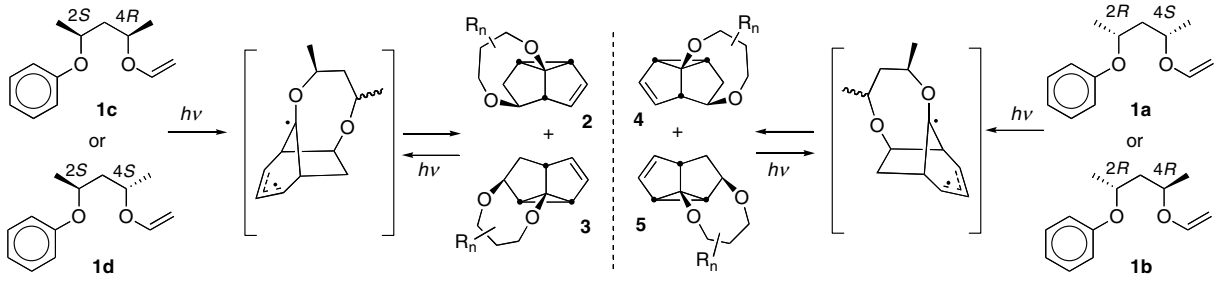
Abstract—Photochemical reactions of substrates consisting of phenyl and vinyl groups, which are tethered with a chiral diol, resulted in intramolecular *meta*-arene–alkene cycloaddition; the reaction efficiency as well as the stereoselectivity was studied. 1,3-Butanediol, 2-substituted 1,3-propanediols, 2-methyl-2,4-penetanediol, and 2,6-dimethyl-3,5-heptanediol were employed as tethers, and the results are compared with those obtained with 2,4-pentanediol (PD) tether, which are known to show high stereoselectivity and moderate efficiency. All the reactions with the lower analogues were less efficient than with PD, although one of the butanediol-tethered reactions afforded a single stereoisomer as PD did. The dimethylheptanediol tether showed similar efficiency but lower stereoselectivity than PD. The results suggest that the PD tether has an optimized structure having a proper flexibility.

1. Introduction

The chiral tethered reaction is applicable to a wide range of asymmetric syntheses when the tether is made of optically active 2,4-pentanediol (PD).[1] The *meta*-arene–alkene photocycloaddition[2] is one of such examples that display high stereoselectivities unattainable by intermolecular reactions. By the photoirradiation of **1a** having (2*R*,4*S*)-PD or **1b** having (2*R*,4*R*)-PD, the vinyl group adds to the 2,6-position of the phenyl group under sufficient differentiation of the stereofaces of the vinyl group to give a pair of the regioisomers, **4** and **5**, but their stereoisomers, **2** and **3**, were not produced (Scheme 1).[3] The stereochemistries of the photoproducts indicate that the PD tethers in **1a** and **1b** exclusively promote the addition at the *si*-face of the vinyl group. The regioisomeric ratio **4**/**5** is different between **1a** and **1b**. The ratio originates not only from the reactivities of the generated biradical intermediates, but largely from the difference in extinction coefficients of the products, which affects their interconversion, and so it depends on the reaction conditions.



Scheme 1. The PD-tethered *meta*-arene–alkene photocycloadditions.

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The essential difference between the two substrates is in the efficiency of their intermolecular photocycloaddition. Under the same reaction conditions, the transformation of **1a** to **4a** and **5a** is 2.6 times faster than that of **1b** to **4b** and **5b**. Considering the equal absorption of **1a** and **1b**, the quantum yield of the addition reaction (ϕ_{add}) is larger with **1a** than that with **1b** by the same ratio of 2.6. The efficiency in this reaction system is a crucial factor to obtain the product in a good yield because of the potential formation of polymeric products under photoirradiation. The isolated product yield was 70% in the reaction of **1a**, while 55% in that of **1b** under the optimized conditions. Although those yields are very high for *meta*-arene–alkene photocycloadditions, the performance of the PD-tether to promote the intramolecular addition is still not always high. For example, when the reaction of **1a** was applied to either isomer of the tolyl analogues, the yield of the photoadducts is only in a range of 29–33%, which further decreases to 19% when the substrate has a 3,5-xylyl group.[3b]

The PD-tether is flexible during the reaction, and the flexibility regulated by the two methyl groups. Herein, we consider the structure of the tether with regard to its ability to cause the intramolecular *meta*-photocycloaddition, and found that the PD tether has an optimized structure in terms of both selectivity and yield.[4]

2. Results and discussion

Substrates **1c**–**k** for the photoreaction were prepared according to the reported procedure with some modifications (Fig. 1). The PD-tethered substrates **1c** and **1d** were prepared as standards for the present study, and are the enantiomers of **1a** and **1b**. The photoreaction was carried out in pentane (2 mM) with a low-pressure mercury lamp and a Vycor filter at room temperature. The reaction was continued until the substrate became undetectable by TLC analysis. All possible internal adducts were isolated by silica gel column chromatography, and their structures determined by ^{1}H NMR and MS spectra. The isolated yields of *meta*-cycloadducts **2**–**5** are given in Table 1 together with the previously reported results with **1a** and **1b**. Stereochemistries of two cycloadducts **4e** and **2f** were determined by their conversion to optically active **8** as shown in Scheme 2,[3] and the other products were assigned by comparison of the CD spectra and the photoconversion to the corresponding regioisomers.

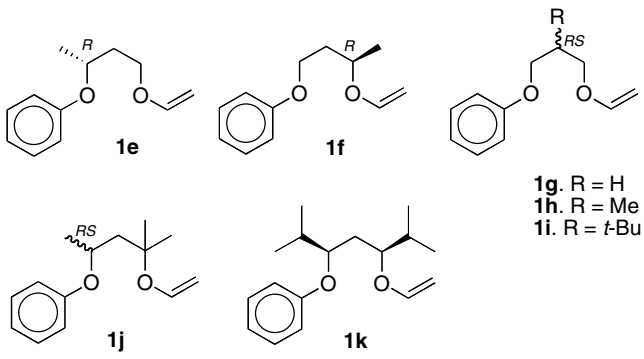


Figure 1.

Under the present photochemical conditions, the total yields with **1c** and **1d** were a little lower than the reported yields with **1a** and **1b** under the optimized conditions (Table 1, entries 1–4). The stereochemical outcomes observed suggest that the stereodirection by the 2-methyl group (α-methyl) on the tether is stronger than that by the 4-methyl group (γ-methyl). This postulation can be proved by the reaction with substrates **1e** and **1f** having a singly methylated tether. The reaction of **1e** having (*R*)-α-methyl proceeded through the addition exclusively at *si*-face of the vinyl group to give a regioisomeric mixture of **4e** and **5e** (entry 5). The strict stereocontrol attained by the single methyl group indicates strong stereocontrollability of the chiral tethered reactions.[5] In the case of **1f** having (*R*)-γ-methyl, the addition at *re*-face was preferred to the *si*-face addition, but the stereocontrol was not rigorous to give pairs of regioisomers in a ratio of (**2f** + **3f**)/(**4f** + **5f**) = 79/21 (entry 6). The stereodirection as well as its degree observed with **1e** and **1f** is well consistent with the results obtained with **1c** and **1d**. The results indicate that the reaction with a PD-tether is efficient when the two methyl groups match in their stereodirection.

The consumption rates of the reactants **1e** and **1f** were even slower than that with **1d** carrying the mismatched PD-tether, but were obviously faster than that with **1g** having no methyl group on the tether (entry 7). Such phenomena, the methyl substitution on a linear molecule accelerates its cyclization, is known as the Thorpe–Ingold effect.[6,7] However, when substrate **1h**, a regioisomer of **1e** and **1f**, was photoirradiated under the same reaction conditions, consumption of the reactant was very slow and no internal cycloadduct was obtained (entry 8). Its bulkier analogue **1i** having *t*-butyl group instead of the methyl group showed a similar consumption rate to those with **1e** and **1f**. The total yield of the adducts of **1i** was moderately high, 32%, but the stereoselectivity was poorer than that with **1f** (entry 9).

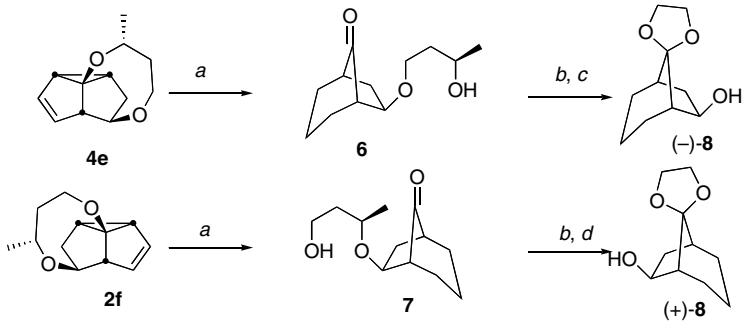
Expecting a result contrasting to that with the lower and simpler analogues **1e**–**h**, we next studied substrates having higher analogues of the PD tether, **1j** and **1k**. The tether of **1j** has an additional methyl group on the tether of **1c** (or **1d**) at the α-position. The substrate **1j** is also considered to be a higher analogue of **1e** with two *gem*-methyl groups at the γ-position. With three methyl groups on the tether, the photoreaction of **1j** was, however, slow and sluggish. The produced cycloadducts were too little to be isolated (<5% for sum of the adducts, entry 10).

With the above results in mind, two bulkier isopropyl groups are introduced in place of the two methyl groups in **1c** to give the higher analogue **1k**. Such a modification is commonly employed in asymmetric synthesis to enhance the stereoselectivity, and the efficiency may also be improved if the effect of the methyl groups in **1c** can simply be amplified.[8] Substrate **1k** was prepared

Table 1. Isolated yield and stereoselectivity in the reaction of the tethered substrates

Entry	Subst.	Concn/mM	Reaction time/h	Isolated yield/%					Stereoselectivity (2 + 3):(4 + 5)
				2	3	4	5	Total	
1	**1a**	1.1	4[a]	—	—	<1	70	70	0:100
2	**1b**	0.8	9[a]	—	—	40	15	55	0:100
3	**1c**	2.0	2	24	38	—	—	60	100:0
4	**1d**	2.0	6	14	30	—	—	45	100:0
5	**1e**	2.0	10	—	—	16	27	43	0:100
6	**1f**	2.0	9	34	<1	9	<1	43	79:21
7	**1g**	2.0	44	(–)[b]	—	(–)[b]	—	19[b]	50:50
8	**1h**	2.0	30	—	—	—	—	0	—
9	**1i**	2.0	10	(–)[c]	—	(–)[c]	—	32[c]	72:28
10	**1j**	2.0	10	—	—	—	—	<5	—
11	**1k**	2.0	2	11	40	(6)[d]	—	57	89:11

[a] The reaction was carried out until the photostationary state of the equilibrium of the regioisomers.[3]
[b] Racemic product (a mixture of **2** and **4**) was obtained.
[c] The cycloadducts **2i** and **4i** were not separable. The ratio of the isomers as well as their structure was determined by ^{1}H NMR.
[d] Not isolated. The yield was calculated from the amount of the crude product and its ^{1}H NMR spectra.



Scheme 2. Reagents and conditions: (a) 4 M HCl/acetone (or THF), and then H_2/Pd–C; (b) ethylene glycol/TsOH; (c) PCC, and then K_2CO_3/MeOH; (d) PDC, MeMgBr, PCC, and then K_2CO_3/MeOH.

from optically active (3*S*,5*S*)-2,6-dimethyl-3,5-heptanediol in a stereochemically pure form by a similar process to that for **1c**. The photoreaction of **1k** proceeded smoothly to give a mixture of **2k** and **3k** in 51% yield (entry 11). However, the third isomeric product was detected by ^{1}H NMR and GC–MS analyses of the reaction mixture. This isomer could not be isolated, but the structure was suggested to be **4k** from the ^{1}H NMR spectra. The estimated amount of **4k** was ca. 6%.

The efficiency of the photoreaction was compared between **1c** and **1k** by monitoring the reaction by GLC. A pentane solution of the substrate (3.0 mM) containing a standard compound (decane or tetradecane) was irradiated, and the consumption of the substrates and the formation of the cycloadducts during the reaction determined. As shown in Figure 2, the consumption rates of **1c** and **1k** were confirmed to be similar to each other. Considering the almost identical extinction coefficients of **1c** and **1k** at the irradiation wavelength, the quantum

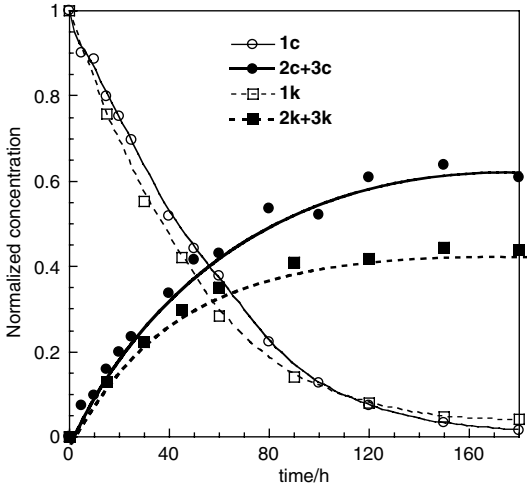


Figure 2. Normalized concentration of reactants, **1c** (open circles) and **1k** (open squares), and sum of the cycloadducts, **2c** and **3c** (filled circles) and **2k** and **3k** (filled squares) during the photoreactions.

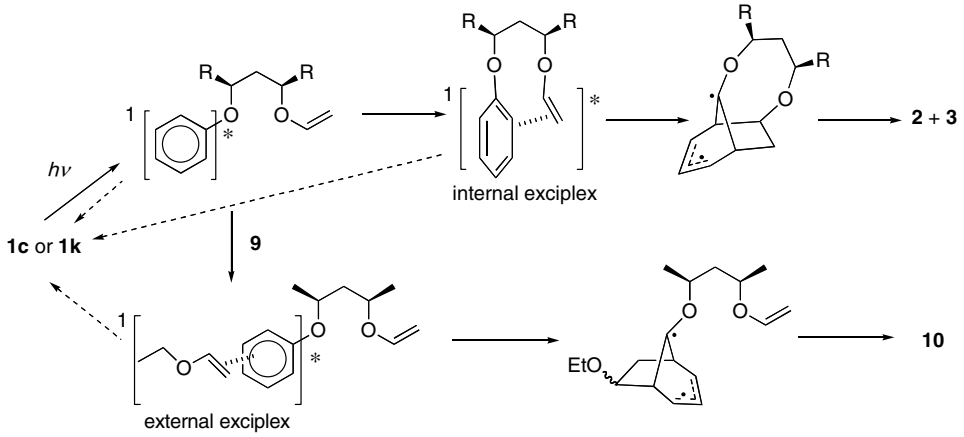


Figure 3.

yields for intramolecular addition (ϕ_{add}) of **1k** is only 1.1-fold larger than that of **1c**. The observed similarity, however, does not mean a similarity in nature of the two tethers for the intramolecular reaction as follows.

When a pentane solution of **1c** (2 mM) was irradiated in the presence of ethyl vinyl ether **9** (1 or 2 M), the products obtained were the internal adducts, **2c** and **3c**, and an isomeric mixture of external adduct **10**; the ethyl vinyl ether adducts mainly at the 2,6-position of **1c**.[9] The ratio of **2c** + **3c**:**10** = 50:50 at [**9**] = 2 M and 74:26 at [**9**] = 1 M. The relative rate of the internal against the external addition given as [**2c** + **3c**][**9**]/[**10**] was 2 M, which corresponds to the effective molarity in ground state reactions. In contrast, the photoreaction of **1k** was not affected by the presence of **9** (up to 10 M), and **1k** was consumed at a similar rate without producing any external adducts (<3%). The effective molarity for the intramolecular reaction of **1k** was calculated to be $>10^2$ M. The large difference between **1c** and **1k** can partly originate from a slower external reaction of **1k** than **1c** due to the steric interference of the isopropyl groups.

The reactions of **1c** and **1k** to give the *meta*-cycloadducts start with the excitation at the phenyl moiety. The excited phenyl produced is quenched by a vinyl moiety to form an exciplex, and then the exciplex converted to the adduct of a ground-state biradical intermediate, which then transformed into the final products (Fig. 3).[2a] The chiral tether having the bulky isopropyl groups in the appropriate stereochemistry must have better efficiency to access the vinyl moiety to the excited phenyl, and thus, the internal quenching of **1k** is faster than **1c** to result in the higher effective molarity. The quantum yield of the overall reaction (ϕ_{add}) is governed by the quantum yields of the exciplex formation (ϕ_1) and its reaction (ϕ_2) following the equation, $\phi_{add} = \phi_1 \times \phi_2$. To estimate the ϕ_1 values, the relative intensity of emission from the S_1 state of the phenyl group was determined. Compared to anisole ($\phi_{fl} = 0.24$), synthetic precursors of **1c** and **1k** (hydroxy analogues at the vinyloxy group) showed a similar emission efficiency (1.1 ± 0.2 times of anisole), while the emission spectra of **1c** and **1k** were different in the intensity; **1k** was much weaker (0.3 ± 0.1-fold) but **1c** was only slightly weaker (0.8 ± 0.2-fold) than anisole. The strong emission from the S_1 state of **1c** indicates a small ϕ_1 value, and the weak emission with **1k** indicates a larger ϕ_1. This difference in ϕ_1, ϕ_1(**1c**) < ϕ_1(**1k**), leads to an inverse relationship of ϕ_2, ϕ_2(**1c**) > ϕ_2(**1k**), since ϕ_{add}(**1c**) ≈ ϕ_{add}(**1k**).

This explanation seems to be reasonable because the addition to form the two σ-bonds necessitates more accurate geometrical arrangement of the phenyl and vinyl groups than the exciplex formation, and the isopropyl groups can cause larger strain energy when the two reactants are placed at proper positions for the formation of the two σ-bonds. The loss of the stereoselectivity may also originate from this strain.

3. Conclusions

Through the study of the asymmetric *meta*-arene–alkene photocycloaddition with various chiral tethers, we found that the substituent on the tether must be properly designed in its number, position, and size to achieve the efficient and stereocontrolled *meta*-arene–alkene-photocycloaddition. A suitable tether part has a function to force the internal reaction sites closer, but too much restriction of the tether flexibility may result in lose of the efficiency of the intramolecular reaction. So far studied for the *meta*-arene–alkene-photocycloaddition, the tether made of the optically active 2,4-pentanediol has the most appropriate structure. The conformation of the PD tether is rightly regulated in keeping the flexibility.

4. Experimental

4.1. General

All products were characterized by NMR spectrometry using a JEOL EXcalibur-400 spectrometer at 400 MHz for proton and 100 MHz for carbon, and by IR with a

JASCO IR-88 or IR-810 spectrophotometer. A JEOL ECA-600 recorded at 600 and 150 MHz was employed for some compounds as indicated in the spectral data. UV spectra were obtained by an Agilent 8453, and fluorescence was observed by a JASCO FP-770. Optical rotations were measured with a Perkin-Elmer 243B polarimeter. CD spectra were obtained using a JASCO J-720. High resolution MS was obtained by a JEOL JMS-AX505HF (EI) or a JEOL JMS-T100LC (APCI). Analytical GLC was performed on a Shimadzu GC17A. MPLC was carried out using FMI pump (10 mL min^{-1}) and a Lover column (Merck Si-60, type B). Pentane for the photoreactions was treated with concentrated H_2SO_4 before distillation. All other solvents were purified by distillation with proper drying agents.

4.2. Preparation of the mono-phenyl ethers as precursors of 1e–k

4.2.1. (*R*)-3-Phenoxy-1-butanol and (*R*)-4-phenoxy-2-butanol. To a solution of cyclohexanone acetal of (*R*)-1,3-butanediol (5.20 g, >99% ee) in THF (100 mL) was added pyridinium perbromide (26.8 g, 2.7 equiv) at −78 °C. The mixture was warmed up to rt for 2 h, and pyridine (1.5 mL), sodium bicarbonate (10% aqueous solution, 15 mL), and then sodium sulfite (ca. 1 g) added to the mixture. The organic layer was separated, and the resulting aqueous solution extracted with benzene (50 mL × 3). The combined organic layer was washed with brine (150 mL), dried over $MgSO_4$, concentrated, and passed through a short silica gel column to give a pale yellow oil (6.02 g, 60%). This oil was added to a solution of sodium methoxide (6.16 g, 6.2 equiv) in DMSO (100 mL), and the mixture stirred for 3 days at rt. After the addition of water (50 mL), the mixture was extracted with ether (100 mL × 4). The combined extract was washed with brine (150 mL), dried over $MgSO_4$, and purified by column chromatography on silica gel (elution with 3% ethyl acetate in hexane) to give a mixture of the phenyl ethers as a colorless oil (1.40 g, 45.9%). This mixture was separated by MPLC (elution with 25% ethyl acetate in hexane) to give (*R*)-3-phenoxy-1-butanol {782 mg, 25.6%, $[\alpha]_D^{25} = -61.9$ (*c* 1.0, methanol)} and (*R*)-4-phenoxy-2-butanol {489 mg, 16.0%, $[\alpha]_D^{25} = -79.2$ (*c* 1.1, methanol)}. The spectral data are identical with those reported for the product prepared by another method.[5b]

4.2.2. 3-Phenoxy-2-methyl-1-propanol. To a solution of 2-methyl-1,3-propanediol (6.31 g), phenol (6.36 g, 1.1 equiv), triphenylphosphine (19.2 g, 1.1 equiv) in THF (400 mL) was added a solution of diisopropyl azodicarboxylate (14.5 mL, 1.1 equiv) in THF (400 mL) at rt for 70 min. After 12 h, the mixture was concentrated and purified by column chromatography on silica gel (elution with 25% ethyl acetate in hexane) to give 7.89 g of a colorless oil (67% yield). IR (neat, cm^{-1}) 3360, 2960, 2930, 2880, 1600, 1500, 1390, 1300, 1250, 1170, 1040, 750, 690; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28–7.26 (m, 2H), 6.95–6.92 (m, 1H), 6.89 (d, J = 8.2 Hz, 2H), 3.96–3.90 (m, 2H), 3.69 (br s, 2H), 2.19 (m, 1H), 1.97 (br s, 1H), 1.02 (d, J = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.78, 129.44, 120.83, 114.46, 71.11, 66.14, 35.62, 13.59. HRMS (EI) *m*/*z* (M^+) calcd for $C_{10}H_{14}O_2$ 166.0993, found 166.0987.

4.2.3. 3,3-Dimethyl-2-phenoxymethyl-1-butanol. 2-Hydroxymethyl-3,3-dimethylbutyl acetate was obtained by the mono-acetylation of 2-hydroxymethyl-3,3-dimethyl-1-butanol[10] in 38.5% yield. To a solution of the acetate ester (1.02 g), phenol (0.58 g, 1.0 equiv), and triphenylphosphine (1.68 g, 1.1 equiv) in THF (45 mL) was added diisopropyl azodicarboxylate (1.3 mL, 1.1 equiv) at rt, and the reaction monitored by TLC analysis. After 15 h, the mixture was concentrated and purified by column chromatography on silica gel (elution with 6% ethyl acetate in hexane) to give 1.19 g of 3,3-dimethyl-2-(phenoxymethyl)butyl acetate as a colorless oil (81.6% yield). A solution of the acetate obtained (0.993 g) and K_2CO_3 (2.3 mg) in methanol (40 mL) and water (13 mL) was stirred for 1.5 h, and extracted with ether (×3). The combined organic layer was washed with water (×2), and then dried over Na_2SO_4. The filtrate was concentrated to give 0.762 g of 3,3-dimethyl-2-phenoxymethyl-1-butanol (81.5% yield). IR (neat, cm^{-1}) 3392, 2960, 1600, 1576, 1498, 1496, 1471, 1456, 1244, 1029, 753; ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 2H), 6.97–6.91 (m, 3H), 4.19 (dd, J = 9.3, 3.9 Hz, 1H), 4.03 (dd, J = 9.3, 7.8 Hz, 1H), 3.79 (br s, 1H), 3.75 (m, 1H), 2.53 (s, 1H, OH), 1.75 (tt, J = 7.8, 3.9 Hz, 1H), 0.96 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 158.5, 129.3, 129.2, 120.8, 114.4, 68.0, 62.3, 49.82, 49.80, 31.8, 28.41, 28.39, 28.35; HRMS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{20}O_2$ 208.1463, found 208.1440.

4.2.4. 2-Methyl-4-phenoxy-2-pentanol. To a solution of diphenyliodonium chloride (4.14 g) and 2-methyl-2,4-pentanediol (7.54 g) in THF was added Na (0.31 g) under argon, and the mixture heated at 60 °C. After 18 h, the mixture was cooled to rt, poured into water, and extracted with dichloromethane (×3). The combined organic layer was washed with water (×2) and dried over Na_2SO_4. The solvent was removed, and the residue purified by column chromatography on silica gel (elution with 30% ethyl acetate in hexane) to give 2-methyl-4-phenoxy-2-pentanol (1.08 g, 41.2% yield) as a colorless oil. IR (neat, cm^{-1}) 3410, 2970, 1600, 1500, 1380, 1240, 1150, 1050, 910, 880, 750; ^{1}H NMR ($CDCl_3$) δ 7.29–7.25 (m, 2H), 6.97–6.91 (m, 3H), 4.69 (m, 1H), 2.97 (s, 1H), 2.00 (dd, J = 14.9, 10.0 Hz, 1H), 1.66 (dd, J = 14.9, 2.4 Hz, 1H), 1.25 (s, 3H), 1.23 (s, 3H), 1.21 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 156.7, 129.5, 121.2, 116.1, 71.9, 70.3, 49.1, 49.0, 30.5, 29.0, 20.4; HRMS (EI) *m*/*z* (M^+) calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1308.

4.2.5. (3*S*,5*R*)-2,6-Dimethyl-5-phenoxy-3-heptanol. To a solution of (3*S*,5*S*)-2,6-dimethyl-3,5-heptanediol (0.60 g), phenol (0.39 g, 1.0 equiv), and triphenylphosphine (3.52 g, 1.1 equiv) in THF (16 mL), a solution of diisopropyl azodicarboxylate (0.9 mL, 1.1 equiv) in THF (15 mL) was added over 1.5 h at rt. The mixture was stirred overnight. The concentrated mixture was purified by column chromatography on silica gel (elution with 6% ethyl acetate in hexane) to give 0.55 g of (3*S*,5*R*)-2,6-dimethyl-5-phenoxy-3-heptanol as a

colorless oil (61.5% yield). $[\alpha]_D^{20} = -24$ (*c* 1.2, methanol); IR (neat, cm^{-1}) 3445, 2961, 1597, 1493, 1469, 1387, 1290, 1242, 1172, 1028, 876; ^1H NMR ($CDCl_3$) δ 7.27–7.24 (m, 5H), 6.95–6.92 (m, 3H), 4.36 (m, 1H), 3.58 (td, $J = 8.8$, 4.9 Hz, 1H), 2.61 (d, $J = 2.4$ Hz, 1H), 2.07 (m, 1H), 1.74–1.66 (m, 4H), 0.93–0.90 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 126.9 (×2), 121.2, 116.5 (×2), 82.7, 75.9, 33.9, 32.9, 29.9, 18.5, 17.9, 17.2, 16.8. HRMS (EI) *m/z* (M^+) calcd for $C_{15}H_{24}O_2$ 236.1176, found 231.1155.

4.3. Preparation of the substrates 1c–k

General procedure for the formation of the vinyl ethers, **1c**–**k**, from the corresponding mono-phenyl ethers is as follows: A solution of the phenyl ether (0.10–0.88 g) with 0.3 equiv of mercuric acetate in ethyl vinyl ether (10–50 mL) was refluxed for 5–7 days. The ethanol generated was removed by azeotropic distillation with pentane twice during the reaction. The concentrated mixture was purified by column chromatography on deactivated alumina with 10% water to give the vinyl ether. For the details of the preparation of **1c** and **1d**, see Ref. 3. Compound **1e**: (colorless oil, 86.6% yield) $[\alpha]_D^{25} = -51.7$ (*c* 0.7, methanol); IR (neat, cm^{-1}) 2950, 2900, 1640, 1620, 1600, 1500, 1240, 1200; ^1H NMR ($CDCl_3$) δ 7.30–7.25 (m, 2H), 6.95–6.89 (m, 3H), 6.46 (dd, $J = 14.3$, 6.8 Hz, 1H), 4.57 (m, 1H), 4.19 (dd, $J = 14.3$, 6.7 Hz, 1H), 3.99 (dd, $J = 6.8$, 2.0 Hz, 1H), 3.89–3.79 (m, 2H), 2.09 (m, 1H), 1.95 (m, 1H), 1.33 (d, $J = 6.1$ Hz, 3H); Anal. Calcd for $C_{12}H_{16}O_2$ C: 74.97, H: 8.39. Found C: 75.41, H: 8.75. Compound **1f**: (colorless oil, 83.8% yield) $[\alpha]_D^{25} = -57.4$ (*c* 1.1, methanol); IR (neat, cm^{-1}) 2950, 2900, 1640, 1600, 1500, 1470, 1240, 1200, 1100; ^1H NMR ($CDCl_3$) δ 7.27 (m, 2H), 6.97–6.89 (m, 3H), 6.32 (dd, $J = 14.0$, 6.6 Hz, 1H), 4.31 (dd, $J = 14.0$, 1.5 Hz, 1H), 4.21–4.01 (m, 3H), 3.99 (dd, $J = 6.6$, 1.5 Hz, 1H), 2.09–1.92 (m, 2H), 1.30 (d, $J = 6.4$ Hz, 3H); Anal. Calcd for $C_{12}H_{16}O_2$ C: 74.97, H: 8.39. Found C: 74.59, H: 8.28. Compound **1g**: (colorless oil, 94.3% yield) IR (neat, cm^{-1}) 2950, 1740, 1600, 1500, 1480, 1320, 1250, 1200, 1060; ^1H NMR ($CDCl_3$) δ 7.29 (m, 2H), 6.97–6.89 (m, 3H), 6.48 (dd, $J = 14.2$, 6.8 Hz, 1H), 4.21 (dd, $J = 14.2$, 2.2 Hz, 1H), 4.08 (t, $J = 6.1$ Hz, 2H), 4.01 (dd, $J = 6.8$, 2.2 Hz, 1H), 3.88 (t, $J = 6.1$ Hz, 2H), 2.14 (tt, $J = 6.1$, 6.1 Hz, 2H); Anal. Calcd for $C_{11}H_{14}O_2$ C: 74.13, H: 7.92. Found C: 73.81, H 7.95. Compound **1h**: (colorless oil, 81.2%) IR (neat, cm^{-1}) 2930, 2880, 1600, 1500, 1250, 1200, 1280, 1040, 1010, 1000, 753; ^1H NMR ($CDCl_3$) δ 7.26 (m, 2H), 6.94–6.88 (m, 3H), 6.46 (dd, $J = 14.2$, 6.8 Hz, 1H), 4.18 (dd, $J = 14.2$, 6.8 Hz, 1H), 3.94 (dd, $J = 9.0$, 5.6 Hz, 1H), 3.86 (dd, $J = 9.0$, 5.6 Hz, 1H), 3.75 (dd, $J = 9.8$, 5.9 Hz, 1H), 3.67 (dd, $J = 9.8$, 5.9 Hz, 1H), 2.31 (m, 1H), 1.09 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 159.00, 151.94, 129.37, 120.59, 115.32, 114.48, 86.35, 69.69, 69.47, 33.47; HRMS (EI) *m/z* (M^+) calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1140. Compound **1i**: (colorless oil, 60.5% yield) IR (neat, cm^{-1}) 3040, 2960, 1600, 1500, 1470, 1400, 1340, 1320, 1250, 1170, 1080, 1030, 960; ^1H NMR ($CDCl_3$) δ 7.26 (dd, $J = 8.3$, 7.3 Hz, 2H), 6.91 (dd, $J = 10.7$, 7.3 Hz, 3H), 6.45 (dd, $J = 14.2$, 6.8 Hz, 1H), 4.18 (dd, $J = 14.2$, 2.0 Hz, 1H), 4.09 (dd, $J = 9.8$, 4.4 Hz, 1H), 4.03 (dd, $J = 9.5$, 6.1 Hz, 1H), 3.95 (dd, $J = 6.8$, 2.0 Hz, 1H), 3.90 (dd, $J = 9.8$, 4.4 Hz, 1H), 3.85 (dd, $J = 10.3$, 6.3 Hz, 1H), 1.85 (tt, $J = 6.3$, 4.4 Hz, 1H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 159.0, 152.0, 129.4, 120.5, 114.5, 111.8, 86.3, 65.9, 65.6, 47.4, 44.3, 32.1, 28.6; HRMS (M^+) *m/z* calcd for $C_{15}H_{22}O_2N$ 234.1620, found 234.1577. Compound **1j**: (colorless oil, 50.2% yield) IR (neat, cm^{-1}) 2976, 1652, 1637, 1634, 1243, 753; ^1H NMR ($CDCl_3$) δ 7.24 (m, 2H), 6.91–6.87 (m, 3H), 6.43 (dd, $J = 13.7$, 6.4 Hz, 1H), 4.61 (br s, 1H), 4.40 (d, $J = 13.7$ Hz, 1H), 4.03 (d, $J = 6.4$ Hz, 1H), 2.02 (dd, $J = 14.2$, 7.8 Hz, 1H), 1.83 (dd, $J = 14.2$, 2.9 Hz, 1H), 1.29 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 145.9, 129.4, 120.6, 116.1, 91.4, 77.2, 76.7, 70.6, 48.3, 27.4, 25.9, 21.2; HRMS (M^+) *m/z* calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1465. Compound **1k**: (colorless oil, 79.8% yield) IR (neat, cm^{-1}) 2960, 1630, 1600, 1490, 1470, 1390, 1370, 1290, 1240, 1110, 1030, 820; ^1H NMR (600 MHz, $CDCl_3$) δ 7.24 (m, 2H), 6.91–6.87 (m, 3H), 6.30 (dd, $J = 7.3$, 6.8 Hz, 1H), 4.31 (dd, $J = 14.2$, 1.5 Hz, 1H), 4.19 (td, $J = 6.1$, 4.1 Hz, 1H), 3.95 (dd, $J = 6.8$, 1.5 Hz, 1H), 3.67 (dt, $J = 6.8$, 1.5 Hz, 1H), 2.01 (tt, $J = 6.8$, 2.9 Hz, 1H), 1.93 (dt, $J = 14.6$, 6.8 Hz, 1H), 1.84 (dt, $J = 14.6$, 6.8 Hz, 1H), 1.77 (dt, $J = 14.6$, 6.8 Hz, 1H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.6, 152.1, 129.5 (×2), 120.4, 115.8 (×2), 87.8, 82.1, 78.8, 31.4, 30.4, 18.3, 18.1, 17.4, 17.3; HRMS (EI) *m/z* (M^+) calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1890.

4.4. Photoreaction of 1c–k

A solution of the vinyl ether **1** (40–160 mg) in pentane (2.0 mmol dm^{-3}) was placed in a quartz photoreactor and deareated by argon bubbling. This was irradiated by a low-pressure mercury lamp (100 W, Eiko-sha, Japan) through a Vycor filter at room temperature until consumption of the substrate. The resulting mixture was purified by MPLC on silica gel (elution with 10–15% ethyl acetate in hexane) to give a colorless oil. Compound **4e**: (16.7% yield) $[\alpha]_D^{25} = +128.7$ (*c* 0.8, methanol); IR (neat, cm^{-1}) 2950, 1420, 1380, 1200, 1140, 1100, 770; ^1H NMR ($CDCl_3$) δ 5.54 (dd, $J = 5.6$, 2.4 Hz, 1H), 5.47 (ddd, $J = 5.6$, 2.8, 1.6 Hz, 1H), 4.31 (m, 1H), 4.13 (d, $J = 4.3$ Hz, 1H), 4.12 (m, 1H), 3.83 (m, 1H), 3.55 (m, 1H), 2.34 (d, $J = 8.3$ Hz, 1H,), 2.05–1.96 (m, 3H), 1.66 (ddd, $J = 14.6$, 4.3, 1.2 Hz), 1.25 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 129.3, 128.5, 87.3, 85.0, 72.1, 61.8, 56.3, 39.2, 38.7, 34.5, 29.5, 22.4; HRMS (APCI) *m/z* (M^+) calcd for $C_{12}H_{16}NaO_2$ 215.1048, found 215.1040. Compound **5e**: (27.3% yield) $[\alpha]_D^{25} = +74.1$ (*c* 2.0, methanol); IR (neat, cm^{-1}) 2950, 1420, 1220, 1160, 1100, 1080, 880, 780; ^1H NMR ($CDCl_3$) δ 5.65 (dddm, $J = 5.6$, 2.9, 1.0 Hz, 1H), 5.44 (dd, $J = 5.6$, 2.3 Hz, 1H), 4.51 (dd, $J = 6.8$, 2.0 Hz, 1H), 4.51(dd, $J = 6.8$, 1.2 Hz, 1H), 4.13–4.03 (m, 2H), 3.94 (ddd, $J = 14.0$, 6.6, 1.4 Hz, 1H), 3.31 (ddm, $J = 8.5$, 2.9, 1.5 Hz, 1H), 2.48 (dddm, $J = 14.7$, 8.5, 2.0 Hz, 1H,), 2.36–2.30 (m, 2H), 2.04–1.96 (m, 2H), 1.85 (ddd, $J = 14.7$, 6.8, 1.5 Hz, 1H), 1.29 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 139.0, 123.6, 87.0, 81.0, 76.9, 61.4,

53.9, 43.9, 42.5, 39.6, 38.0, 22.9; HRMS (APCI) *m/z* (M^+) calcd for $C_{12}H_{16}NaO_2$ 215.1048, found 215.1044. Compound **2f**: (34% yield) mp 53.0–55.5 °C; $[\alpha]_D^{25} = -140$ (*c* 0.6, methanol); IR (KBr) 2950, 2870, 1460, 1400, 1380, 1200, 1140, 1100, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.55 (dd, $J = 5.6$, 2.4 Hz, 1H), 5.44 (ddd, $J = 5.6$, 2.9, 1.5 Hz, 1H), 4.13 (m, 1H), 4.05 (m, 1H), 3.90 (m, 1H), 3.78 (m, 1H), 3.44 (m, 1H), 2.51 (dm, $J = 8.1$ Hz, 1H), 2.24 (m, 1H), 1.98 (m, 1H), 1.84 (ddd, $J = 13.9$, 6.4, 2.7 Hz, 1H), 1.61 (m, 1H), 1.44 (m, 1H), 1.18 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 128.6, 87.4, 87.0, 66.7, 65.5, 56.8, 42.2, 39.6, 31.4, 30.0, 25.5; HRMS (APCI) *m/z* (M^+) calcd for $C_{12}H_{16}NaO_2$ 215.1048, found 215.1040. Compound **4f**: (9.2% yield) $[\alpha]_D^{25} = +119$ (*c* 0.8, methanol); IR (neat, cm^{-1}) 2950, 1420, 1380, 1240, 1200, 1160, 1100; ^1H NMR ($CDCl_3$) δ 5.50 (ddd, $J = 5.6$, 2.6, 1.6 Hz, 1H), 5.47 (dd, $J = 5.6$, 2.2 Hz, 1H), 4.16 (d, $J = 5.1$ Hz, 1H), 4.06–3.80 (m, 3H), 3.22 (t-like, $J = 2.6$ Hz, 1H), 2.33 (dm, $J = 8.3$ Hz, 1H), 2.23 (dt, $J = 8.3$, 1.2 Hz, 1H), 2.12 (m, 1H), 2.07 (dd, $J = 6.4$, 2.6 Hz, 1H), 1.79 (ddd, $J = 15.6$, 5.1, 1.2 Hz, 1H), 1.68 (dd, $J = 16.8$, 5.6 Hz, 1H), 1.21 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 130.8, 127.2, 88.1, 85.6, 71.4, 70.9, 60.5, 41.7, 40.1, 32.0, 28.6, 26.4; HRMS (APCI) *m/z* (M^+) calcd for $C_{12}H_{16}NaO_2$ 215.1048, found 215.1045. Compound **2g** + **4g**: (racemic mixture, 19% yield) IR (neat, cm^{-1}) 3050, 2950, 2850, 1460, 1420, 1240, 1200, 1140, 1100, 840, 780, 740; ^1H NMR ($CDCl_3$) δ 5.33 (dd, $J = 5.6$, 2.2 Hz, 1H), 4.13 (d, $J = 4.6$ Hz, 1H), 3.84–3.75 (m, 2H), 3.56 (t, $J = 11.4$ Hz, 1H), 3.49 (ddd, $J = 13.5$, 7.4, 2.8 Hz, 1H), 3.22 (dm, $J = 2.6$ Hz, 1H), 2.34 (dm, $J = 7.6$ Hz, 1H), 1.99–1.89 (m, 3H), 1.63 (ddm, $J = 13.4$, 4.6 Hz, 1H), 1.37 (m, 1H); HRMS (APCI) *m/z* (M^+) calcd for $C_{11}H_{14}NaO_2$ 201.0891, found 201.0887. Compound **2i**: (23% yield) ^1H NMR ($CDCl_3$) δ 5.58 (dd, $J = 5.5$, 2.7 Hz, 1H), 5.45 (d, $J = 4.8$, 2.7 Hz, 1H), 4.15 (s, 1H), 4.04 (t-like, $J = 2.7$ Hz, 1H), 3.90 (dd, $J = 13.4$, 8.6 Hz, 1H), 3.75 (dd, $J = 13.8$, 9.6 Hz, 1H), 3.53 (br s, 1H), 2.59 (d, $J = 6.9$ Hz, 1H), 1.99 (t-like, $J = 6.9$ Hz, 1H), 1.84 (ddd, $J = 13.7$, 6.9, 2.7 Hz, 1H), 1.46 (d, $J = 13.7$ Hz, 1H), 0.98 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 128.6, 128.3, 87.8, 68.4, 62.6, 55.8, 52.1, 49.8, 43.6, 42.0, 33.2, 31.7, 29.4, 28.8, 27.1; HRMS (APCI) *m/z* (M^+) calcd for $C_{15}H_{22}NaO_2$ 257.1517, found 257.1510. Compound **4i**: (9% yield) ^1H NMR ($CDCl_3$) δ 5.51 (dd, $J = 5.5$, 2.7 Hz, 1H), 5.45 (m, 1H), 4.06 (d, $J = 3.4$ Hz, 1H), 3.90 (m, 2H), 3.78 (dd, $J = 13.7$, 6.2 Hz, 1H), 3.69 (dd, $J = 13.7$, 7.6 Hz, 1H), 3.36 (br s, 1H), 2.45 (d, $J = 8.2$ Hz, 1H), 2.03 (t-like, $J = 7.6$ Hz, 1H), 1.98–1.88 (m, 2H), 1.53–1.57 (m, 2H), 0.88 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 128.6, 128.3, 87.8, 68.4, 62.6, 55.8, 52.1, 49.8, 43.6, 42.0, 33.2, 31.7, 29.4, 28.8, 27.1; HRMS (APCI) *m/z* (M^+) calcd for $C_{15}H_{22}NaO_2$ 257.1517, found 257.1512. Compound **2k**: (11.2% yield) $[\alpha]_D^{20} = -65.6$ (*c* 0.9, methanol); CD (pentane) λ_{ext} 240 nm ($\Delta\varepsilon$ +19.3); IR (neat, cm^{-1}) 2959, 2873, 1405, 1385, 1097, 1082, 997; ^1H NMR (600 MHz, $CDCl_3$) δ 5.55 (dd, $J = 5.4$, 2.4 Hz, 1H), 5.39 (ddd, $J = 5.4$, 2.4, 1.5 Hz, 1H), 4.06 (d, $J = 2.9$ Hz, 1H), 3.77 (m, 1H), 3.75 (br s, 1H), 3.53 (m, 1H), 2.26 (d, $J = 5.4$ Hz, 1H), 2.03 (dd, $J = 7.3$, 6.8 Hz, 1H), 1.89 (ddd, $J = 13.7$, 6.3, 2.9 Hz, 1H), 1.81–1.52 (m, 4H), 0.94–0.85 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 129.1, 128.3, 86.9, 85.4, 83.4, 80.1, 52.82, 38.1, 36.5, 35.6, 34.7, 34.7, 33.6, 19.1, 18.4, 18.2, 18.0; HRMS (EI) *m/z* (M^+) calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1911. Compound **3k**: (55.7% yield) $[\alpha]_D^{20} = -15.2$ (*c* 0.3, methanol); CD (pentane) λ_{ext} 220 nm ($\Delta\varepsilon$ −44.9); IR (neat, cm^{-1}) 2957, 1469, 1421, 1384, 1292, 1261, 1098; ^1H NMR (600 MHz, $CDCl_3$) δ 5.61 (dd, $J = 5.4$, 2.4 Hz, 1H), 5.42 (d, $J = 5.4$ Hz, 1H), 4.49 (dd, $J = 6.8$, 2.4 Hz), 3.92 (dd, $J = 6.3$, 3.4 Hz, 1H), 3.69 (dd, $J = 7.3$, 3.4 Hz, 1H,), 3.21 (dd, $J = 8.3$, 2.4 Hz, 1H), 2.47–2.41 (m, 2H), 2.06–1.92 (m, 2H), 1.79–1.68 (m, 2H), 1.56 (d, $J = 17.6$ Hz, 1H), 0.89 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.7, 123.6, 87.8, 87.3, 81.5, 79.8, 54.4, 48.6, 40.9, 40.7, 35.9, 34.4, 33.4, 17.8 (×2), 17.7 (×2); HRMS (EI) *m/z* (M^+) calcd for $C_{17}H_{26}O_2$ 262.1933, found 262.1909.

4.5. Conversion of 4e to (−)-8

A solution of **4e** (78 mg, 0.41 mmol) in acetone (8 mL) and aqueous HCl (4 M, 2 mL) was stirred for 5 days. The solution was heated to reflux for an additional 2 days. The mixture was diluted with water (15 mL), and extracted with CH_2Cl_2 (15 mL × 3). The combined organic layer was washed with satd aqueous $NaHCO_3$, and dried over $MgSO_4$. Filtration, concentration, and purification by MPLC on silica gel (elution with 65% ethyl acetate in hexane) gave 32 mg of a yellow oil (40% yield). $[\alpha]_D^{25} = -48.2$ (*c* 0.3, methanol); IR (neat, cm^{-1}) 3450, 3050, 2950, 1760, 1640, 1440, 1380, 1340, 1300, 1200, 1100, 1050, 940, 920, 880, 860, 780, 740, 680; ^1H NMR ($CDCl_3$) δ 5.86 (m, 1H), 5.45 (dt, $J = 6.3$, 3.2 Hz, 1H), 3.95–3.90 (m, 2H), 3.60–3.49 (m, 2H), 2.94 (m, 1H), 2.67–2.55 (m, 4H), 2.38 (m, 1H), 1.91 (m, 1H), 1.68–1.64 (m, 2H), 1.17 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 215.2, 133.6, 124.9, 81.2, 67.7, 67.0, 49.4, 45.3, 41.0, 39.6, 38.3, 23.5; HRMS (EI) *m/z* (M^+) calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1240.

Hydrogenation of the above product (35 mg, 0.17 mmol) over Pd–C (ca. 30 mg) in ethyl acetate (5 mL) proceeded smoothly to give essentially pure **6** (24 mg, 67.9% yield). Compound **6**: $[\alpha]_D^{25} = -17.7$ (*c* 0.5, methanol); IR (neat, cm^{-1}) 3450, 2950, 2850, 1750, 1640, 1460, 1420, 1380, 1340, 1300, 1260, 1200, 1180, 1100, 1040, 1020, 960, 920, 840, 760; ^1H NMR ($CDCl_3$) δ 3.95 (q, $J = 6.1$ Hz, 1H), 3.90 (dd, $J = 8.1$, 2.4 Hz, 1H), 3.61 (m, 1H), 3.53 (m, 1H), 2.43 (m, 1H), 2.33 (m, 1H), 2.22 (dd, $J = 14.4$, 8.1 Hz, 1H), 2.05–1.85 (m, 6H), 1.69–1.53 (m, 4H), 1.18 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 220.5, 78.3, 67.22, 67.17, 51.3, 45.6, 38.3, 36.4, 34.6, 33.6, 23.5, 18.0; HRMS (EI) *m/z* (M^+) calcd for $C_{12}H_{20}O_3$ 212.1412, found 212.1412.

A solution of **6** (23 mg, 0.11 mmol) and ethylene glycol (2 mL) in benzene (40 mL) was heated to reflux in the presence of TsOH·pyridine and the generated water removed by a Dean–Stark trap. After 2.5 h, the mixture was cooled to rt, and extracted with ether (30 mL × 3). The combined organic layer was dried over $MgSO_4$,

filtered, and concentrated. The residue was purified by column chromatography on silica gel (elution with 20% ethyl acetate in hexane) to give the acetal as a colorless oil (42 mg, 97% yield). $[\alpha]_D^{25} = -13.9$ (*c* 0.8, methanol); IR (neat, cm^{-1}) 3450, 2950, 2850, 1720, 1450, 1380, 1260, 1240, 1180, 1120, 1020, 940, 860, 740; ^1H NMR ($CDCl_3$) δ 3.99–3.84 (m, 5H), 3.67–3.62 (m, 2H), 3.51 (td, $J = 9.7$, 3.2 Hz, 1H), 2.04 (m, 1H), 1.94 (m, 1H), 1.90–1.88 (m, 2H), 1.87–1.68 (m, 4H), 1.62 (m, 1H), 1.50 (m, 1H), 1.44–1.29 (m, 3H), 1.17 (d, $J = 6.1$ Hz, 3H).

A suspension of the acetal (42 mg, 0.16 mmol), PCC (ca. 60 mg), and powdered molecular sieves (3A) in dichloromethane (25 mL) was stirred for 10 h. The mixture was allowed to stand with additional PCC (ca. 30 mg) for 6 h. The mixture was filtered and the filtrate was extracted with dichloromethane (30 mL × 5). The combined organic layer was washed with water (50 mL) and dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to give the ketone as a colorless oil (44 mg, 106%). The ketone was dissolved in methanol (4 mL), and stirred with K_2CO_3 (ca. 10 mg) at rt to give (−)-**8**, the spectra of which were identical with the reported ones.[11] The optical rotation was observed after purification by the preparative GLC (NPGS, 160 °C). $[\alpha]_D^{25} = -15.2$ (*c* 0.05, methanol), lit.[11] for (1*R*,5*S*,6*R*)-**8**: $[\alpha]_D = -16$.

4.6. Conversion of 2f to (+)-8

A solution of **2f** (91 mg) in THF (10 mL) containing aqueous HCl (4 mol dm^{-3}, 0.5 mL) was heated to reflux for 2 days. Extraction with dichloromethane (20 mL × 2) and purification by MPLC (elution with 60% ethyl acetate in hexane) gave a colorless oil (11 mg, 11% yield). $[\alpha]_D^{25} = -0.5$ (*c* 0.8, methanol); IR (neat, cm^{-1}) 3400, 2950, 1760, 1640, 1440, 1380, 1320, 1300, 1200, 1120, 1080, 1020, 940, 740; ^1H NMR ($CDCl_3$) δ 5.88 (m, 1H), 5.48 (dt, $J = 9.0$, 2.9 Hz, 1H), 4.07 (dd, $J = 8.3$, 4.2 Hz, 1H), 3.63–3.59 (m, 3H), 2.95 (m, 1H), 2.65 (dd, $J = 4.2$, 3.2 Hz, 1H), 2.60 (m, 2H), 2.40 (m, 1H), 1.93 (m, 1H), 1.68–1.64 (m, 2H), 1.17 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 215.6, 133.7, 125.0, 78.0, 72.3, 59.8, 49.6, 45.3, 42.0, 39.5, 39.2, 19.7; HRMS (EI) *m*/*z* (M^+) calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1244.

A solution of this compound (39 mg) in ethyl acetate (5 mL) was stirred vigorously under hydrogen atmosphere in the presence of Pd–C (ca. 30 mg) for 30 min. Filtration and evaporation gave essentially pure **7** as a colorless oil (39 mg, 99% yield). $[\alpha]_D^{25} = -53.7$ (*c* 0.8, methanol); IR (neat, cm^{-1}) 3450, 2950, 1750, 1460, 1380, 1340, 1200, 1140, 1100, 1060, 960, 870, 760; ^1H NMR ($CDCl_3$) δ 4.01 (dd, $J = 8.3$, 2.4 Hz, 1H), 3.73–3.60 (m, 3H), 2.41–2.34 (m, 3H), 2.24 (dd, $J = 14.4$, 8.3 Hz, 1H), 2.00–1.84 (m, 5H), 1.70–1.51 (m, 4H), 1.15 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 221.1, 75.0, 71.5, 59.6, 51.3, 45.5, 39.1, 36.2, 34.5, 34.4, 19.8, 18.0; HRMS (EI) *m*/*z* (M^+) calcd for $C_{12}H_{20}O_3$ 212.1412, found 212.1399.

A solution of **7** (38.5 mg), ethylene glycol (2 mL), and TsOH·pyridine (10 mg) in benzene (40 mL) was heated to reflux while removing generated water by a Dean–Stark trap. After 2 h, the mixture was extracted with ether (30 mL × 3), dried over $MgSO_4$, and concentrated to give a crude acetal (54.8 mg), which was purified by column chromatography on silica gel (elution with 30% ethyl acetate in hexane) to give 45.3 mg of a colorless oil (97.4% yield). $[\alpha]_D^{25} = -43.9$ (*c* 0.9, methanol); IR (neat, cm^{-1}) 3450, 2950, 1450, 1380, 1240, 1180, 1120, 1080, 1060, 1020, 940, 760; ^1H NMR ($CDCl_3$) δ 3.99–3.87 (m, 4H), 3.81 (dd, $J = 8.1$, 3.9 Hz, 1H), 3.76–3.66 (m, 2H), 3.60 (m, 1H), 2.03 (m, 1H), 1.94–1.67 (m, 7H), 1.59 (m, 1H), 1.49 (m, 1H), 1.43–1.33 (m, 2H), 1.21 (m, 1H), 1.14 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 115.9, 77.3, 74.6, 64.5, 63.9, 61.9, 44.6, 40.5, 39.3, 36.0, 28.2, 27.5, 19.6, 17.1.

The acetal obtained above (43 mg) was dissolved in dichloromethane (30 mL) with powdered molecular sieves (3 Å, 300 mg). To this suspension was added PDC (104 mg, 1.6 equiv) at rt, and the mixture stirred for 3 h. The filtrate was washed with satd aqueous $NaHCO_3$, which was re-extracted with dichloromethane (100 mL). The combined extract was dried over $MgSO_4$, concentrated and purified by column chromatography on silica gel (elution with 30% ethyl acetate in hexane) to give the aldehyde as a colorless oil (33.7 mg, 79% yield). $[\alpha]_D^{25} = -46.0$ (*c* 0.7, methanol); IR (neat, cm^{-1}) 2950, 1730, 1440, 1380, 1310, 1240, 1200, 1180, 1120, 1080, 1060, 1020, 980, 950, 930, 870, 760; ^1H NMR ($CDCl_3$) δ 9.80 (t, $J = 2.2$ Hz, 1H), 3.95–3.84 (m, 5H), 3.81 (dd, $J = 8.3$, 3.8 Hz, 1H), 2.69 (ddd, $J = 16.1$, 8.3, 2.2 Hz, 1H), 2.38 (ddd, $J = 16.1$, 4.6, 2.2 Hz, 1H), 2.03 (m, 1H), 1.90–1.77 (m, 6H), 1.49–1.33 (m, 3H), 1.21 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 202.5, 115.8, 78.5, 69.4, 64.3, 64.0, 50.7, 44.5, 40.9, 36.1, 28.3, 27.6, 20.3, 17.2; HRMS (EI) *m*/*z* (M^+) calcd for $C_{14}H_{22}O_4$ 254.1218, found 254.1502.

A solution of the aldehyde (30 mg) in ether (7 mL) was added to a solution of methyl magnesium bromide (2 M in ether, 1 mL). Extraction and column chromatography on silica gel afforded 37 mg of a colorless oil (100%). To a solution of this oil (29 mg) in dichloromethane (20 mL) was added PCC (46 mg) and powdered molecular sieves (3 Å, 210 mg) at rt. After 2 h, the mixture was filtered, extracted (CH_2Cl_2, 20 mL × 4), dried over $MgSO_4$, and purified by a flash column (silica gel, 20% ethyl acetate in hexane) to give 27.9 mg of the ketone (97% yield). $[\alpha]_D^{25} = -29$ (*c* 0.6, methanol); IR (neat, cm^{-1}) 2950, 1720, 1380, 1240, 1130, 1060, 1020; ^1H NMR ($CDCl_3$) δ 3.93–3.83 (m, 5H), 3.77 (dd, $J = 8.1$, 3.8 Hz, 1H), 2.76 (dd, $J = 15.3$, 8.1 Hz, 1H), 2.33 (dd, $J = 15.3$, 4.8 Hz, 1H), 2.19 (s, 3H), 2.02 (br s, 1H), 1.92–1.77 (m, 5H), 1.48–1.34 (m, 2H), 1.30–1.18 (m, 2H), 1.16 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 208.5, 115.8, 78.5, 77.3, 70.8, 64.2, 63.8, 50.9, 44.2, 41.0, 36.1, 28.3, 27.7, 20.2, 17.2.

The ketone obtained above (23 mg) was dissolved in methanol (5 mL) with K_2CO_3 (50 mg). After stirring for 3 days, the mixture extracted was identical to (−)-**8**

except for the specific rotation obtained after the GLC purification (NPGS, 160 °C). $[\alpha]_D^{25} = +14$ (*c* 0.1, methanol).

4.7. GLC analysis of the reaction of 1c and 1k

A solution of **1c** (1.58 mg) in pentane (2.5 mL) containing decane (0.46 mg) was placed in a UV cell, de-aerated by argon bubbling, and then this was photoirradiated by a low-pressure mercury lamp. A part of solution was taken out by a microsyringe every hour during the photoirradiation, and was subjected to GLC analysis. (OV-1, 0.25 mm i.d. × 30 m, 120 °C, 30 cm s^{-1}). The retention times were as follows (min); decane: 5.1, **1c**: 12.9, **2c**: 16.3, **3c**: 20.1. The sensitivities among **1c**, **2c**, and **3c** were predicted to be the same. Photoreaction of **1k** was carried out in the same way except for the use of tetradecane as a standard. The GLC analysis was performed at 150 °C. The retention times were as follows (min); tetradecane: 5.3, **1k**: 12.3, **2k**: 17.1, **3k**: 22.6. The sensitivities among **1k**–**3k** were predicted to be the same. The results are shown in Figure 2.

4.8. Determination of the effective molarity for the reaction of 1c and 1k

A solution of **1c** (8.3 mg) and ethyl vinyl ether (3.8 mL or 1.9 mL) in pentane (20 mL) was placed in a quartz photo reactor, de-aerated by argon bubbling, and then photo-irradiated for 16 h by the low pressure mercury lamp. The mixture was subjected to GLC analysis (OV-1, 120 °C, 30 cm s^{-1}). The retention times for the intermolecular products were at 59–67 (showing five peaks). One of the intermolecular adducts was isolated from the reaction mixture and used as a standard for the calibration of the GLC peaks. ^{1}H NMR ($CDCl_3$) δ 6.27 (ddd, J = 14.6, 6.8, 1.5 Hz, 1H), 5.57 (dd, J = 5.9, 2.0 Hz, 1H), 5.45 (m, 1H), 4.25 (dtd, J = 14.2, 2.9, 1.5 Hz, 1H), 4.02 (q, J = 6.3 Hz, 1H), 3.95 (dq, J = 6.3, 1.5 Hz, 1H), 3.88 (td, J = 5.9, 1.5 Hz, 1H), 3.60 (dd, J = 5.9, 4.4 Hz, 1H), 3.42 (dtd, J = 19.5, 6.8, 2.4 Hz, 2H), 3.20 (s, 1H), 2.16 (d, J = 3.4 Hz, 1H), 1.97 (dt, J = 13.7, 7.3 Hz, 2H), 1.59 (dd, J = 14.6, 4.9 Hz, 1H), 1.45 (m, 1H), 1.24–1.16 (m, 6H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 150.59, 129.27, 128.59, 88.89, 88.06, 87.48, 72.94, 71.87, 63.20, 58.12, 43.92, 37.77, 34.89, 30.58, 20.97, 19.96, 15.48; HRMS (EI) *m*/*z* (M^+) calcd for $C_{17}H_{26}O_3$ 278.1882, found 278.1826.

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