Tetrahedron 65 (2009) 8668–8676

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Stereocontrolled one-pot synthesis of cycloalkane derivatives possessing a quaternary carbon using allyl phenyl sulfone

Koichiro Ota, Takao Kurokawa, Etsuko Kawashima, Hiroaki Miyaoka *

School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

ARTICLE INFO

Article history:
Received 2 June 2009
Received in revised form 22 August 2009
Accepted 25 August 2009
Available online 28 August 2009

Keywords:
Allyl phenyl sulfone
One-pot synthesis
Cyclopentane
Cyclopropane

ABSTRACT

Stereocontrolled one-pot synthesis of cyclopentane derivatives possessing quaternary carbon using allyl phenyl sulfone and epoxyiodide was presented. Furthermore, application of this protocol to the synthesis of cycloalkane derivatives with different ring sizes was successful.

1. Introduction

To date, a variety of carbon–carbon bond formation reactions have been developed for the construction of carbon frameworks. In particular, the use of alkylsulfones has frequently been employed to synthesize medicinal and natural organic compounds since the sulfonylcarbanion generated by an appropriate base readily facilitated carbon–carbon bond formation following reaction with alkyl halide, epoxide, ester, acyl halide or aldehyde.[1] We previously reported on the one-pot synthesis of cycloalkane derivatives **IVa** using allyl phenyl sulfone and disubstituted epoxide **Ia** having a leaving group (X) via alkyl sulfone **IIa** and anion **IIIa** (Fig. 1).[2] The protocol we developed comprises a sequence of coupling and cyclization reactions. The sulfonylcarbanion generated from allyl phenyl sulfone reacted with disubstituted epoxymesylate **Ia** (X=OMs) to afford epoxysulfone **IIa**, and was followed by cyclization of regenerated sulfonylcarbanion **IIIa** by excess base in situ. Here, by selecting an appropriate stereochemistry of the epoxide, it was possible to control the stereochemistry of the hydroxy group at the neighboring position of the cycloalkane. Additionally, converting the vinyl group to a formyl group in cycloalkane **IVa** facilitated control of the stereochemistry at the α-position of the aldehyde. Moreover, a new carbon–carbon bond could readily be constructed from the aldehyde, and so this one-pot protocol enabled us to synthesize cycloalkane derivatives **Va**, which possess three contiguous stereocenters. In our laboratory, we have achieved the total synthesis of marine eicosanoides bacillariolides[3,4] and constanolactone E[5,6] using this one-pot protocol synthesis of cycloalkane derivatives.

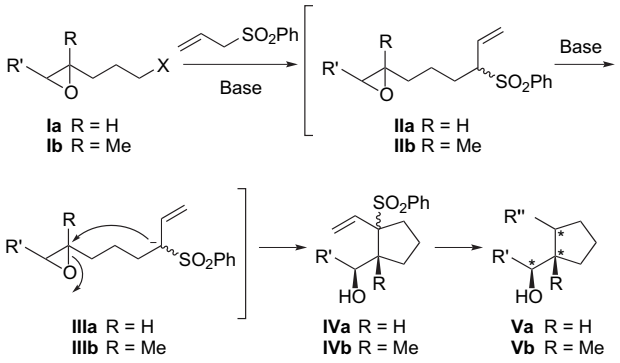


Figure 1. One-pot synthesis of cyclopentane derivatives from epoxide possessing a leaving group and allyl phenyl sulfone via epoxysulfone.

Marine-derived natural products often have the common partial structure **Vb**, which possesses a chiral quaternary carbon. Reiswigin A (a potent anti-herpes virus marine terpenoid),[7] cyanthiwigin E (a potent anti-tumor marine terpenoid),[8] and aragusterol A (a potent anti-tumor marine steroid)[9] are just some examples that have been reported (Fig. 2). We supposed that the common partial structure **Vb** could be successfully constructed using the aforementioned one-pot reaction. With this view in mind, trisubstituted epoxide **Ib** (R=Me) was employed in the one-pot protocol. The carbanion of

* Corresponding author.
E-mail address: miyaokah@ps.toyaku.ac.jp (H. Miyaoka).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.08.058

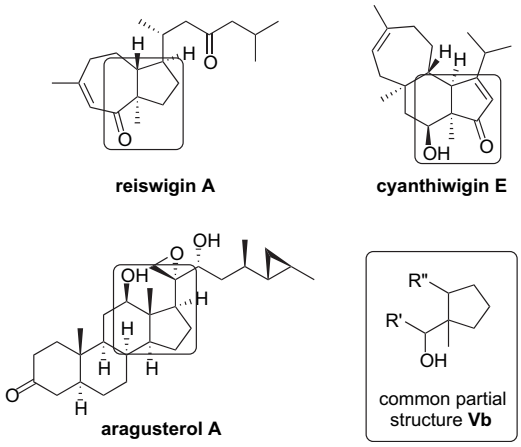
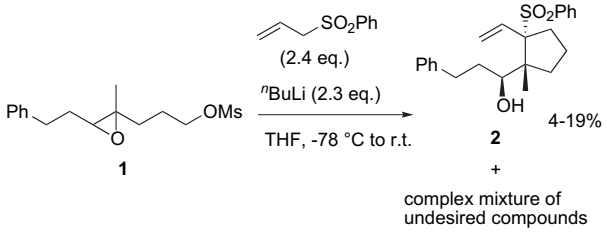


Figure 2. Marine natural products possessing a common partial structure.

allyl phenyl sulfone reacted with trisubstituted epoxide **Ib** to generate epoxysulfone **IIb**, and deprotonation of epoxysulfone **IIb** afforded carbanion **IIIb**. The cyclization of carbanion **IIIb** generated cyclopentane **IVb**, which possesses a quaternary chiral center. Cyclopentane **IVb** could then readily be converted to the common partial structure **Vb** (Fig. 1). In this paper, we wish to report on the stereocontrolled one-pot synthesis of cycloalkane derivatives possessing a quaternary carbon using allyl phenyl sulfone and trisubstituted epoxyiodide.

2. Results and discussion

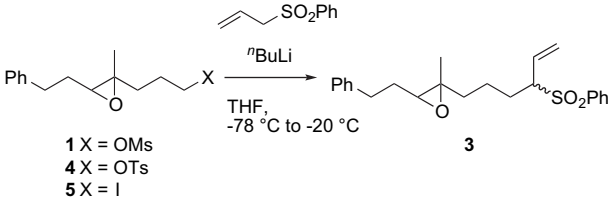
One-pot synthesis of the cycloalkane was initially performed according to a previously reported method.[2] Epoxymesylate **1**, which was synthesized from 3-phenylpropanal, was reacted with the sulfonylcarbanion generated by deprotonation of allyl phenyl sulfone (2.4 equiv) with ^{n}BuLi (2.3 equiv) to afford a small amount of cyclopentane **2** (4–19% yield) and a large amount of complex mixtures comprising undesired compounds (Scheme 1). This one-pot reaction consisted of a coupling process (the coupling of allyl phenyl sulfone and epoxymesylate) and a cyclization process (the cyclization of epoxysulfone). Since epoxymesylate **1** essentially decomposed under these reaction conditions, we decided to optimize the reaction conditions in each process.



Scheme 1. One-pot synthesis of cyclopentane derivative **2** under previously reported reaction conditions.

At first, the coupling process involving trisubstituted epoxide and allyl phenyl sulfone was optimized (Table 1). We have synthesized epoxytosylate **4** and epoxyiodide **5** from 3-phenylpropanal to select the leaving group (entries 1–3). The sulfonylcarbanion, which was generated from allyl phenyl sulfone (2.4 equiv) and ^{n}BuLi (2.3 equiv) was then reacted separately with epoxymesylate **1**, epoxytosylate **4**, and epoxyiodide **5**. Epoxyiodide **5**, which possesses iodine as the leaving group was reacted with the carbanion of allyl phenyl sulfone to generate epoxysulfone **3** in quantitative yield (entry 3). The amount of these reagents was then optimized using epoxyiodide **5** (entries 4–6). Epoxyiodide **5** was reacted with the sulfonylcarbanion generated from allyl phenyl sulfone (1.2 equiv) and ^{n}BuLi (1.1 equiv) to generate epoxysulfone **3** in 57% yield and epoxyiodide **5** (43% recovered) (entry 4). Epoxysulfone **3** was successfully obtained in 99% yield using allyl phenyl sulfone (1.2 equiv) and ^{n}BuLi (2.3 equiv) (entry 6).

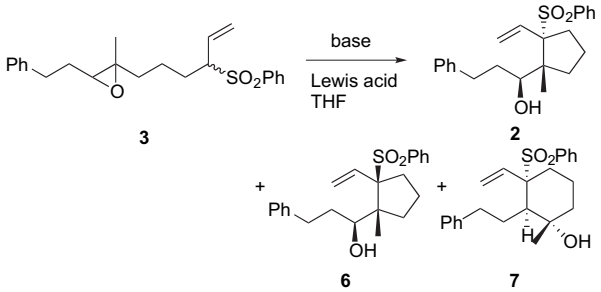
Table 1
Coupling reaction of epoxide possessing a leaving group and allyl phenyl sulfone to epoxysulfone **3**



Entry	SM	X	Allyl phenyl sulfone (equiv)	^{n}BuLi (equiv)	Yield (%)
1	**1**	OMs	2.4	2.3	35
2	**4**	OMs	2.4	2.3	43
3	**5**	I	2.4	2.3	Quant.
4	**5**	I	1.2	1.1	57
5	**5**	I	1.7	1.6	82
6	**5**	I	1.2	2.3	99

Next, we investigated conditions for the 5-*exo* cyclization process of epoxysulfone **3** (Table 2). In order to confirm the regioselectivity of the cyclization reaction, epoxysulfone **3** was treated with ^{n}BuLi or LDA to generate a mixture of 5-*exo* cyclization product **2** (16 or 21%) and 6-*endo* cyclization product **7** (35 or 42%) (entries 1 and 2). Generally, the intramolecular cyclization reaction of an epoxide with base generates a 5-*exo* cyclization product. The 5-*exo* cyclization reaction was inhibited as a result of steric hindrance by the methyl group, thereby resulting in the generation of cyclohexane **7**. We supposed that undesired cyclization was due to low reactivity of the epoxide group. Consequently, we investigated the addition of Lewis acid to elevate the reactivity of the epoxide group (entries 3–7). Initially, the activating ability of Lewis acids (1.1 equiv) such as $EtAlCl_2$, Et_2AlCl, Me_3Al, $BF_3\cdot OEt_2$, and $TiCl(O^iPr)_3$ for epoxide was investigated to promote cyclization of the sulfonylcarbanion, which was generated from epoxysulfone **3** and ^{n}BuLi (1.1 equiv). When Lewis acid was added, cyclopentane **2** and its diastereomer **6** were also obtained. Of the Lewis acids investigated,

Table 2
Cyclization of epoxysulfone **3** to cyclopentane derivatives



Entry	Base (1.1 equiv)	Lewis acid (1.1 equiv)	Temp	Yield (%)		
				2	**6**	**7**
1	^{n}BuLi	—	−78 °C to 0 °C	16	—	35
2	LDA	—	−78 °C to 0 °C	21	—	42
3	^{n}BuLi	$EtAlCl_2$	−78 °C to 0 °C	52	32	—
4	^{n}BuLi	Et_2AlCl	−78 °C to rt	64	16	—
5	^{n}BuLi	Me_3Al	−78 °C to rt	66	12	—
6	^{n}BuLi	$BF_3\cdot OEt_2$	−78 °C to 0 °C	31	28	—
7	^{n}BuLi	$TiCl(O^iPr)_3$	−78 °C to rt	26	11	—

Me_3Al was found to be the most effective in terms of chemical yield and selectivity (entry 5).

The relative configuration of cyclopentanes **2** and **6** was determined by NOESY spectrum analysis and chemical conversions. Firstly, configuration of the vinyl and 1-hydroxy-3-phenylpropyl groups was determined from the NOESY spectrum (Fig. 3). trans-Configuration of the vinyl and 1-hydroxy-3-phenylpropyl groups in **2** was determined by NOE correlation between vinyl and methyl protons. cis-Configuration of the vinyl and 1-hydroxy-3-phenylpropyl groups in **6** was determined by NOE correlation between the vinyl proton and methine proton of the hydroxy group. Next, the relative configuration of the methyl and hydroxy groups was determined by chemical conversions and NOESY spectrum analysis (Scheme 2). Cyclopentane **6** was converted to γ-lactone **8** by ozonolysis and oxidation of the hemiacetal. The NOE correlation between methyl and methine protons of γ-lactone in **8** suggested that the methyl group and methine proton of γ-lactone were oriented on the same face of the lactone ring. Therefore, the stereochemistry of the hydroxy group in **6** was found to be in the β-configuration. The stereochemistry of the hydroxy group in **2** was elucidated following chemical conversions. Cyclopentane **6** was converted to (*E*)-alkene **9** by rearrangement of the phenylsulfonyl group with BPO. Cyclopentane **2** was also converted to (*E*)-alkene **9** by rearrangement of the phenylsulfonyl group with BPO. Therefore, the stereochemistry of the hydroxy group in **2** was also found to be in the β-configuration.

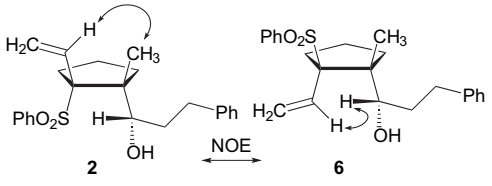
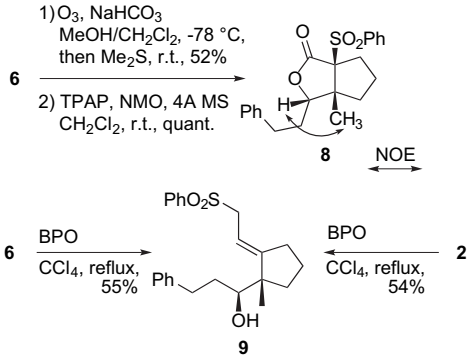


Figure 3. Selected NOE correlations of **2** and **6**.



Scheme 2. Chemical conversion of β-sulfone **6** to lactone **8** and chemical conversions of β-sulfone **6** and α-sulfone **2** to sulfone **9**.

The relative configuration of cyclohexane **7** was determined by examination of the NOESY spectrum (Fig. 4). The NOE correlation between methyl and vinyl protons and between the vinyl proton and one of methylene protons suggested that the methyl, vinyl, and 2-phenylethyl groups were oriented on the same face of the cyclohexane ring. The relative configuration of **7** was therefore determined to be that shown in Figure 4.

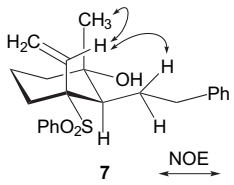
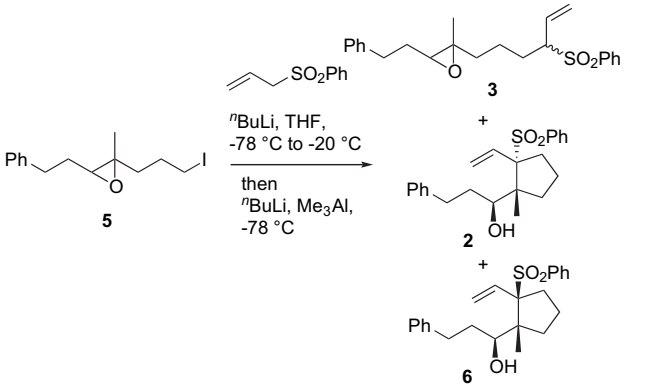


Figure 4. Selected NOE correlations of **7**.

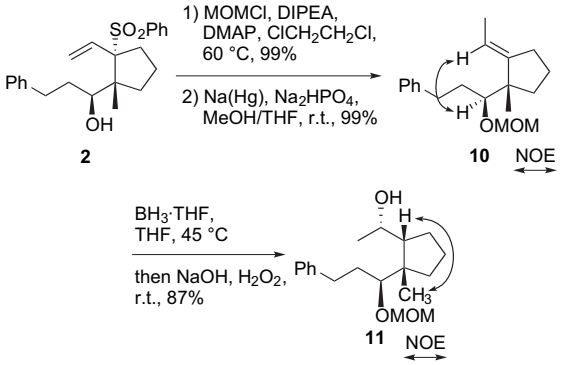
Finally, we optimized conditions of the one-pot protocol to synthesize cyclopentane derivatives by combining the best conditions determined for each step (Table 3). The sulfonylcarbanion, prepared from allyl phenyl sulfone (1.2 equiv) and ^{n}BuLi (2.3 equiv), was reacted with epoxyiodide **5** at −78 °C. Following confirmation of the disappearance of epoxyiodide **5** by TLC, Me_3Al (1.1 equiv) was added to the reaction mixture to generate epoxysulfone **3** (50%), α-sulfone **2** (8%), and β-sulfone **6** (4%) (entry 1). Since epoxysulfone **3** was obtained as a major product, these conditions were insufficient for the 5-*exo* cyclization reaction. ^{n}BuLi was then added after completing a coupling reaction (entries 2–5). Following confirmation of the generation of epoxysulfone **3**, ^{n}BuLi (2.1 equiv) and Me_3Al (2.2 equiv) were added to generate α-sulfone **2** (66%) and β-sulfone **6** (18%) (entry 5). However, the chemical yield of cyclopentane derivatives **2** and **6** was not very high when excess ^{n}BuLi was used from the beginning (entry 6).

Table 3
One-pot synthesis of cyclopentane derivatives from epoxyiodide **5** and allyl phenyl sulfone



Entry	^{n}BuLi (first) (equiv)	Allyl phenyl sulfone (equiv)	^{n}BuLi (second) (equiv)	Me_3Al (equiv)	Yield (%)		
					3	**2**	**6**
1	2.3	1.2	—	1.1	50	8	4
2	2.3	1.2	1.1	1.1	9	38	14
3	2.3	1.2	1.1	2.2	—	54	12
4	2.3	1.2	2.1	2.2	—	59	18
5	2.3	2.4	2.1	2.2	—	66	18
6	4.4	1.2	—	2.2	—	55	14

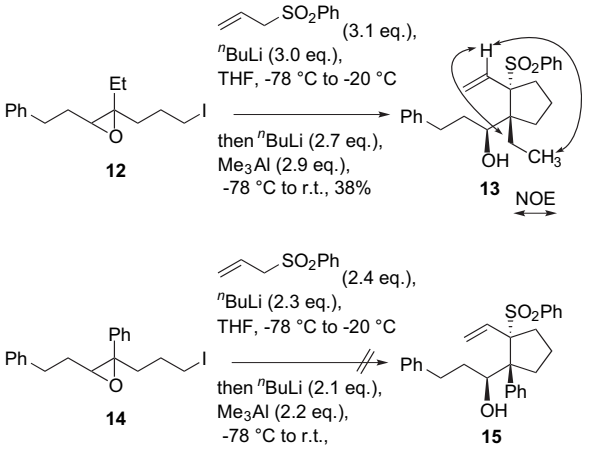
Next, generated cyclopentane **2** was easily converted to the common partial structure **Vb** by removal of the phenylsulfonyl group (Scheme 3). The hydroxy group in cyclopentane **2** was protected as a MOM ether and the phenylsulfonyl group was



Scheme 3. Conversion of cyclopentane derivative **2** to a common partial structure.

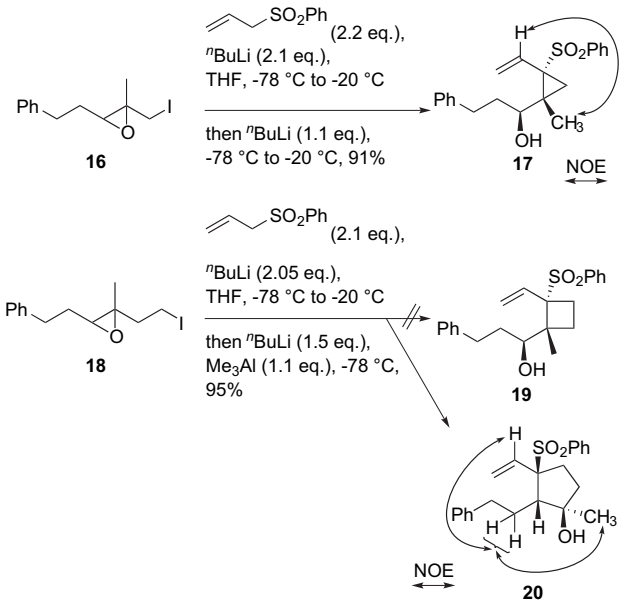
eliminated using Na(Hg) and Na_2HPO_4 to generate trisubstituted (*E*)-olefin **10**. The stereochemistry of the olefin in **10** was elucidated by examination of the NOESY spectrum. Trisubstituted olefin **10** was converted to alcohol **11**, which corresponds to partial structure **Vb**, via stereoselective hydroboration using BH_3/THF. The stereochemistry of alcohol **11** was elucidated by examination of the NOESY spectrum. It therefore became possible to introduce various functional groups using alcohol **11**. The one-pot protocol to synthesize cyclopentane derivatives was successfully extended to the use of trisubstituted epoxide.

Next, the synthesis of cyclopentane derivatives possessing ethyl or phenyl groups in lieu of methyl groups was examined (Scheme 4). The sulfonylcarbanion that was generated using ^{n}BuLi (3.0 equiv) and allyl phenyl sulfone (3.1 equiv) was reacted with epoxyiodide **12** possessing an ethyl group. Following completion of the coupling reaction, ^{n}BuLi (2.7 equiv) and Me_3Al (2.9 equiv) were added to give cyclopentane **13** as a single diastereomer in moderate yield (38%). The relative configuration of **13** was determined by examination of the NOESY spectrum. The one-pot synthesis of epoxyiodide **14** possessing a phenyl group with the sulfonylcarbanion under similar reaction conditions did not generate cyclopentane **15**, but a degradation product. Further examination of the reaction conditions is necessary for a one-pot synthesis of the cyclopentane possessing ethyl or phenyl groups.



Scheme 4. One-pot synthesis of cyclopentane derivatives from epoxyiodides **12** and **14** with allyl phenyl sulfone.

Furthermore, the developed protocol was applied to the synthesis of cycloalkane derivatives possessing different ring sizes (Scheme 5). The sulfonylcarbanion that was generated by ^{n}BuLi (2.1 equiv) and allyl phenyl sulfone (2.2 equiv) was reacted with epoxyiodide **16**. Following completion of the coupling reaction, ^{n}BuLi (1.1 equiv) was added to the reaction mixture. As a result, the 3-*exo* cyclization reaction was carried out without addition of a Lewis acid, to generate cyclopropane **17** as a single diastereomer in good yield (91%). The relative configuration of **17** was determined by examination of the NOESY spectrum. Under the reaction conditions developed, a one-pot reaction of epoxyiodide **18** with the sulfonylcarbanion did not generate the 4-*exo* product cyclobutane **19**, but generated the 5-*endo* product cyclopentane **20** as a single diastereomer in good yield (95%). The relative configuration of **20** was determined by examination of the NOESY spectrum. We supposed that the regioselectivity of the cyclization reaction resulted from steric strain derived from the generated cyclobutane and steric hindrance of the substituted group of epoxide **18**.



Scheme 5. One-pot synthesis of cyclopropane and cyclopentane derivatives.

3. Conclusion

In summary, we have successfully expanded an efficient protocol for the synthesis of cyclopentane derivatives using trisubstituted epoxide. Furthermore, application of this protocol to the synthesis of cycloalkane derivatives possessing different ring sizes was successful. Optically active cycloalkane derivative is produced by this one-pot synthesis using optically active epoxyiodide, which is prepared by asymmetric epoxidation. The synthesis of natural products by application of the present one-pot reaction is now being undertaken.

4. Experimental

4.1. General

Melting points (mps) were measured using a Yazawa melting point apparatus BY-2 and are uncorrected. IR spectra were recorded using a Jasco FT-IR/620 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer. Chemical shifts are given on the δ (ppm) scale using tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br, broad). High resolution ESIMS (HRESIMS) spectra were obtained using a Micromass LCT spectrometer. Elemental analysis data were obtained using an Elemental Vavio EL.

4.2. (2*S**,3*S**)-2-(3-Iodopropyl)-2,3-dimethyl-3-phenethyloxirane (5)

To a solution of (*E*)-4-methyl-7-phenylhept-4-en-1-ol[10] (4.79 g, 23.5 mmol) in CH_2Cl_2 (59.0 mL) were added DMAP (4.30 g, 53.2 mmol) and *p*-toluenesulfonyl chloride (5.14 g, 27.0 mmol) at 0 °C. The mixture was stirred for 30 min at rt. The reaction mixture was diluted with Et_2O, washed with H_2O and brine, dried, and then concentrated to afford the crude tosylate. To a solution of the crude tosylate in CH_2Cl_2 (120 mL) were added Na_2HPO_4 (10.0 g, 70.4 mmol) and *m*-CPBA (7.50 g, 28.2 mmol) at 0 °C. The mixture was stirred for 1 h at rt. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=3:1) to generate epoxytosylate **4** (7.43 g, 85% yield) as a colorless oil. IR

(neat) 2925, 1356, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.77 (2H, m), 7.35–7.26 (5H, m), 7.19 (3H, m), 4.01 (2H, m), 2.81 (1H, m), 2.69 (2H, m), 2.44 (3H, s), 1.90–1.64 (4H, m), 1.49 (2H, m), 1.09 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 144.7, 141.2, 133.1, 129.8, 128.4, 128.4, 127.9, 126.1, 70.3, 62.7, 60.2, 34.3, 32.6, 30.4, 24.5, 21.6, 16.4; HRESIMS (*m*/*z*) calcd for $C_{21}H_{27}O_4S$ $(M+H)^+$ 375.1611, found 375.1630. Anal. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00. Found: C, 67.45; H, 7.24.

To a solution of epoxytosylate **4** (49.5 mg, 132 μmol) in acetone (1.30 mL) were added $NaHCO_3$ (12.2 mg, 145 μmol) and NaI (198 mg, 1.32 mmol) at rt. The mixture was stirred for 2 h at the same temperature. The reaction mixture was diluted with Et_2O and then filtered through a silica gel pad. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=9:1) to generate epoxyiodide **5** (38.8 mg, 89% yield) as a colorless oil. IR (neat) 2925 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.37–7.24 (5H, m), 3.21 (2H, m), 2.95–2.72 (3H, m), 2.04–1.83 (4H, m), 1.64 (2H, m), 1.19 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.2, 128.4, 128.4, 126.1, 62.8, 60.2, 39.3, 32.7, 30.4, 29.2, 16.5, 6.2; HRESIMS (*m*/*z*) calcd for $C_{14}H_{20}OI$ $(M+H)^+$ 331.0559, found 331.0545. Anal. Calcd for $C_{14}H_{19}OI$: C, 50.92; H, 5.80. Found: C, 51.00; H, 5.92.

4.3. (2*S**,3*S**)-2-(4-Benzenesulfonylhex-5-enyl)-2-methyl-3-phenethyloxirane (3)

To a solution of allyl phenyl sulfone (129 mg, 0.710 mmol) in THF (4.50 mL) was added ^{n}BuLi (0.680 mmol, hexane solution) at −78 °C and the mixture was warmed to 0 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, a solution of epoxyiodide **5** (99.0 mg, 0.300 mmol) in THF (1.50 mL) was added and the reaction mixture was warmed to rt for over 5 h. After stirring for 1 h at ambient temperature, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=2:1) to generate epoxysulfone **3** (113 mg, 99%) as a colorless viscous oil. IR (neat) 2929, 1305, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.82 (2H, m), 7.62 (2H, m), 7.28 (2H, m), 7.19 (3H, m), 5.60 (1H, m), 5.28 (1H, dd, *J*=10.3, 6.0 Hz), 5.03 (1H, dd, *J*=17.1, 6.0 Hz), 3.47 (1H, m), 2.82 (1H, m), 2.69 (2H, m), 2.07 (1H, m), 1.84 (2H, m), 1.66 (1H, m), 1.58–1.24 (4H, m), 1.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.2, 137.3, 133.6, 130.2, 129.1, 128.8, 128.4, 126.0, 123.7, 123.7, 69.8 (69.7), 62.8 (62.8), 60.5 (60.5), 38.0 (37.9), 32.6, 30.4 (30.4), 26.8, 22.1 (22.0), 16.4 (16.3); HRESIMS (*m*/*z*) calcd for $C_{23}H_{28}O_3S$ $(M+H)^+$ 385.1837, found 385.1823. Anal. Calcd for $C_{23}H_{28}O_3S$: C, 71.84; H, 7.34. Found: C, 71.57; H, 7.38.

4.4. (*S**)-1-[(1*R**,2*S**)-2-Benzenesulfonyl-1-methyl-2-vinylcyclopentyl]-3-phenylpropan-1-ol (2) and (*S**)-1-[(1*R**,2*R**)-2-benzenesulfonyl-1-methyl-2-vinylcyclopentyl]-3-phenylpropan-1-ol (6)

To a solution of epoxysulfone **3** (30.4 mg, 0.079 mmol) in THF (0.79 mL) was added ^{n}BuLi (0.087 mmol, hexane solution) at −78 °C. The mixture was stirred for 30 min at the same temperature. Me_3Al (0.087 mmol, hexane solution) was added and the reaction mixture was warmed to 0 °C for over 5 h. After stirring for 1 h at the same temperature, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to generate α-sulfone **2** (20.1 mg, 66%) and β-sulfone **6** (3.7 mg, 12%) as colorless solids. Compound **2**: mp 154–157 °C. IR (neat) 3551, 2974, 1281, 1129 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.75 (2H, m), 7.54 (1H, m), 7.44 (2H, m), 7.26 (4H, m), 7.16 (1H, m), 6.31 (1H, dd, *J*=17.4, 10.9 Hz), 5.12 (1H, d, *J*=10.9 Hz), 4.72 (1H, d, *J*=17.4 Hz), 4.48 (1H, m), 3.39 (1H, m), 3.01 (1H, ddd, *J*=13.5, 11.2, 4.9 Hz), 2.72 (1H, ddd, *J*=13.5, 11.2, 5.5 Hz), 2.44 (1H, ddd, *J*=14.1, 10.8, 5.1 Hz), 2.29 (1H, ddd, *J*=13.0, 10.2, 4.4 Hz), 2.06 (2H, m), 1.93 (1H, m), 1.75 (1H, m), 1.61 (1H, m), 1.48 (1H, m), 1.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 143.0, 137.8, 135.9, 133.4, 130.1, 128.6, 128.3, 128.1, 125.6, 119.1, 80.4, 75.1, 57.5, 35.3, 34.5, 33.6, 31.0, 21.0, 20.7; HRESIMS (*m*/*z*) calcd for $C_{23}H_{28}O_3S$ $(M+H)^+$ 385.1837, found 385.1834. Anal. Calcd for $C_{23}H_{28}O_3S$: C, 71.84; H, 7.34. Found: C, 71.91; H, 7.20. Compound **6**: mp 148–150 °C. IR (neat) 3491, 2948, 1278, 1128 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.76 (2H, m), 7.57 (1H, m), 7.45 (2H, m), 7.25 (5H, m), 6.39 (1H, dd, *J*=17.5, 10.8 Hz), 5.23 (1H, d, *J*=10.8 Hz), 4.83 (1H, d, *J*=17.5 Hz), 3.72 (1H, ddd, *J*=16.7, 10.1, 6.0 Hz), 2.90 (1H, ddd, *J*=14.1, 10.1, 4.9 Hz), 2.61 (1H, ddd, *J*=13.7, 9.6, 6.9 Hz), 2.22 (2H, m), 2.03 (3H, m), 1.85 (1H, m), 1.71 (2H, m), 1.63 (1H, m), 1.52 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 142.1, 137.6, 135.2, 133.2, 130.5, 128.5, 128.4, 127.9, 125.8, 119.4, 81.0, 75.8, 56.3, 34.5, 34.1, 33.1, 31.4, 20.7, 20.2; HRESIMS (*m*/*z*) calcd for $C_{23}H_{28}O_3S$ $(M+H)^+$ 385.1837, found 385.1834. Anal. Calcd for $C_{23}H_{28}O_3S$: C, 71.84; H, 7.34. Found: C, 71.61; H, 7.15.

4.5. (3*S**,3a*R**,6a*S**)-6a-Benzenesulfonyl-3a-methyl-3-phenethylhexahydrocyclopenta[*c*]furan-1-one (8)

A cold (−78 °C) solution of β-sulfone **6** (50.0 mg, 0.130 mmol) in CH_2Cl_2 (1.30 mL) and MeOH (1.30 mL) was treated with ozone until a blue color persisted for more than 10 h. Excess ozone was removed using an argon flow. The reaction mixture was treated with excess Me_2S (0.095 mL, 1.30 mmol), allowed to warm slowly to rt for over 1 h, and then stirred for 12 h at the same temperature. The mixture was diluted with Et_2O, washed with H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography ($CHCl_3$/AcOEt=15:1) to generate the hemiacetal (26.3 mg, 52%) as a colorless solid. Mp 171–179 °C. IR (KBr) 3429, 2953, 1283, 1131 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.88 (2H, m), 7.60 (1H, m), 7.51 (2H, m), 7.29 (2H, m), 7.20 (3H, m), 5.75 (1H, d, *J*=5.7 Hz), 3.79 (1H, dd, *J*=12.4, 12.4 Hz), 3.03 (1H, d, *J*=5.7 Hz), 2.87 (1H, ddd, *J*=13.7, 8.6, 8.6 Hz), 2.62 (1H, ddd, *J*=13.7, 8.1, 8.1 Hz), 2.27 (1H, m), 2.06 (1H, m), 1.93 (1H, m), 1.80 (3H, m), 1.64 (1H, m), 1.57 (3H, s), 1.49 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.7, 139.2, 133.6, 129.6, 128.8, 128.5, 128.3, 126.0, 97.6, 82.9, 81.4, 59.1, 37.2, 33.6, 31.3, 30.6, 20.6; HRESIMS (*m*/*z*) calcd for $C_{22}H_{26}O_4S$ $(M-OH)^+$ 369.1524, found 369.1529.

To a solution of the above hemiacetal (5.0 mg, 13.0 μmol) in CH_2Cl_2 (650 μL) were added 4 Å MS (6.5 mg), NMO (7.5 mg, 65.0 μmol), and TPAP (0.5 mg, 1.30 μmol) and the mixture was stirred at rt for 30 min. The reaction mixture was diluted with Et_2O and then filtered through a silica gel pad. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=2:1) to generate lactone **8** (5.0 mg, quantitative yield) as colorless plates. Mp 169–170 °C. IR (KBr) 2935, 1766, 1306, 1145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.84 (2H, m), 7.68 (1H, m), 7.55 (2H, m), 7.32 (2H, m), 7.23 (3H, m), 4.80 (1H, dd, *J*=10.5, 2.4 Hz), 3.00 (1H, ddd, *J*=13.8, 10.9, 4.9 Hz), 2.76 (1H, ddd, *J*=13.8, 10.5, 6.6 Hz), 2.56 (1H, m), 2.08 (1H, m), 1.89 (4H, m), 1.72 (1H, m), 1.61 (3H, s), 1.58 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 172.8, 141.0, 137.4, 134.4, 130.2, 128.6, 128.6, 128.3, 126.3, 86.0, 80.0, 56.8, 35.7, 33.3, 32.8, 31.6, 23.0, 18.5; HRESIMS (*m*/*z*) calcd for $C_{22}H_{24}O_4S$ $(M+H)^+$ 385.1474, found 385.1492. Anal. Calcd for $C_{22}H_{24}O_4S$: C, 68.72; H, 6.29. Found: C, 68.68; H, 6.58.

4.6. (*S**)-1-{(*S**)-2-[(*E*)-2-Benzenesulfonylethylidene]-1-methylcyclopentyl}-3-phenylpropan-1-ol (9)

To a solution of β-sulfone **6** (23.2 mg, 60.0 μmol) in CCl_4 (600 μL) was added BPO (1.2 mg, 3.60 μmol) and the mixture was refluxed

for 8 h. The reaction mixture was diluted with Et_2O, washed with aqueous NaOH solution (1 M), saturated aqueous $Na_2S_2O_3$ solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by TLC (hexane/AcOEt=2:1) to generate sulfone **9** (12.6 mg, 54% yield) as a colorless oil. IR (neat) 3520, 2956, 1306, 1147 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.88 (2H, m), 7.66 (1H, m), 7.55 (2H, m), 7.29 (2H, m), 7.21 (3H, m), 5.16 (1H, m), 3.85 (2H, m), 3.52 (1H, dd, J=10.3, 10.3 Hz), 2.94 (1H, m), 2.61 (1H, m), 2.14 (1H, m), 1.88 (3H, m), 1.73 (1H, br s), 1.61 (2H, m), 1.32 (2H, m), 0.89 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 161.8, 142.4, 139.0, 133.7, 129.2, 128.5, 128.4, 128.3, 125.8, 106.6, 76.5, 57.6, 51.5, 33.4, 33.1, 33.0, 31.2, 24.6, 22.7; HRESIMS (m/z) calcd for $C_{23}H_{28}O_3S$ $(M+H)^+$ 385.1837, found 385.1862.

4.7. (*S**)-1-{(*S**)-2-[(*E*)-2-Benzenesulfonylethylidene]-1-methylcyclopentyl}-3-phenylpropan-1-ol (9)

To a solution of α-sulfone **2** (25.0 mg, 65.0 μmol) in CCl_4 (650 μL) was added BPO (1.3 mg, 3.90 μmol) and the mixture was refluxed for 8 h. The reaction mixture was diluted with Et_2O, washed with aqueous NaOH solution (1 M), saturated aqueous $Na_2S_2O_3$ solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by TLC (hexane/AcOEt=2:1) to generate sulfone **9** (13.7 mg, 55% yield) as a colorless oil.

4.8. (*S**)-1-[(1*R**,2*S**)-2-Benzenesulfonyl-1-methyl-2-vinylcyclopentyl]-3-phenylpropan-1-ol (2) and (*S**)-1-[(1*R**,2*R**)-2-benzenesulfonyl-1-methyl-2-vinylcyclopentyl]-3-phenylpropan-1-ol (6) (one-pot procedure)

To a solution of allyl phenyl sulfone (133 mg, 0.730 mmol) in THF (4.50 mL) was added ^{n}BuLi (0.700 mmol, hexane solution) at −78 °C and the mixture was warmed to 0 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, a solution of epoxyiodide **5** (102 mg, 0.310 mmol) in THF (1.50 mL) was added and the reaction mixture was warmed to −20 °C for over 5 h. The mixture was stirred for 1 h at the same temperature. After cooling to −78 °C, ^{n}BuLi (0.640 mmol, hexane solution) was added and the reaction mixture was warmed to −20 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, Me_3Al (0.680 mmol, hexane solution) was added. After stirring for 30 min at the same temperature, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to generate α-sulfone **2** (78.7 mg, 66%) and β-sulfone **6** (21.5 mg, 18%) as colorless solids.

4.9. (*S**)-[(1*S**,2*E*)-3-(2-Ethylidene-1-methylcyclopentyl)-3-methoxymethoxypropyl]benzene (10)

To a solution of α-sulfone **2** (60.2 mg, 0.157 mmol) in 1,2-dichloroethane (1.60 mL) were added *N*,*N*-diisopropylethylamine (0.136 mL, 0.785 mmol), chloromethyl methyl ether (0.060 mL, 0.785 mmol), and DMAP (19.1 mg, 0.157 mmol) and the mixture was stirred at 60 °C for 2 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to generate the MOM ether (66.7 mg, 99%) as a colorless solid. Mp 119–121 °C. IR (KBr) 2937 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.72 (2H, m), 7.51 (1H, m), 7.39 (2H, m), 7.24 (4H, m), 7.13 (1H, m), 6.31 (1H, dd, J=17.4, 11.0 Hz), 5.15 (1H, d, J=11.0 Hz), 4.83 (1H, d, J=6.3 Hz), 4.74 (1H, d, J=6.3 Hz), 4.65 (1H, d, J=17.4 Hz), 4.43 (1H, d, J=9.1 Hz), 3.41 (3H, s), 2.89 (1H, m), 2.78 (1H, m), 2.59 (1H, m), 2.29 (1H, m), 2.09–1.98 (2H, m), 1.86–1.72 (4H, m), 0.87 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 143.4, 136.8, 134.9, 133.3, 130.7, 128.6, 128.3, 127.9, 125.5, 121.0, 99.3, 85.3, 81.0, 56.5, 56.2, 38.7, 36.3, 33.5, 31.3, 19.6, 19.1; HRESIMS (m/z) calcd for $C_{25}H_{32}O_4S$ $(M+Na)^+$ 451.1919, found 451.1928. Anal. Calcd for $C_{25}H_{32}O_4S$: C, 70.06; H, 7.53. Found: C, 69.79; H, 7.54.

To a solution of the above MOM ether (43.7 mg, 0.102 mmol) in MeOH/THF (2.00 mL, 1:1) were added Na_2HPO_4 (870 mg) and 5% Na–Hg (2.40 g). After stirring for 2 h at rt, the reaction mixture was diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/AcOEt=20:1) to generate *E*-olefin **10** (30.2 mg, 99%) as a colorless viscous oil. IR (neat) 2954 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.23 (5H, m), 5.21 (1H, m), 4.68 (1H, d, J=6.6 Hz), 4.61 (1H, d, J=6.6 Hz), 3.41 (3H, s), 3.39 (1H, m), 2.86 (1H, m), 2.58 (1H, m), 2.37 (1H, m), 2.10–1.86 (4H, m), 1.71 (2H, m), 1.58 (3H, d, J=6.6 Hz), 1.32 (1H, m), 0.98 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 149.9, 142.8, 128.4, 128.3, 125.7, 114.7, 98.2, 84.5, 55.9, 50.0, 35.8, 33.8, 33.4, 30.1, 24.3, 22.6, 14.7; HRESIMS (m/z) calcd for $C_{19}H_{28}O_2$ $(M+Na)^+$ 311.1987, found 311.2011. Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 78.84; H, 9.71.

4.10. (*S**)-1-{(1*R**,2*S**)-2-[(*S**)-1-Methoxymethoxy-3-phenylpropyl]-2-methylcyclopentyl}ethanol (11)

To a solution of *E*-olefin **10** (10.8 mg, 0.036 mmol) in THF (0.36 mL) was added BH_3/THF (0.109 mmol, THF solution) at 0 °C. The reaction mixture was warmed to 45 °C and stirred for 2 h. To the resulting solution were added 1 M NaOH solution (73 μL) and 35% aqueous H_2O_2 solution (73 μL) at rt. After stirring for 1 h, the resultant mixture was diluted with Et_2O, washed with H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to generate alcohol **11** (9.6 mg, 87%) as a colorless viscous oil. IR (neat) 3432 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.41–7.23 (5H, m), 4.82 (2H, dd, J=15.9, 6.8 Hz), 4.01 (1H, m), 3.92 (1H, br s), 3.51 (3H, s), 3.46 (1H, m), 2.98 (1H, m), 2.65 (1H, m), 2.14–1.98 (2H, m), 1.79–1.31 (7H, m), 1.25 (3H, s), 1.19 (3H, d, J=6.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 142.1, 128.5, 128.4, 125.9, 98.3, 88.3, 68.8, 59.1, 56.3, 49.1, 38.8, 35.2, 34.8, 32.0, 30.2, 23.0, 22.9; HRESIMS (m/z) calcd for $C_{19}H_{30}O_3$ $(M+Na)^+$ 329.2093, found 329.2098. Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.18; H, 9.79.

4.11. (2*S**,3*S**)-2-Ethyl-2-(3-iodopropyl)-3-methyl-3-phenethyloxirane (12)

To a solution of 2-bromobut-1-ene (3.29 g, 24.4 mmol) in Et_2O (97.6 mL) was added ^{t}BuLi (26.8 mmol, hexane solution) at −78 °C. After stirring for 15 min at the same temperature, commercially available 3-phenylpropanal (3.47 g, 25.6 mmol) was added and the mixture was warmed to rt. The mixture was stirred for 1.5 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, dried, and then concentrated to afford the crude alcohol. To the crude alcohol were added triethyl orthoacetate (15.8 g, 97.7 mmol) and propionic acid (180.7 mg, 2.44 mmol) at rt and the mixture was warmed to 140 °C. The mixture was stirred for 38 h under reflux and then heated to 160 °C. Following removal of excess triethyl orthoacetate, the residue was filtered through a silica gel pad (hexane/AcOEt=20:1). The filtrate was concentrated under reduced pressure to give the crude ester. To a solution of the crude ester in Et_2O (122 mL) was added $LiAlH_4$ (1.85 g, 48.8 mmol) at 0 °C. After stirring for 30 min at the same temperature, the reaction mixture was diluted with Et_2O and $Na_2SO_4 \cdot 10H_2O$ was added. The mixture was dried over $MgSO_4$ and Na_2SO_4. Removal of the solvent gave

a residue, which was purified by silica gel column chromatography (hexane/AcOEt=5:1) to generate the alcohol (413.1 mg, 8% yield) as a colorless oil. IR (neat) 3349, 1453 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.30–7.27 (2H, m), 7.20–7.16 (3H, m), 5.18 (1H, t, J=7.1 Hz), 3.61 (2H, br t), 2.65 (2H, dd, J=7.4, 8.2 Hz), 2.33 (2H, dd, J=7.6, 15.4 Hz), 2.07 (2H, dd, J=7.5, 7.7 Hz), 2.01 (2H, q, J=7.6 Hz), 1.65 (2H, m), 1.28 (1H, br s), 0.92 (3H, t, J=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 142.3, 141.2, 128.4, 128.2, 125.7, 123.4, 62.9, 36.4, 32.7, 31.0, 29.6, 23.0, 13.1; HRESIMS (m/z) calcd for $C_{15}H_{22}ONa$ $(M+Na)^+$ 241.1568, found 241.1585. Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.24; H, 10.02.

To a solution of the above alcohol (410 mg, 1.88 mmol) in CH_2Cl_2 (37.6 mL) were added DMAP (528 mg, 4.32 mmol) and *p*-toluenesulfonyl chloride (430 mg, 2.26 mmol) at 0 °C. The mixture was stirred for 3 h at rt. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude tosylate. To a solution of the crude tosylate in CH_2Cl_2 (37.6 mL) were added $NaHCO_3$ (474 mg, 5.64 mmol) and *m*-CPBA (749 mg, 2.82 mmol) at rt. The mixture was stirred for 20 min at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude epoxytosylate. To a solution of the crude epoxytosylate in acetone (37.6 mL) were added $NaHCO_3$ (237 mg, 2.82 mmol) and NaI (1.41 g, 9.41 mmol) at rt. The mixture was stirred for 3 h at 50 °C. The reaction mixture was diluted with Et_2O and filtered through a silica gel pad. The filtrate was concentrated to give a residue, which was purified by silica gel column chromatography (hexane/AcOEt=15:1) to generate epoxyiodide **12** (67.7 mg, 11% yield) as a colorless oil. IR (neat) 2968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.32–7.28 (2H, m), 7.22–7.19 (3H, m), 3.17 (2H, ddd, J=6.8, 6.8, 3.4 Hz), 2.88–2.69 (2H, m), 2.78 (1H, dd, J=6.5, 5.8 Hz), 1.92–1.80 (4H, m), 1.67–1.58 (3H, m), 1.46–1.37 (1H, m), 0.96 (3H, t, J=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.3, 128.5, 128.4, 126.1, 63.5, 63.0, 35.4, 32.9, 30.1, 28.8, 23.2, 9.3, 6.4; HRESIMS (m/z) calcd for $C_{15}H_{22}OI$ $(M+H)^+$ 345.0715, found 345.0698. Anal. Calcd for $C_{15}H_{21}OI$: C, 52.34; H, 6.15. Found: C, 52.50; H, 6.31.

4.12. (*S**)-1-[(1*R**,2*R**)-2-Benzenesulfonyl-1-ethyl-2-vinylcyclopentyl]-3-phenylpropan-1-ol (13)

To a solution of allyl phenyl sulfone (87.5 mg, 0.480 mmol) in THF (3.00 mL) was added ^{n}BuLi (0.479 mmol, hexane solution) at −78 °C and the mixture was warmed to 0 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, a solution of epoxyiodide **12** (53.2 mg, 0.155 mmol) in THF (1.00 mL) was added and the reaction mixture was warmed to −20 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, ^{n}BuLi (0.417 mmol, hexane solution) was added and the reaction mixture was warmed to −20 °C and then stirred for 30 min at the same temperature. After cooling to −78 °C, Me_3Al (0.448 mmol, hexane solution) was added. After stirring for 2 h at the same temperature, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=3:1) to generate α-sulfone **13** (23.6 mg, 38%) as a colorless viscous oil. IR (neat) 3423 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.78 (2H, d, J=7.4 Hz), 7.60 (1H, t, J=7.4 Hz), 7.48 (2H, t, J=7.8 Hz), 7.32–7.18 (5H, m), 6.39 (1H, dd, J=18.0, 11.4 Hz), 5.21 (1H, d, J=10.8 Hz), 4.78 (1H, d, J=17.4 Hz), 4.55 (1H, dd, J=9.3, 4.5 Hz), 3.57 (1H, d, J=5.4 Hz), 3.08 (1H, dt, J=8.6, 2.3 Hz), 2.76 (1H, dt, J=7.7, 2.6 Hz), 2.58 (1H, dt, J=7.5, 3.1 Hz), 2.28 (1H, dt, J=8.0, 3.1 Hz), 2.05–1.97 (2H, m), 1.91–1.85 (2H, m), 1.63 (1H, quint., J=7.6 Hz), 1.56 (2H, m), 1.43 (1H, quint., J=7.6 Hz), 1.01 (3H, t, J=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 143.0, 138.0, 135.6, 133.4, 130.5, 128.7, 128.3, 128.0, 125.7, 119.3, 82.0, 73.8, 61.1, 34.9, 33.6, 33.6, 32.4, 28.1, 21.1, 9.8; HRESIMS (m/z) calcd for $C_{24}H_{31}O_3S$ $(M+H)^+$ 399.1994, found 399.1980.

4.13. (2*R**,3*S**)-2-(3-Iodopropyl)-3-methyl-3-phenethyl-2-phenyloxirane (14)

To a solution of α-bromostylene (5.00 g, 24.6 mmol) in Et_2O (98.4 mL) was added ^{t}BuLi (27.1 mmol, hexane solution) at −78 °C. After stirring for 15 min at the same temperature, commercially available 3-phenylpropanal (3.47 g, 25.6 mmol) was added and the reaction mixture was warmed to rt. The mixture was stirred for 1.5 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, dried, and then concentrated to afford the crude alcohol. To the crude alcohol were added triethyl orthoacetate (15.9 g, 98.0 mmol) and propionic acid (182.2 mg, 2.46 mmol) at rt and the mixture was warmed to 140 °C. The mixture was stirred for 22 h under reflux and then heated to 160 °C. Following removal of excess triethyl orthoacetate, the residue was filtered through a silica gel pad (hexane/AcOEt=15:1). The filtrate was concentrated under reduced pressure to give the crude ester. To a solution of the crude ester in Et_2O (123 mL) was added $LiAlH_4$ (1.90 g, 49.2 mmol) at 0 °C. After stirring for 35 min at the same temperature, the reaction mixture was diluted with Et_2O and $Na_2SO_4 \cdot 10H_2O$ was added. The mixture was dried over $MgSO_4$ and Na_2SO_4. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to generate the alcohol (533.6 mg, 8% yield) as a colorless oil. IR (neat) 3343, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.32–7.18 (6H, m), 7.11 (2H, d, J=7.2 Hz), 7.04 (2H, d, J=7.0 Hz), 5.53 (1H, t, J=7.2 Hz), 3.60 (2H, br t), 2.65 (2H, dd, J=7.4, 7.8 Hz), 2.42 (2H, dd, J=7.4, 7.5 Hz), 1.56 (2H, m), 1.29 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.8, 141.1, 140.8, 128.5, 128.3, 128.2, 128.0, 126.7, 126.5, 125.7, 62.4, 36.2, 35.5, 31.0, 30.7; HRESIMS (m/z) calcd for $C_{19}H_{23}O$ $(M+H)^+$ 267.1749, found 267.1744. Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.54; H, 8.40.

To a solution of the above alcohol (467 mg, 1.75 mmol) in CH_2Cl_2 (17.5 mL) were added DMAP (492 mg, 4.03 mmol) and *p*-toluenesulfonyl chloride (400 mg, 2.10 mmol) at 0 °C and the mixture was warmed to rt. The mixture was stirred for 3 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude tosylate. To a solution of the crude tosylate in CH_2Cl_2 (17.5 mL) were added $NaHCO_3$ (441 mg, 5.25 mmol) and *m*-CPBA (697 mg, 2.63 mmol) at 0 °C and the mixture was warmed to rt. The mixture was stirred for 2 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with 10% aqueous NaOH solution, H_2O and brine, dried, and then concentrated to afford the crude epoxytosylate. To a solution of the crude epoxytosylate in acetone (17.5 mL) were added $NaHCO_3$ (221 mg, 2.63 mmol) and NaI (1.31 g, 8.74 mmol) at rt. The mixture was warmed to 50 °C and then stirred for 12 h at the same temperature. The reaction mixture was diluted with Et_2O and filtered through a silica gel pad. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=15:1) to generate epoxyiodide **14** (568.4 mg, 83% yield) as a colorless oil. IR (neat) 3026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.35–7.22 (7H, m), 7.17 (1H, m), 7.04 (2H, m), 3.13 (2H, dt, J=2.7, 6.8 Hz), 3.10 (1H, t, J=6.1 Hz), 2.66 (2H, m), 2.31 (1H, m), 1.91 (1H, m), 1.75 (1H, m), 1.63 (1H, m), 1.48 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.1, 137.6, 128.4, 128.3, 128.1, 127.4, 126.8, 125.9, 65.2, 64.0, 38.5, 32.3, 30.4, 28.9, 6.5; HRESIMS (m/z) calcd for $C_{19}H_{22}OI$ $(M+H)^+$ 393.0715, found 393.0731. Anal. Calcd for $C_{19}H_{21}OI$: C, 58.17; H, 5.40. Found: C, 58.21; H, 5.48.

4.14. (2*R**,3*S**)-2-Iodomethyl-2,3-dimethyl-3-phenethyloxirane (16)

To a solution of (*E*)-2-methyl-5-phenylpent-2-en-1-ol[11] (966 mg, 5.48 mmol) in CH_2Cl_2 (55.0 mL) were added $NaHCO_3$ (2.30 g, 27.4 mmol) and *m*-CPBA (2.18 g, 8.20 mmol) at 0 °C. The mixture was stirred for 15 min at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude epoxyalcohol. To a solution of the crude epoxyalcohol in CH_2Cl_2 (25.0 mL) were added imidazole (1.10 g, 16.2 mmol), Ph_3P (2.25 g, 8.59 mmol), I_2 (2.18 g, 8.59 mmol), and 2-methyl-but-2-ene (2.70 mL, 25.3 mmol) at 0 °C. The mixture was stirred for 3 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $Na_2S_2O_3$ solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=15:1) to generate epoxyiodide **16** (808.8 mg, 49% yield) as a colorless oil. IR (neat) 2963 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.36–7.23 (5H, m), 3.24 (1H, m), 3.11 (1H, m), 2.96 (1H, t, *J*=6.3 Hz), 2.91–2.74 (2H, m), 1.99–1.83 (2H, m), 1.41 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 140.9, 128.5, 128.4, 126.2, 65.9, 60.2, 32.5, 30.9, 16.0, 13.9; HRESIMS (*m*/*z*) calcd for $C_{12}H_{15}OINa$ $(M+Na)^+$ 325.0065, found 325.0088. Anal. Calcd for $C_{12}H_{15}OI$: C, 47.70; H, 5.00. Found: C, 47.81; H, 5.22.

4.15. (*S**)-1-[(1*R**,2*S**)-2-Benzenesulfonyl-1-methyl-2-vinylcyclopropyl]-3-phenylpropan-1-ol (17)

To a solution of allyl phenyl sulfone (242 mg, 1.34 mmol) in THF (6.00 mL) was added ^{n}BuLi (1.27 mmol, hexane solution) at −78 °C and the mixture was warmed to 0 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, a solution of epoxyiodide **16** (183 mg, 0.604 mmol) in THF (6.10 mL) was added and the reaction mixture was warmed to −20 °C. The mixture was stirred for 1 h at the same temperature. After cooling to −78 °C, ^{n}BuLi (0.664 mmol, hexane solution) was added and the mixture was warmed to 0 °C. After stirring for 3 h at the same temperature, the mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=3:1) to generate cyclopropane **17** (195 mg, 91%) as a colorless viscous oil. IR (neat) 3522, 2937, 1303, 1147 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.77 (2H, m), 7.60 (1H, m), 7.48 (2H, m), 7.33–7.15 (5H, m), 5.90 (1H, dd, *J*=17.2, 10.2 Hz), 5.19 (1H, d, *J*=10.2 Hz), 4.85 (1H, d, *J*=17.2 Hz), 4.71 (1H, m), 2.99–2.75 (2H, m), 2.23 (1H, m), 1.95 (3H, m), 1.19 (1H, d, *J*=4.1 Hz), 1.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 142.3, 140.0, 133.1, 130.6, 128.8, 128.6, 128.5, 128.3, 125.7, 124.1, 71.8, 54.3, 38.3, 37.0, 33.3, 24.8, 15.3; HRESIMS (*m*/*z*) calcd for $C_{21}H_{24}O_3S$ $(M+Na)^+$ 379.1344, found 379.1357.

4.16. (2*S**,3*S**)-2-(2-Iodoethyl)-2,3-dimethyl-3-phenethyloxirane (18)

To a solution of (*E*)-2-methyl-5-phenylpent-2-en-1-ol[11] (1.38 g, 7.80 mmol) in CH_2Cl_2 (78.0 mL) were added 4 Å MS (2.34 g), NMO (1.19 g, 10.1 mmol), and TPAP (95.9 mg, 0.27 mmol) at rt. The mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with Et_2O, filtered through a silica gel pad (AcOEt only), and then concentrated to afford the crude aldehyde. To a solution of methyltriphenylphosphonium iodide (28.4 g, 70.2 mmol) in THF (100 mL) was added ^{n}BuLi (62.4 mmol, hexane solution) at 0 °C. The mixture was stirred for 30 min at the same temperature and a solution of the above crude aldehyde in THF (11.0 mL) was added dropwise at rt. After stirring for 30 min, the reaction mixture was diluted with Et_2O, and to this was added saturated aqueous NH_4Cl solution. The mixture was filtered through a Celite pad (Et_2O). The filtrate was washed with H_2O and brine and then dried over $MgSO_4$. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane only) to generate the diene (358.6 mg, 27% yield) as a colorless oil.

To a solution of cyclohexene (102.1 mg, 1.24 mmol) in THF (2.0 mL) was added BH_3/THF (0.62 mmol, THF solution) dropwise at 0 °C. The mixture was stirred for 1 h at the same temperature and a solution of the above diene (97.3 mg, 0.56 mmol) in THF (1.0 mL) was added dropwise at rt. After stirring for 12 h, 3 M NaOH solution (1.1 mL) and 35% aqueous H_2O_2 solution (210 μL) were added to the mixture at rt. After stirring for 30 min, the resultant mixture was diluted with Et_2O, washed with H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=4:1) to give the alcohol (103.5 mg, 96% yield) as a colorless oil.

To a solution of the above alcohol (269.0 mg, 1.41 mmol) in CH_2Cl_2 (3.50 mL) were added DMAP (396 mg, 3.24 mmol) and *p*-toluenesulfonyl chloride (323 mg, 1.69 mmol) at 0 °C. The mixture was stirred for 30 min at rt. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude tosylate. To a solution of the crude tosylate in CH_2Cl_2 (14.1 mL) were added $NaHCO_3$ (592 mg, 7.05 mmol) and *m*-CPBA (562 mg, 2.12 mmol) at 0 °C. The mixture was stirred for 30 min at rt. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, H_2O and brine, dried, and then concentrated to afford the crude epoxytosylate. To a solution of the crude epoxytosylate in acetone (7.1 mL) were added $NaHCO_3$ (178 mg, 2.12 mmol) and NaI (1.10 g, 7.05 mmol) at rt. The mixture was stirred for 4 h at the same temperature. The reaction mixture was diluted with Et_2O and then filtered through a silica gel pad. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=10:1) to generate epoxyiodide **18** (214.9 mg, 48% yield) as a colorless oil. IR (neat) 2925 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.32–7.19 (5H, m), 3.14 (2H, m), 2.90–2.71 (2H, m), 2.85 (1H, t, *J*=6.2 Hz), 2.20 (1H, m), 1.98 (1H, m), 1.87 (2H, m), 1.17 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 141.2, 128.5, 128.4, 126.1, 62.8, 61.1, 42.6, 32.7, 30.4, 15.9, −0.8; HRESIMS (*m*/*z*) calcd for $C_{13}H_{18}OI$ $(M+H)^+$ 317.0402, found 317.0396. Anal. Calcd for $C_{13}H_{17}OI$: C, 49.38; H, 5.42. Found: C, 49.44; H, 5.58.

4.17. (1*R**,2*S**,3*R**)-3-Benzenesulfonyl-1-methyl-2-phenethyl-3-vinylcyclopentanol (20)

To a solution of allyl phenyl sulfone (140 mg, 0.770 mmol) in THF (4.50 mL) was added ^{n}BuLi (0.752 mmol, hexane solution) at −78 °C and the mixture was warmed to 0 °C. The mixture was stirred for 30 min at the same temperature. After cooling to −78 °C, a solution of epoxyiodide **18** (116 mg, 0.367 mmol) in THF (2.80 mL) was added and the reaction mixture was warmed to −20 °C. The mixture was stirred for 1 h at the same temperature. After cooling to −78 °C, ^{n}BuLi (0.550 mmol, hexane solution) was added. After the mixture was stirred for 1 h at the same temperature, Me_3Al (0.734 mmol, hexane solution) was added. After stirring for 1.5 h at the same temperature, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl solution, H_2O and brine, and then dried. Removal of the solvent gave a residue, which was purified by silica gel column chromatography (hexane/AcOEt=2:1) to generate cyclopentane **20** (129 mg, 95%) as a colorless viscous oil. IR (neat) 3501, 2965 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 7.76 (2H, m), 7.59 (1H, m), 7.47 (2H, m), 7.28 (4H, m), 7.18 (1H, m), 6.28 (1H, dd, *J*=17.4, 10.7 Hz), 5.16 (1H, d, *J*=10.7 Hz), 4.82 (1H, d, *J*=17.4 Hz), 2.92 (2H, m), 2.61 (1H, m), 2.26 (2H, m), 2.05 (2H, m), 1.72 (2H, m),

1.64 (1H, br s), 1.59 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 142.2, 137.4, 137.1, 133.4, 130.4, 128.6, 128.3, 128.1, 125.7, 116.5, 81.3, 76.6, 60.2, 40.4, 35.3, 29.5, 27.6, 23.6; HRESIMS (m/z) calcd for $C_{22}H_{26}O_3S$ $(M+Na)^+$ 393.1500, found 393.1480.

References and notes

1. Simokin, N. S. *Sulphones in Organic Synthesis*; Pergamon: Oxford, 1993.
2. Miyaoka, H.; Shigemoto, T.; Shinohara, I.; Suzuki, A.; Yamada, Y. *Tetrahedron* **2000**, *56*, 8077–8081.
3. Miyaoka, H.; Tamura, M.; Yamada, Y. *Tetrahedron Lett.* **1998**, *39*, 621–624.
4. Miyaoka, H.; Tamura, M.; Yamada, Y. *Tetrahedron* **2000**, *56*, 8083–8094.
5. Miyaoka, H.; Shigemoto, T.; Yamada, Y. *Tetrahedron Lett.* **1996**, *37*, 7407–7408.
6. Miyaoka, H.; Shigemoto, T.; Yamada, Y. *Heterocycles* **1998**, *47*, 415–428.
7. Kashman, Y.; Hirsch, S.; Koehn, F.; Cross, S. *Tetrahedron Lett.* **1987**, *28*, 5461–5464.
8. Peng, J.; Walsh, K.; Weedman, V.; Bergthold, J. D.; Lynch, J.; Lieu, K. L.; Braude, I. A.; Kelly, M.; Hamann, M. T. *Tetrahedron* **2002**, *58*, 7809–7819.
9. Iguchi, K.; Fujita, M.; Nagaoka, H.; Mitome, H.; Yamada, Y. *Tetrahedron Lett.* **1993**, *34*, 6277–6280.
10. Abouabdellah, A.; Bonnet-Delpon, D. *Tetrahedron* **1994**, *50*, 11921–11932.
11. Browder, C. C.; Marmsaeter, F. P.; West, F. G. *Org. Lett.* **2001**, *3*, 3033–3035.