δ 1.13 (d, J = 8 Hz, 3 H), 1.42–1.56 (m, 1 H), 2.13–2.27 (m, 1 H), 2.33–2.50 (m, 1 H), 2.50–2.63 (m, 1 H), 2.87–3.04 (m, 1 H), 6.73 (dd, J_1 = 4.0, J_2 = 2.0 Hz, 1 H), 9.75 (s, 1 H).

2,8,8-Trimethyl-2,3-oxa-7,9-dioxalcyclo[4.3.0]non-4-ene (4a). To a mixture of **13**[3] (200 mg, 1.2 mmol) in 1,2-dichloroethane (8 mL) and borax buffer pH 8 (10 mL) was added MCPBA (80% purity, 250 mg, 1.2 mmol) at room temperature. The reaction was stirred overnight and then diluted with $CHCl_3$ (1 × 15 mL). The solution washed with saturated Na_2SO_3 (1 × 10 mL), saturated $NaHCO_3$ (1 × 10 mL), and H_2O (1 × 10 mL) and dried over Na_2SO_4, and solvent was evaporated to give crude **4a**. Column chromatography (10% deactivated silica, hexane/ethyl acetate, 90:10) gave 73 mg (40%) of pure **4a**: R_f 0.3 (hexane/ethyl acetate, 3:1); IR (neat) 3030, 2980, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (s, 6 H), 1.50 (s, 3 H), 3.12 (d, J = 4 Hz, 1 H), 4.48 (s, 2 H), 5.68 (dd, J_1 = 10, J_2 = 2 Hz, 1 H), 5.94 (ddd, J_1 = 10, J_2 = 4, J_3 = 2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.4 (CH_3), 26.2 (CH_3), 27.9 (CH_3), 53.9 (CH), 72.4 (CH), 75.1 (CH), 110.1 (C), 123.3 (CH), 132.5 (CH); mass spectrum (70 eV), m/e (relative intensity) 167 (2), 156 (24), 139 (90), 111 (52), 73 (100); calcd for $C_9H_{11}O_3$ (M − 15) 167.0708, found 167.0681.

Acknowledgment. We acknowledge generous financial support by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the NIH (Grant AI-00564). We also thank Professor D. T. Gibson for providing us with the initial cultures of Pp-39D.

Registry No. 1, 41977-20-2; **2b**, 114763-34-7; **4a**, 114763-41-6; **5**, 104010-72-2; **6**, 114818-65-4; **7**, 114818-64-3; **9**, 592-57-4; **10**, 1700-10-3; **12**, 114818-66-5; **13**, 114763-30-3; **14**, 4216-41-5; **15**, 105582-16-9; **17**, 114763-37-0; **18**, 114763-38-1; **19**, 638-37-9; **20**, 1072-21-5; **21**, 61031-76-3; **22a**, 114763-31-4; **22b**, 114763-35-8; **22c**, 114763-36-9; **23**, 114763-32-5; **24**, 114763-33-6; **25a**, 41977-21-3; **25b**, 41977-22-4; **26a**, 114763-39-2; **26b**, 114763-40-5; **28**, 65986-73-4; **29**, 114763-28-9; **30**, 114763-29-0; toluene, 108-88-3; chlorobenzene, 108-90-7; vinylbenzene, 100-42-5; phenylacetylene, 536-74-3.

Enantioselective Total Synthesis of (+)-12,13-Epoxytrichothec-9-ene and Its Antipode†,[1]

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Contribution from the Department of Chemistry, Kansas State University, Manhattan, Kansas 66506. *Received November 9, 1987*

Abstract: The 1,4-addition reactions of the anions derived from various cyclic allylic sulfoxides and 2-cyclopentenones were examined. Methyl substitution at C-3 of 2-cyclopentenones hinders the 1,4-addition. The activated enone, 2-(methoxycarbonyl)-3-methyl-2-cyclopentenone (**4**), however, afforded excellent chemical and optical yields of the 1,4-adducts. (+)-12,13-Epoxytrichothec-9-ene [(+)-**1**] and its antipode (−)-**1** were enantioselectively synthesized from (*S*)-(−)-4-methyl-2-cyclohexenone in 11 steps.

The intense interest in trichothecenes[3] stems from the fact that many of the trichothecenes, especially the macrocyclic trichothecene esters, exhibit a wide range of significant biological activities, including antibiotic, antifungal, and particularly antitumor properties. A variety of synthetic studies of trichothecenes has been reported;[4] however, only one deals with the synthesis of an optically active trichothecene, anguidine.[4a] As part of our continuing studies to utilize the enantioselective 1,4-addition reactions of chiral sulfinylallyl anions with cyclic enones,[5] the synthesis of the family of trichothecenes was undertaken. Herein, we report the full account of the first synthesis of optically pure (+)-12,13-epoxytrichothec-9-ene [(+)-**1**][6] and its antipode (−)-**1**.

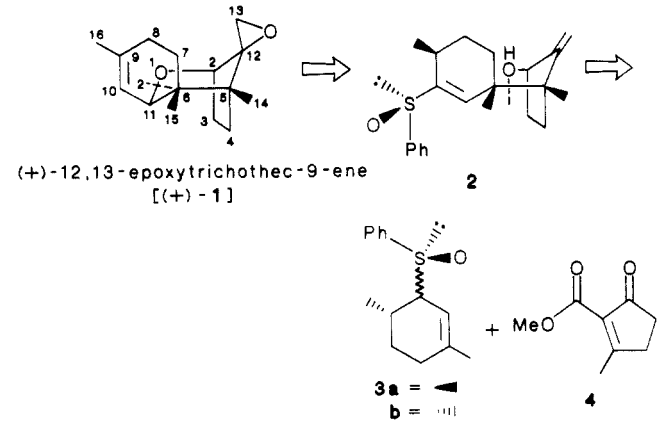
Results and Discussion

A convergent synthesis of the trichothecene skeleton is assembled from the addition of an A-ring unit to a C-ring unit followed by an intramolecular cyclization providing the B ring (Scheme I). We expect bond 1 in structure **2** could be formed via the conjugate addition of a *trans*-sulfinylallyl anion to an enone. Bond 2 would be contructed via the intramolecular Michael-type reaction of the hydroxyl and α,β-unsaturated sulfoxide moieties.[7]

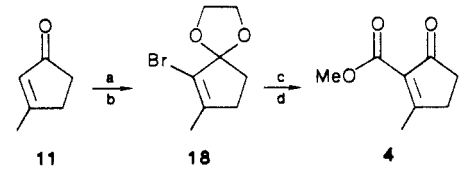
The scope of the 1,4-addition reactions of various racemic cyclic allylic sulfoxides and cyclopentenones was examined first. The results are summarized in Table I. The general procedure for these reactions consists in treating the sulfoxide with 1 equiv of lithium diisopropylamide (LDA) in THF at −78 °C for 1 h, and then treating this solution with 1 equiv of the cyclic enone at −78 °C. The relative stereochemistry is predicted from earlier results.[5,8,9]

Racemic sulfoxide **6** was prepared from 3-methyl-2-cyclohexen-1-ol in a two-stage reaction sequence: (i) tosylation with CH_3Li and *p*-toluenesulfonyl chloride (TsCl) followed by displacement with sodium benzenethiolate and (ii) oxidation of the resulting sulfide with 1 equiv of 30% H_2O_2 in acetic acid (AcOH).

Scheme I



Scheme II[a]



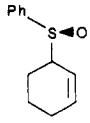
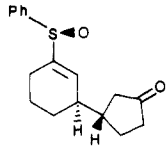
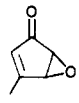
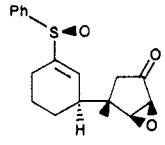
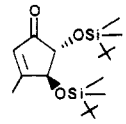
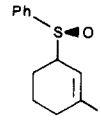
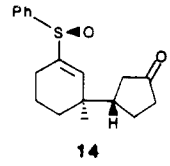
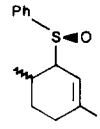
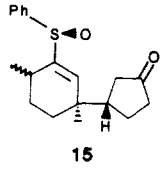
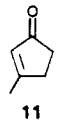
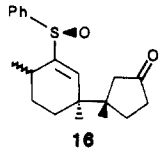
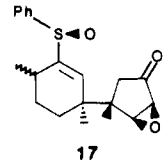
[a] (a) Br_2/Et_3N, CCl_4; (b) ethylene glycol, H^+; (c) *n*-BuLi, $ClCO_2Me$; (d) $(CO_2H)_2$, THF, H_2O.

† This paper is dedicated to E. J. Corey on the occasion of his 60th birthday.

(1) Part of this work is taken from the Ph.D. Dissertation of S. Venkataraman, Kansas State University.

0002-7863/88/1510-4741$01.50/0

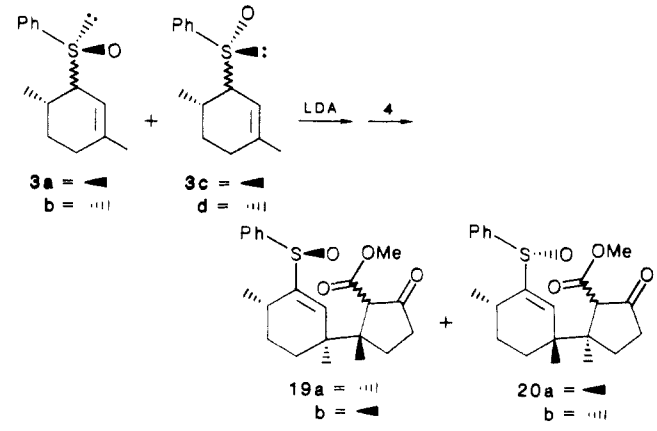
Table I

entry	racemic sulfoxide	enone	1,4-adduct	% yield[a]
1	 **5**	 **8**	 **12**	50
2	**5**	 **9**	 **13**	15
3	**5**	 **10**	none	
4	 **6**	**8**	 **14**	60
5	**6**	**9**	none	
6	 **7**	**8**	 **15**	61
7	**7**	 **11**	 **16**	5
8	**7**	**9**	 **17**	5

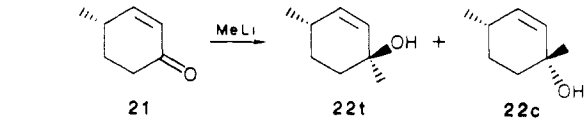
[a] Starting sulfoxides and enones were also recovered.

By the same method, racemic sulfoxide **3** was made from 3,6-dimethyl-2-cyclohexen-1-ol.

Scheme III

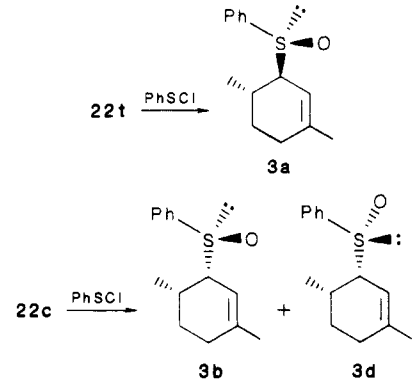


Scheme IV



Scheme V

Scheme VI



The results shown in Table I clearly indicate that the presence of a methyl group at the C-3 of 2-cyclopentenones prevents the addition reactions. Raising the reaction temperature (to −50 or −30 °C) leads to decomposition of the sulfinylallyl anions. Presumably, this C-3 methyl group sterically hinders the 1,4-addition.[10]

(2) To whom correspondence should be addressed.

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(6) Isolation of **1**: (a) Machida, Y. Nozoe, S. *Tetrahedron* **1972**, *28*, 5113. Trichothecene **1** was isolated from the mycelium as an oil in extremely minute amount, and the optical rotation was not reported. Synthesis of (±)-**1**: (b) Fujimoto, Y.; Yokura, S.; Nakamura, T.; Morikawa, T.; Tatsuno, T. *Tetrahedron Lett.* **1974**, 2523. (c) Masuoka, N.; Kamikawa, T. *Tetrahedron Lett.* **1976**, 1691.

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(9) The 1,4-addition reactions of cyclic allylic sulfoxides of this type and cyclic enones has not been reported previously.

To circumvent this problem, the activated enone, i.e., **4**, was used as the substrate for the 1,4-addition reaction. Enone **4** was prepared from **11** by following the method of Smith et al.[11] (Scheme II) in a four-step reaction sequence: (i) bromination with Br_2 in CCl_4 followed by dehydrobromination with Et_3N, (ii) ketalization with ethylene glycol and *p*-TsOH in refluxing benzene,[12] (iii) lithiation with *n*-BuLi in THF followed by carbomethoxylation with methyl chloroformate, and (iv) deprotection with oxalic acid in THF and H_2O.

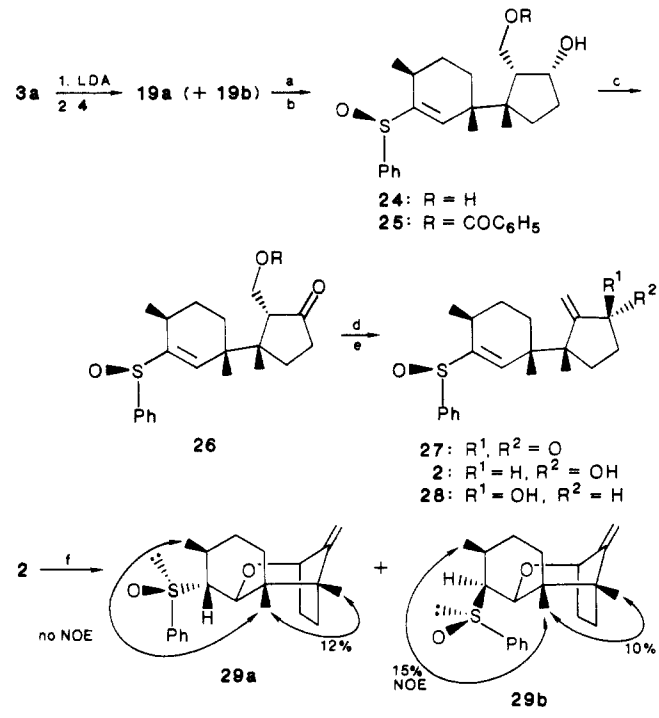
Addition of the sulfinylallyl anion [derived from the reaction of racemic sulfoxides **3** (total of four diastereomers) with LDA] to enone **4** afforded 87% yield (based on unrecovered starting sulfoxides; 30% starting sulfoxide was recovered) of two racemic 1,4-adducts **19a** and **20a**, and 5% of their C-12 epimers (**19b** and **20b**; Scheme III). The relative stereochemistries at sulfur, C-5, -6, -9, and -12 were determined in the studies using chiral sulfoxides **3** (vide infra). Adduct **19a** and **20a** are separable by column chromatography. This promising result encouraged us to use the optically active sulfoxides **3a** and **3b**. The sulfenate rearrangement[5f,13] was applied in the synthesis of these optically active sulfoxides.

Treatment of (*S*)-(−)-4-methyl-2-cyclohexen-1-one (**21**)[14] with methyllithium in ether provided 1,2-adducts **22t** and **22c** (2.2:1) in 92% yield (Scheme IV). The formation of the trans alcohol **22t** as the major product agrees with the results of Reich and Wollowitz who used aryllithium.[13] The cis alcohol **22c** was reported by Marino and Abe,[15] but their ^1H NMR data[15] are not sufficient to distinguish between **22t** and **22c**. To firmly establish the stereochemistry, **22t** and **22c** were separately subjected to hydrogenation to produce the known alcohols **23t** and **23c**[16] (Scheme V).

Treatment of pure **22t** with 1.2 equiv of benzenesulfenyl chloride[13] and 2.4 equiv of Et_3N in benzene[5f] gave 80% yield of a single sulfoxide, **3a** (Scheme VI). *S*(*R*)-**3c** was not detected under these conditions.[17] The absolute configuration at sulfur of **3a** was determined from ^1H NMR NOE experiments with **29a** and **29b** (vide infra). On the other hand, the reaction of pure **22c** with PhSCl–Et_3N in benzene gave an 1:1 mixture of **3b** and **3d** (78% yield). Because of the thermal decomposition[18,5f] of these types of allylic sulfoxides, **3a**, **3b**, and **3d** were used in next reactions without delay. At room temperature, **3a** is not converted into **3c**. The reverse reaction of the allyl sulfenate–allyl sulfoxide rearrangement[13] in this type of cyclic system is relatively slow.[19]

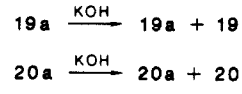
Reduction of **3a**, **3b**, and **3d** (4:1:1) with Zn–AcOH provided the corresponding sulfides, and oxidation of these sulfides with 1 equiv of 50% H_2O_2 in AcOH at 0–5 °C gave mixture of sulfoxides **3a–d** (2:1:2:1).

Scheme VII[a]



[a] (a) $LiBH_4$, THF; (b) PhCOCN, Et_3N; (c) PCC; (d) DBN, toluene; (e) $CeCl_3 \cdot 7H_2O$, $NaBH_4$, MeOH; (f) KOH, *t*-BuOH.

Scheme VIII



Addition of the sulfinylallyl anion (derived from the reaction of sulfoxide **3a** with 1 equiv of LDA in THF at −78 °C) to 1 equiv of enone **4** in THF at −78 °C and maintaining the mixture for 15 min afforded 93% yield (isolated; based on unrecovered starting sulfoxide, 30% of which was recovered) of adducts **19a** and **19b** (ratio of 93:7) (Scheme VII). The stereochemistry at C-12 of **19a** and **19b** were presumed on the basis of our earlier findings that in the pentalenolactone E synthesis[5g] the acid (AcOH; −78 °C) approaches the enolate ion (resulting from 1,4-γ-addition) predominantly from the opposite side of the bulkier cyclohexenyl group. Pure adduct **19a**, when treated with 0.2 equiv of KOH in MeOH at 0 °C for 15 min, provided an 1:1 mixture of **19a** and **19b** in 98% yield (Scheme VIII). Similarly, isomerization of pure adduct **20a** [obtained from column chromatographic separation of the 1,4-adducts from the reaction of mixture of **3b** and **3d**, and enone **4** (**19a** was formed from **3b**)] with KOH gave a mixture of **20a** and **20b** (1:1) in 97% yield. It should be noted that same product distributions (**19a**:**19b** or **20a**:**20b**) were obtained either with optically active sulfoxides (e.g., pure 3a) or with a mixture of racemic sulfoxides as starting materials (see Scheme III) and that the diastereomers with the opposite stereochemistry at C-5 and C-6 were not isolated. Less than 5% of a mixture of compounds, having similar R_f values and ^1H NMR spectral properties, was separated from column chromatography of the crude 1,4-adduct; however, a pure compound could not be obtained for identification. In practice, a mixture of sulfoxides **3a**, **3b**, and **3d** can be used in the addition reaction with enone **4** to provide adducts **19a**, **19b**, **20a**, and **20b**. Pure **19a** (least polar) and pure **20a** (most polar) can be separated and isolated by column chromatography.

Reduction of **19a** with lithium borohydride in THF at 25 °C produced diol **24** in 67% yield along with 16% recovered starting **19a** (Scheme VII). Only starting material was recovered in our attempts (*t*-BuOK–*t*-BuOH, 80 °C) to form the tetrahydropyran ring (forming bond 2; Scheme I) from the C-13 monobenzyloxy

(10) Also, electronic effect of C-3 methyl group of cyclic enones decreases the reduction potential. The E_{red} value of 3-methyl-2-cyclopentenone is predicted to be about −2.3 V: (a) House, H. O.; Huber, L. E.; Umen, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 8471. (b) House, H. O.; Wilkins, J. M. *J. Org. Chem.* **1978**, *43*, 2443. Both steric and electronic effects work against the 1,4-addition.

(11) (a) Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B. III *Tetrahedron Lett.* **1978**, 4661. (b) Smith, A. B. III; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. M.; Korn, A. *Org. Synth.* **1983**, *61*, 65.

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(15) Marino, J. P.; Abe, H. *J. Org. Chem.* **1981**, *46*, 5379.

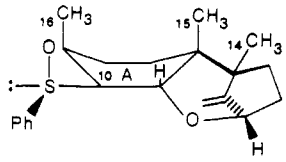
(16) (a) Senda, Y.; Ishiyama, J.; Imaizumi, S. *Tetrahedron* **1975**, *31*, 1601. (b) Grenier-Loustalot, M. F.; Zahidi, A.; Bonastre, J.; Grenier, P. *Bull. Chim. Soc. Fr.* **1979**, 229. The ^{13}C NMR chemical shifts of the C-1 bearing an equatorial OH group in 3- and 4-substituted 1-methylcyclohexanols showed the resonances at about 70.56 ppm and those of isomeric counterparts at about 68.80 ppm. We have independently prepared **23t** from the ozonolysis of *cis*-1,4-dimethylcyclohexane absorbed on silica gel[16c] (this method provided only **23t**) and **23c** from *trans*-1,4-dimethylcyclohexane.[16c] The ^{13}C NMR data of these alcohols obtained from ozonation show that the above ^{13}C NMR chemical shift predictions are correct. (c) Cohen, Z.; Keinan, E.; Mazur, Y.; Varkony, T. H. *J. Org. Chem.* **1975**, *40*, 2141.

(17) The ^1H and ^{13}C NMR spectra of **3a**, **3b**, **3c**, and **3d** are all different. The mechanism of this sulfenate–sulfoxide [2,3] sigmatropic rearrangement is being studied.

(18) Snider, B. B. *J. Org. Chem.* **1981**, *46*, 3155.

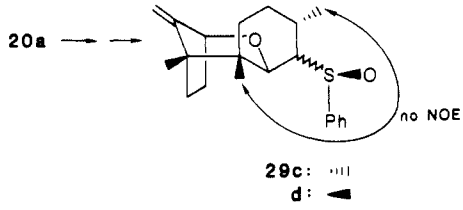
(19) The rate of the rearrangement reaction from allylic sulfoxides to allylic sulfenates in these cyclic systems has not been reported.

Scheme IX



29b

Scheme X



29c: ···|
d: ◄

derivative of **24** (obtained from the monobenzylation of **24** with NaH and 1 equiv of benzyl bromide). Presumably, the C-12 (benzyloxy)methyl group internally hinders attack of the C-2 alkoxide on C-11 of the C_{10}=C_{11}. Providing a double bond between C_{12} and C_{13} might circumvent this problem.

Selective monobenzoylation of **24** with 1.0 equiv of benzoyl cyanide and 0.1 equiv of Et_3N in CH_3CN at −10 °C[20] afforded 70% yield of monobenzoate **25** and 17% recovery of diol **24**. Oxidation of **25** with 1.4 equiv of pyridinium chlorochromate (PCC) in CH_2Cl_2[21] generated ketone **26** in 84% yield. Dehydrobenzoylation of **26** to enone **27** was effected with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in toluene at 80 °C for 1.5 h (82% yield). 1,2-Reduction of enone **27** with $CeCl_3 \cdot 7H_2O$ and $NaBH_4$ in methanol[22] at −10 °C produced 92% yield of a mixture of alcohol **2** and **28** (ratio of 9:1). When the reducing reagent diisobutylaluminum hydride (in toluene at −78 °C) was used, 51% of a 1:1 mixture of these alcohols along with 20% of the 1,4-reduction product were obtained. Alcohols **2** and **28** could not be separated and were used in the next cyclization reaction. Alcohol **2** underwent ring closure (intramolecular Michael-type reaction) when treated with KOH in *t*-BuOH under reflux for 3 h to give 84% yield of tricyclic ethers **29a** and **29b** (ratio of 3:1), which were separated by column chromatography. Alcohol **28** was unaffected and was recovered (91%) from the mixture, and reoxidized to ketone **27** with PCC in CH_2Cl_2 (85% yield). The stereochemistry and structures of **29a** and **29b** were fully confirmed by ^1H NMR NOE, 2D NOESY, 2D COSY, and 2D *J*-resolved experiments and by their transformation to (+)-12,13-epoxytrichothec-9-ene [(+)-**1**] (vide infra). The NOE studies on **29b** were especially helpful in the assignment of the stereochemistry at sulfur of sulfoxide **3a**. Irradiation at the upfield methyl singlet (C-15) of **29b** induced 15% signal enhancement in the C-16 methyl doublet and 10% in the C-14 methyl singlet (also confirmed by 2D NOESY). With **29a**, irradiation either at upfield singlet C-15 (8% signal enhancement of C-11 H; 12% enhancement of C-14 methyl) or at downfield singlet C-14 induced no signal enhancement in the C-16 methyl (also confirmed by 2D NOESY). The induced NOE between C-15 and C-16 in **29b** can be realized readily from its molecular model (Scheme IX). The all-cis juxtaposition of C-15 methyl, C-16 methyl, and C-10 phenylsulfinyl forces the cyclohexane (A) ring of **29b** to maintain the skew-boat conformation. This conformation allows the C-10 phenylsulfinyl group to assume an equatorial position, thereby avoiding the 1,3-diaxial interaction with C-15 methyl, which would arise in the chair conformation. Hence, the 1,4-diaxial interaction between the C-15 and C-16 methyls in the skew-boat conformation would provide a large NOE effect.

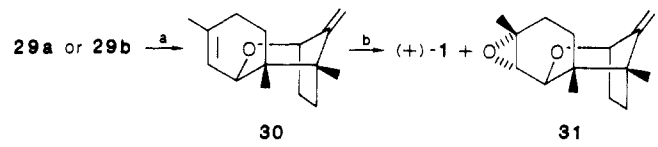
1,4-Adduct **20a** was also converted into tricyclic ethers **29c** and **29d** (Scheme X) by the identical sequence of reactions described above (Scheme VII). The NOE studies performed on both **29c** and **29d** indicated no NOE between the C-15 and C-16 methyls.

The absolute configuration at C-9 in **29b** allows us to deduce the absolute configuration of all chiral centers in **29b** from the above NMR experiments. The absolute stereochemistry of **29a** and **29b** match those of verrucarin A.[23]

Finally, (+)-12,13-epoxytrichothec-9-ene [(+)-**1**] was obtained by a two-step reaction sequence (Scheme XI): (i) dehydrosulfenylation[5f,24] of **29a** and/or **29b** (independently or as a mixture) with 1,4-diazabicyclo[2.2.2]octane (Dabco) in 1,3,5-trimethylbenzene at 250 °C in a sealed tube (70% yield of **30**) and (ii) selective monoepoxidation of the resulting diene with 1.0 equiv of *m*-chloroperbenzoic acid (MCPBA) and Na_2HPO_4 in CH_2Cl_2[6b,c] [50% yield of (+)-**1**, 30% yield of isomeric 9,10-epoxide **31**, 10% yield of the 9,10- and 12,13-diepoxide, and 8% recovery of **30**]. The spectral properties (NMR and IR) of **30** and (+)-**1** were identical with those of authentic materials.[25] The epoxide moiety at C-9 and C-10 of **31** are assumed to orient at the β face. This orientation is the same as that in trichothecene triepoxide baccharin.[23c] In fact, the ^1H NMR chemical shifts of C-14 and C-16 methyls of **31** are similar to those of baccharin.

Antipode (−)-**1** was also synthesized from **29c** and **29d** as described above.

Scheme XI[a]



30 31

[a] (a) Dabco, 1,3,5-trimethylbenzene; (b) MCPBA.

Conclusions

The utility of the asymmetric induction reaction of chiral sulfinylallyl anions with enones has de novo been extended to another skeletal class. The method leading to the total synthesis of (+)-12,13-epoxytrichothec-9-ene [(+)-**1**] is stereocontrolled, short, and effective and should be applicable to the construction of other highly oxidized members of optically pure trichothecenes.

The intramolecular anionic ring closure utilizing the C-2 hydroxyl and α,β-unsaturated sulfoxide moieties has further demonstrated the use of sulfoxides in organic synthesis. The synthetic route detailed here should provide access to many interesting chiral intermediates for evaluation of biological activity[26] and assessment of structure–activity relationships.

Experimental Section

Nuclear magnetic resonance spectra were obtained in deuteriochloroform on a Bruker WM-400 (400 MHz in ^1H and 100 MHz in ^{13}C) spectrometer and are reported in ppm (δ units) downfield of internal tetramethylsilane. Infrared spectra were recorded on a Perkin-Elmer 1330 spectrophotometer and are reported in wavenumbers (cm^{-1} units). Mass spectra were determined on a Finnigan 4000 automated gas chromatograph/EI-CI mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

3-(Phenylsulfinyl)-1-cyclohexene (5): IR (neat) 3040, 2950, 2920, 1650, 1040 cm^{-1}; ^1H NMR δ 7.7–7.6 (m, 2 H, Ar H), 7.5 (m, 3 H, Ar H), 6.13 (dt, *J* = 12, 2 Hz, 0.5 H, =CH), 6.02 (dt, *J* = 12, 2 Hz, 0.5 H, =CH), 5.65 (dd, *J* = 12, 3 Hz, 0.5 H, SCCH=), 5.15 (dd, *J* = 12, 3 Hz, 0.5 H, SCCH=), 3.36 (m, 0.5 H, CHS), 3.29 (m, 0.5 H, CHS), 2.4–1.6 (m, 6 H); MS, *m/z* 206 (M^+).

(20) Tanaka, M. *Tetrahedron Lett.* **1980**, *21*, 2959.
(21) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(22) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.

(23) Absolute stereochemistry of verrucarin A, a trichothecene, has been established from X-ray analysis: (a) McPhail, A. T.; Sim, G. A. *J. Chem. Soc. C* **1966**, 1394. X-ray analysis of the relative stereochemistry of trichodermin and baccharin: (b) Abrahamsson, S.; Nilsson, B. *Acta Chem. Scand.* **1966**, *20*, 1044. (c) Kupchan, S. M.; Jarvis, B. B.; Dailey, R. G. J.; Bright, W.; Bryan, R. F.; Shizuri, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7092.
(24) Goldberg, S. I.; Sahli, M. S. *J. Org. Chem.* **1967**, *32*, 2059.
(25) The NMR and IR spectra of **1** and **30** were provided by Professor Yasuo Fujimoto of Riken, Japan.
(26) Diol **24** has shown significant inhibitory activity in vitro against P-388 (LD_{50} = 10 μg/mL). The studies of the cytotoxic activity of these synthetic intermediates will be discussed subsequently.

Because of the sensitivity[18] of these types of allylic sulfoxides to thermal decomposition even at room temperature, sulfoxides **3**, **5**, and **6** were not submitted for elemental analysis.

1-Methyl-3-(phenylsulfinyl)-1-cyclohexene (6): IR (neat) 1652, 1045 cm^{-1}; ^1H NMR δ 7.5–7.6 (m, 2 H, ortho H), 7.4–7.5 (m, 3 H, meta and para H), 5.37 (s, 0.6 H, =CH), 4.84 (s, 0.4 H, =CH), 3.30 (s, 0.6 H, CHS), 3.21 (s, 0.4 H, CHS), 1.68 (s, 2 H, $=CCH_3$), 1.62 (s, 1 H, $=CCH_3$), 1.4–2.3 (m, 6 H); ^{13}C NMR δ 143.0, 142.7, 142.2, 130.7, 130.6, 128.5, 124.9, 124.6, 114.0, 113.5, 63.4, 61.9, 29.5, 29.3, 23.9, 23.8, 22.5, 20.7, 20.0, 19.0; MS, m/z 220 (M^+).

2,3-Epoxy-4-methyl-4-cyclopentenone (9). This enone, not previously reported, was prepared in a four-stage reaction sequence: (i) deprotection of 4-(cumyloxy)-1-methyl-2-cyclopenten-1-ol[27] with Na–liquid NH_3, (ii) oxidation of resulted 1-methyl-2-cyclopentene-1,4-diol with pyridinium chlorochromate (PCC) in CH_2Cl_2, (iii) epoxidation of the resulting enone with NaOH–30% H_2O_2, and (iv) dehydration with methanesulfonyl chloride (MsCl) and Et_3N.

1-Methyl-2-cyclopentene-1,4-diol. To a cold solution (−35 °C) of 2.6 g (11.2 mmol) of 4-(cumyloxy)-1-methyl-2-cyclopenten-1-ol[27] in 50 mL of ammonia and 5 mL of ethanol was added 0.515 g (22.4 mmol) of Na in small portions over 10 min. After the mixture was stirred for 5 min, 10 mL of ethanol was added. Ammonia was evaporated, and 1.29 g (22.4 mmol) of acetic acid was added. Since this diol is highly water-soluble, aqueous workup was avoided. The mixture was dissolved in methylene chloride and column chromatographed on silica gel, with hexanes, ethyl acetate, and ethanol as eluents to give 1.13 g (89%) of the diol: IR (neat) 3400, 1650 cm^{-1}; ^1H NMR δ 5.81–5.86 (m, 2 H, =CH), 4.64–4.67 (m, 1 H, CHO), 2.37 (dd, J = 7.2, 14.4 Hz, 1 H, CH_2), 1.79 (dd, J = 14.4, 3.2 Hz, 1 H, CH_2), 1.33 (s, 3 H, CH_3); ^{13}C NMR δ 141.0, 134.0, 81.1, 75.1, 49.5, 27.6; MS, m/z 114 (M^+). Anal. Calcd for $C_6H_{10}O_2$: C, 63.14; H, 8.83. Found: C, 63.01; H, 9.07.

4-Hydroxy-4-methyl-2-cyclopenten-1-one. To a mixture of 11.4 g (0.1 mol) of the alcohol in 550 mL of CH_2Cl_2 were added 70 g of 3A molecular sieves and 43 g (0.2 mol) of PCC. The mixture was stirred at 25 °C for 3 h, diluted with ether, and filtered through Celite. The filtrate was passed through a Florisil column and eluted with ether. The solvent was removed by simple distillation, leaving the crude product, which was purified on a chromatographic column to give 7.5 g (67% yield) of the enone: IR (neat) 3300, 1700, 1610 cm^{-1}; ^1H NMR δ 7.43 (d, J = 5.6 Hz, 1 H, =CH), 6.10 (d, J = 5.6 Hz, 1 H, =CH), 2.54 (s, 2 H, CH_2), 1.55 (s, 3 H, CH_3); ^{13}C NMR δ 207.1, 166.8, 132.7, 76.5, 50.6, 27.6; MS, m/z 112 (M^+).

2,3-Epoxy-4-hydroxy-4-methylcyclopentan-1-one. To a cold solution (15–20 °C) of 6.75 g (60 mmol) of the enone in 60 mL of MeOH was added 20.5 mL of 30% H_2O_2. To this mixture was added 5 mL of 6 N NaOH over a 40-min period while the temperature of the mixture was maintained between 15 and 20 °C. The mixture was then stirred at 20–25 °C for an additional 2.5 h, diluted with brine, and extracted with 3000 mL of CH_2Cl_2 in 150-mL portions. The combined organic extracts were dried ($MgSO_4$), concentrated, and column chromatographed to give 5 g (65% yield) of the epoxy ketone: ^1H NMR δ 3.78 (d, J = 2.3 Hz, 1 H, OCHC=O), 3.52 (d, J = 2.3 Hz, 1 H, CHO), 2.45 (d, J = 17.6 Hz, 1 H, CH_2), 2.20 (d, J = 17.6 Hz, 1 H, CH_2), 1.40 (s, 2 H, CH_3), 1.25 (s, 1 H, CH_3); ^{13}C NMR δ 205.0, 72.5, 63.5, 57.7, 46.6, 29.7, 24.2; MS, m/z 128 (M^+).

2,3-Epoxy-4-methyl-4-cyclopentenone (9). To a cold solution (0 °C) of 0.17 g (1.3 mmol) of the above epoxy ketone in 12 mL of ether was added 0.74 mL (5.3 mmol) of triethylamine followed by 0.31 mL (3.98 mmol) of methanesulfonyl chloride. After the mixture was stirred for 30 min at 25 °C, it was poured into water and extracted three times with ether. The combined ether extracts were washed with water and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 80 mg (55% yield) of epoxy enone **9**: IR (neat) 1700, 1615 cm^{-1}; ^1H NMR δ 5.68 (s, 1 H, =CH), 3.92 (s, 1 H, O=CCHO), 3.65 (s, 1 H, CHO), 2.23 (s, 3 H, CH_3); ^{13}C NMR δ 199, 169.7, 128.1, 55.9, 52.3, 17.8; MS, m/z 110 (M^+). Anal. Calcd for $C_6H_6O_2$: C, 65.45; H, 5.49. Found: C, 65.27; H, 5.61.

The following example serves as the general procedure for the reactions of sulfoxides (**5**, **6**, and **3**) with cyclic enones (Table I).

3-(3-Oxocyclopentyl)-1-(phenylsulfinyl)cyclohex-1-ene (12). To a cold (−78 °C) solution of 0.8 g (3.9 mmol) of sulfoxide **5** in 20 mL of THF was added a cold (−78 °C) solution of LDA (4.27 mmol) in 20 mL of THF via cannula. After the resulting yellow solution was stirred at −78 °C for 30 min, 0.7 mL (4.0 mmol) of HMPA was added, followed after 5 min by the addition of 0.320 g (3.9 mmol) of 2-cyclopentenone, and the solution was stirred at −78 °C for 15 min. After a solution of 0.26 mL (4.2 mmol) of acetic acid (AcOH) in 2 mL of ether was added, the solution was warmed to 25 °C, diluted with aqueous NH_4Cl, and extracted three times with ether. The combined extracts were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.562 g (50% yield) of **5**: IR (neat) 1710, 1600, 1035 cm^{-1}; ^1H NMR δ 7.7–7.6 (m, 2 H, Ar H), 7.4–7.5 (m, 3 H, Ar H), 6.53 (s, 1 H, =CH), 2.5–1.6 (m, 14 H); ^{13}C NMR δ 217.8, 145.26, 142.92, 133.56, 130.90, 129.14, 124.92, 42.79, 41.63, 41.14, 38.54, 27.36, 26.55, 21.18, 20.89; MS, m/z 288 (M^+). Anal. Calcd for $C_{17}H_{20}O_2S$: C, 70.80; H, 6.99; S, 11.12. Found: C, 70.52; H, 7.17; S, 10.83.

3-(2,3-Epoxy-1-methyl-4-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (13): IR (neat) 1710, 1600, 1042 cm^{-1}; ^1H NMR δ 7.4–7.6 (m, 5 H, Ar H), 6.50 (s, 1 H, =CH), 3.7 (s, 1 H, O=CCHO), 3.5 (s, 1 H, CHO), 1.3 (s, 3 H, CH_3), 1.2–2.5 (m, 9 H); MS, m/z 316 (M^+).

3-Methyl-3-(3-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (14): IR (neat) 1705, 1602, 1045 cm^{-1}; ^1H NMR δ 7.57–7.58 (m, 2 H, ortho H), 7.50–7.57 (m, 3 H, meta and para H), 6.43 (s, 1 H, =CH), 1.10 (s, 3 H, CH_3), 1.0–2.5 (m, 13 H); ^{13}C NMR δ 218.07, 143.7, 142.8, 136.8, 131.0, 129.1, 124.9, 46.9, 40.1, 38.7, 37.6, 32.6, 24.4, 23.8, 21.3, 19.1; MS, m/z 302 (M^+). Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.49; H, 7.33. Found: C, 71.17; H, 7.58.

3,6-Dimethyl-3-(3-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (15): IR (neat) 1712, 1600, 1037 cm^{-1}; ^1H NMR δ 7.4–7.7 (m, 5 H, Ar H), 6.49 (s, 0.5 H, =CH), 6.35–6.45 (2 s, 0.2 H, =CH), 6.32 (s, 0.3 H, =CH), 1.14 (s, 1.5 H, CH_3), 1.06 (s, 0.9 H, CH_3), 1–2.5 (m, 12.6 H); MS, m/z 316 (M^+). Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.11; H, 7.64. Found: C, 71.83; H, 7.85.

3,6-Dimethyl-3-(1-methyl-3-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (16): IR (neat) 1706, 1601, 1038 cm^{-1}; ^1H NMR δ 7.6–7.7 (m, 2 H, ortho H), 7.4–7.6 (m, 3 H, meta and para H), 6.65 (s, 1 H, =CH), 1.12 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.08 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR δ 219.0, 147.2, 143.5, 132.7, 131.6, 129.5, 125.9, 48.3, 46.2, 40.8, 36.4, 30.6, 30.0, 29.5, 21.5, 21.4, 19.4; MS, m/z 330 (M^+). Anal. Calcd for $C_{20}H_{26}O_2S$: C, 72.69; H, 7.93. Found: C, 72.29; H, 8.17.

3,6-Dimethyl-3-(2,3-epoxy-1-methyl-4-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (17): ^1H NMR δ 7.4–7.7 (m, 5 H, Ar H), 6.55 (s, 0.5 H, =CH), 6.33 (s, 0.5 H, =CH), 3.72 (d, J = 2.1 Hz, 0.6 H, O=CCHO), 3.67 (d, J = 2.1 Hz, 0.4 H, O=CCHO), 3.4–3.7 (s, 1 H, CHO), 2.23 (d, J = 18.4 Hz, 1 H, CH_2), 2.01 (d, J = 18.4 Hz, 0.6 H, CH_2), 1.98 (d, J = 18.6 Hz, 0.4 Hz, CH_2), 1.36 (s, 1.8 H, CH_3), 1.34 (s, 1.2 H, CH_3), 1.13 (s, 1.2 H, CH_3), 1.10 (d, J = 6.7 Hz, 1.5 H, CH_3), 1.03 (s, 1.8 H, CH_3), 0.95 (d, J = 7.0 Hz, 1.5 H, CH_3). MS, m/z 344 (M^+).

2-(Methoxycarbonyl)-3-methyl-2-cyclopenten-1-one (4). To a cold solution (−78 °C) of 5 g (22.8 mmol) of 2-bromo-3-methyl-2-cyclopentenone ethylene ketal (**18**)[11] in 250 mL of THF was added 18.6 mL (29.6 mmol) of *n*-BuLi (1.6 M in hexane). After the solution was stirred at −78 °C for 45 min, 5.3 mL (68.5 mmol) of methyl chloroformate was added, and the mixture stirred at −78 °C for 30 min and at 25 °C for 15 min. The mixture was diluted with ether and poured into 200 mL of 20% aqueous solution of Na_2HPO_4, and the organic layer was separated. The aqueous layer was again extracted twice with ether, and the combined organic layers were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. The crude product was dissolved in 100 mL of CH_2Cl_2–water mixture (1:1), and 2.8 g (22 mmol) of oxalic acid was added. The mixture was stirred at 25 °C for 12 h, diluted with ether and water, and neutralized with 2 N NaOH, and the ether layer was separated. The aqueous layer was extracted twice with ether, and the organic layers were combined, washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 2.5 g (72% yield) of enone **4**: IR (neat) 2942, 1730, 1700, 1617, 1430, 1250, 1225 cm^{-1}; ^1H NMR, 3.85 (s, 3 H, OCH_3), 2.7 (m, 2 H, CH_2), 2.5 (m, 2 H, CH_2), 2.41 (s, 3 H, CH_3); ^{13}C NMR δ 203.06, 184.98, 163.46, 132.20, 51.46, 34.81, 32.53, 19.07; MS, m/z 154 (M^+). Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.17; H, 6.61.

***trans*-(1*S*,4*S*)- and *cis*-(1*R*,4*S*)-1,4-Dimethyl-2-cyclohexen-1-ol (22t and 22c).** To a cold (−78 °C) solution of 2.0 g (18.2 mmol) of (*S*)-(−)-4-methyl-2-cyclohexenone[14] in 90 mL of THF was added 14.5 mL (21 mM) of CH_3Li (1.5 M in hexane). After being stirred at −78 °C for 30 min and 0 °C for 30 min, the mixture was diluted with a solution of 1.4 g (23.1 mmol) of acetic acid in 10 mL of ether, poured into water, and extracted three times with ether. The combined ether layer was washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 2.1 g (92% yield) of a mixture of isomeric alcohols **22t** and **22c** in a ratio of 2.2:1. These two isomers could be separated and isolated via PTLC. For **22t**: IR (neat) 3400, 1660 cm^{-1}; ^1H NMR δ 5.55 (s, 2 H, =CH), 1.29 (s, 3 H, $OCCH_3$), 0.97 (d, J = 7.2 Hz, 3 H, CH_3), 1.2–2.3 (m, 4 H); ^{13}C NMR δ 134.3, 133.2, 68.9, 36.9, 28.9, 28.8, 27.9, 20.8; MS, m/z 126 (M^+). Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.08; H, 11.21. For **22c**: ^1H NMR δ 5.60 (s, 2 H, =CH), 1.29 (s, 3 H, $OCCH_3$), 1.02 (d, J = 7.2 Hz, 3 H, CH_3), 1.2–2.3 (m, 4 H); ^{13}C NMR

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δ 135.6, 132.6, 73.1, 37.1, 30.7, 30.0, 29.5, 21.2; MS, m/z 126 (M^+).

(3*R*,4*R*,*SS*)-1,4-Dimethyl-3-(phenylsulfinyl)-1-cyclohexene (3a). From Alcohol 22t. To a solution of 0.1 g (0.79 mmol) of alcohol **22t** and 0.67 mL (4.8 mmol) of triethylamine was added a solution of 4.6 mL (1.2 mmol) of phenylsulfenyl chloride in benzene (0.26 M). The resulting mixture was stirred at 25 °C for 30 min, diluted with ether, washed with water and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.148 g (80% yield) of sulfoxide **3a**: IR (neat) 1650, 1038 cm^{-1}; ^1H NMR δ 7.58 (d, J = 6.9 Hz, 2 H, ortho H), 7.48–7.54 (m, 3 H, meta and para H), 4.98 (s, 1 H, =CH), 2.93 (br s, 1 H, CHS), 1.70 (s, 3 H, $=CCH_3$), 1.18 (d, J = 6.7 Hz, 3 H, CH_3), 1.3–2.3 (m, 5 H); ^{13}C NMR δ 143.7, 142.5, 130.4, 128.8, 124.6, 111.9, 69.2, 28.8, 28.3, 28.2, 24.1, 19.8; MS, m/z 234 (M^+).

(3*S*,4*R*,*SS*)- and (3*S*,4*R*,*SR*)-1,4-Dimethyl-3-(phenylsulfinyl)-1-cyclohexene (3b and 3d). From Alcohol 22c. The procedure was the same as that described for the preparation of **3a**, except alcohol **22c** was used. A 1:1 mixture of sulfoxides **3b** and **3d** was obtained: IR (neat) 1650, 1038 cm^{-1}; ^1H NMR δ 7.4–7.8 (m, 5 H, Ar H), 4.88 (s, 0.5 H, =CH), 4.72 (s, 0.5 H, =CH), 3.05 (s, 0.5 H, CHS), 2.5 (s, 0.5 H, CHS), 1.73 (s, 1.5 H, CH_3), 1.65 (s, 1.5 H, $=CCH_3$), 1.42 (d, J = 6.9 Hz, 1.5 H, CH_3), 1.06 (d, J = 6.9 Hz, 1.5 H, CH_3), 0.9–2.2 (m, 5 H); ^{13}C NMR δ 144.3, 142.3, 136.5, 134.3, 133.2, 131.2, 130.2, 128.9, 124.7, 124.4, 112.4, 111.9, 69.8, 67.8, 31.6, 30.0, 27.5, 26.5, 25.6, 25.3, 23.9, 23.8, 18.8, 18.1; MS, m/z 234 (M^+).

Reaction of 3a, 3b, and 3d with Zn–AcOH. Formation of (3*R*,4*S*)- and (3*S*,4*S*)-1,4-Dimethyl-3-(phenylthio)cyclohexene. A mixture of 0.2 g (0.85 mmol) of **3a**, **3b**, and **3d** (4:1:1) and 1 g of activated zinc in 12 mL of AcOH was stirred at 25 °C for 10 h, and the reaction was monitored by TLC. The reaction mixture was diluted with ether, filtered through Celite, and neutralized with 5 N NaOH. The organic layer was separated, and the aqueous layer was extracted twice with ether. The combined ether layers were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.167 g (90% yield) of the sulfide: IR (neat) 1660 cm^{-1}; ^1H NMR δ 7.2–7.4 (m, 5 H, Ar H), 5.4 (s, 0.5 H, =CH), 5.4–5.5 (s, 0.5 H, =CH), 3.8–3.9 (s, 0.4 H, CHS), 3.4–3.5 (s, 0.6 H, CHS), 1.7 (s, 3 H, $=CCH_3$), 1.1 (d, J = 7.0 Hz, 3 H, CH_3), 1.0–2.1 (m, 5 H); MS, m/z 218 (M^+).

Oxidation of (4*S*)-1,4-Dimethyl-3-(phenylthio)cyclohexene. Formation of 3a–d. To a solution of 0.12 g (0.55 mmol) of the sulfide in 2 mL of AcOH at 0 °C was added 40 μL (0.55 mmol) of 50% H_2O_2. The mixture was stirred at 0–5 °C for 30 min, diluted with ether, and neutralized with 2 N NaOH. The organic layer was separated, and the aqueous layer was extracted with ether twice. The combined ether layers were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.116 g (90% yield) of sulfoxides **3** as a mixture of four isomers (**a**–**d**, 2:1:2:1). For **3c**: ^1H NMR δ 4.50 (m, 1 H, =CH), 3.35 (br s, 1 H, CHS), 1.37 (d, J = 6.7 Hz, 3 H, CH_3). The remainder of the proton resonances overlaped with those of isomers **3a**,**b**,**d**.

3,6-Dimethyl-3-[2-(methoxycarbonyl)-1-methyl-3-oxocyclopentyl]-1-(phenylsulfinyl)cyclohexene (19a,b and 20a,b). To a cold solution (−78 °C) of 4.18 g (17.8 mmol) of sulfoxides **3a**, **3b**, and **3d** (4:1:1) in 62 mL of THF was added a cold (−78 °C) solution of LDA (21 mmol) in 62 mL of THF via cannula. The resulting orange solution was stirred for 10 min at −78 °C. A solution of 2.75 g (17.8 mmol) of enone **4** in 35 mL of THF was then added, and the mixture was stirred at −78 °C for 15 min. To it was added a solution of 2.8 g (46.2 mmol) of acetic acid in 20 mL of ether, and the mixture was poured into water and extracted with ether twice. The combined ether extracts were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel with CH_2Cl_2 and ether as eluents to give 3.5 g (50% yield) of **19a**, 0.25 g (4% yield; 5:1) of **19b** and **20b**, 0.7 g (10% yield) of **20a**, and 1.25 g (30% recovery) of starting sulfoxides **3**. For **19a**: $[\alpha]^{22}_D$ −34.29° (c 0.04, $CHCl_3$); IR (neat) 3040, 2940, 1750, 1730, 1630, 1040 cm^{-1}; ^1H NMR δ 7.58 (d, J = 7.9 Hz, 2 H, ortho H), 7.48–7.52 (m, 3 H, meta and para H), 6.43 (s, 1 H, =CH), 3.74 (s, 3 H, OCH_3), 3.39 (s, 1 H, O=CCHC=O), 1.25 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 0.96 (d, J = 7.0 Hz, 3 H, CH_3), 1.1–2.5 (m, 9 H); ^{13}C NMR δ 211.39, 170.16, 137.14, 130.88, 129.12, 128.79, 125.18, 124.80, 61.82, 52.06, 50.13, 42.67, 35.42, 29.99, 28.20, 27.09, 25.86, 21.32, 20.11, 17.48; MS, m/z 388 (M^+). Anal. Calcd for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.26. Found: C, 68.33; H, 7.36. For **20a**: $[\alpha]^{22}_D$ −91.8° (c 0.10, $CHCl_3$); ^1H NMR δ 7.64 (d, J = 7.8 Hz, 2 H, ortho H), 7.48–7.52 (m, 3 H, meta and para H), 6.65 (s, 1 H, =CH), 3.64 (s, 3 H, OCH_3), 3.39 (s, 1 H, O=CCHC=O), 1.20 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 1.09 (d, J = 6.6 Hz, 3 H, CH_3), 1.1–2.5 (m, 9 H); ^{13}C NMR δ 211.8, 170.3, 147.2, 142.8, 131.7, 129.5, 129.1, 126.6, 62.2, 52.0, 51.2, 41.6, 35.3, 30.7, 30.2 (2 C), 29.8, 21.6, 19.3, 16.9; MS, m/z 388 (M^+). Anal. Calcd for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.26. Found: C, 68.17; H, 7.38. For **19b** and **20b**: ^1H NMR δ 6.78 (s, 1 H, =CH, **20b**), 6.64 (s, 1 H, =CH, **19b**), 3.85 (s, 3 H, OMe, **19b**), 3.80 (s, 3 H, OMe, **20b**); MS, m/z 388 (M^+).

When pure sulfoxide **3a** was used, 93% yield (isolated; based on unrecovered starting sulfoxide, 30% of which was recovered) of adducts **19a** and **19b** (ratio of 93:7) was obtained.

(3*S*,6*S*,*SS*,1′*S*,2′*R*,3′*R*)-3,6-Dimethyl-3-[3-hydroxy-2-(hydroxymethyl)-1-methylcyclopentyl]-1-(phenylsulfinyl)cyclohexene (24). To a cold solution (0 °C) of 4.66 g (12 mmol) of **19a** in 30 mL of THF was added 14.4 mL (21.6 mmol) of $LiBH_4$ (1.5 M in THF). The mixture was warmed to 25 °C, stirred for 18 h, and poured into 300 mL of ether. To this solution was added 5 mL of methanol over a 5-min period, followed by the addition of 100 mL of water and then 100 mL of 1 N HCl. The organic layer was separated, and the aqueous layer was extracted twice with CH_2Cl_2–ether mixture (1:1). The combined organic solutions were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 2.93 g (67% yield) of diol **24** and 0.746 g (16% recovery) of **19a**: $[\alpha]^{22}_D$ −91.5° (c 0.92, $CHCl_3$); IR (neat) 3400, 3040, 2940, 1620, 1028 cm^{-1}; ^1H NMR δ 7.3–7.7 (m, 5 H, Ar H), 6.48 (s, 1 H, =CH), 4.44 (br s, 1 H, CHO), 3.98 (m, 1 H, CH_2O), 3.82 (m, 1 H, CH_2O), 1.10 (d, J = 7.0 Hz, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 0.99 (s, 3 H, CH_3), 1.0–2.4 (m, 10 H); ^{13}C NMR δ 147.9, 143.0, 141.6, 130.6, 129.1, 124.8, 75.4, 61.7, 49.6, 48.4, 34.6, 33.2, 30.1, 28.2, 27.1, 26.0, 21.6, 20.6, 19.4; MS, m/z 362 (M^+). Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.57; H, 8.34. Found: C, 69.43; H, 8.41.

(3*S*,6*S*,*SS*,1′*S*,2′*R*,3′*R*)-3-[2-[(Benzoyloxy)methyl]-3-hydroxy-1-methylcyclopentyl]-3,6-dimethyl-1-(phenylsulfinyl)cyclohexene (25). To a cold solution of (−10 °C) of 0.57 g (1.6 mmol) of diol **24** in 16 mL of acetonitrile was added 16 mg (0.16 mmol) of triethylamine and 0.21 mL (1.6 mmol) of benzoyl cyanide. After the mixture was stirred at −10 °C for 2 h, it was poured into water, and the mixture was extracted three times with ether. The ether extracts were combined, washed with water and then brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.51 g (70% yield) of monobenzoate **25**, 27.5 mg (3% yield) of the dibenzoate, and 98.6 mg (17% recovery) of starting diol **24**. For **25**: $[\alpha]^{22}_D$ −67.4° (c 0.17, $CHCl_3$); IR (neat) 3400, 3044, 2950, 1700, 1594, 1550, 1270, 1030 cm^{-1}; ^1H NMR δ 8.03 (d, J = 7.1 Hz, 2 H, ortho H), 7.4–7.7 (m, 8 H, Ar H), 6.48 (s, 1 H, =CH), 4.85 (t, J = 11.2 Hz, 1 H, CHOC=O), 4.45 (dd, J = 11.2, 3.5 Hz, 1 H, CHOC=O), 4.30 (br s, 1 H, CHO), 1.18 (s, 3 H, CH_3), 1.13 (d, J = 7.0 Hz, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 1.4–2.4 (m, 10 H); ^{13}C NMR δ 167.1, 148.7, 143.6, 140.5, 133.0, 130.4, 130.1, 129.6, 128.9, 128.3, 124.7, 74.3, 64.0, 48.9, 48.3, 44.3, 35.5, 33.9, 28.1, 27.0, 25.8, 22.0, 20.4; MS, m/z 466 (M^+). Anal. Calcd for $C_{28}H_{34}O_4S$: C, 72.07; H, 7.34. Found: C, 71.80; H, 7.38.

For the dibenzoate: $[\alpha]^{22}_D$ −98.9° (c 0.46, $CHCl_3$); IR (neat) 3050, 2950, 1700, 1593, 1550, 1040 cm^{-1}; ^1H NMR δ 7.9–8.1 (m, 4 H, ortho H), 7.3–7.7 (m, 11 H, Ar H), 6.55 (s, 1 H, =CH), 5.73 (s, 1 H, CHOC=O), 4.7 (dd, J = 11.2, 4.2 Hz, 1 H, CHOC=O), 4.48 (t, J = 10.7 Hz, 1 H, CHOC=O), 1.33 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 1.09 (d, J = 7.1 Hz, 3 H, CH_3), 1.1–2.7 (m, 9 H); ^{13}C NMR δ 166.5, 165.8, 149.3, 143.8, 139.5, 132.9, 130.6, 130.5, 130.1, 129.7, 129.5, 129.0, 128.9, 128.5, 128.4, 124.9, 124.8, 78.2, 63.1, 49.1, 47.1, 44.1, 35.7, 32.0, 28.2, 27.1, 26.1, 22.1, 20.4, 20.0.

(3*S*,6*S*,*SS*,1′*S*,2′*R*)-3-[2-[(Benzoyloxy)methyl]-1-methyl-3-oxocyclopentyl]-3,6-dimethyl-1-(phenylsulfinyl)cyclohexene (26). To a solution of 0.8 g (1.71 mmol) of monobenzoate **25** in 10 mL of CH_2Cl_2 was added 2 g of 3A molecular sieves and 0.52 g (2.4 mmol) of PCC. The mixture was stirred at 25 °C for 3 h, diluted with ether and ethyl acetate (1:1), filtered through Florisil, and eluted with ether. The solvent was evaporated, and the crude material was column chromatographed on silica gel to give 0.683 g (84% yield) of ketobenzoate **26**: IR (neat) 1750, 1730, 1600, 1042 cm^{-1}; ^1H NMR δ 8.03 (d, J = 8.0 Hz, 2 H, ortho H), 7.39–7.54 (m, 8 H, Ar H), 6.59 (s, 1 H, =CH), 4.85 (d, J = 12.4 Hz, 1 H, CHOC=O), 4.43 (dd, J = 12.4, 6.3 Hz, 1 H, CHOC=O), 1.12 (d, J = 7.0 Hz, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 1.3–2.8 (m, 10 H); ^{13}C NMR δ 215.4, 166.3, 148.7, 143.2, 139.5, 133.1, 130.5, 129.88, 129.6, 129.0, 128.5, 124.6, 61.9, 55.1, 47.7, 42.3, 34.3, 29.2, 28.0, 26.7, 25.5, 21.4, 20.7, 17.0; MS, m/z 464 (M^+). Anal. Calcd for $C_{28}H_{32}O_4S$: C, 72.38; H, 6.94. Found: C, 72.32; H, 7.23.

(3*S*,6*S*,*SS*,1′*S*)-3,6-Dimethyl-3-(1-methyl-2-methylene-3-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (27). To a solution of 0.31 g (0.67 mmol) of ketobenzoate **26** in 3.5 mL of toluene was added 0.10 mL (0.8 mmol) of DBN (1,5-diazabicyclo[4.3.0]non-5-ene), and the mixture was stirred at 80 °C for 1.5 h. After it was cooled to room temperature and poured into 200 mL of ethyl acetate, the mixture was washed with 1 N HCl, water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.1845 g (82% yield) of enone **27**: $[\alpha]^{22}_D$ −155.5° (c 0.25, $CHCl_3$); IR (neat) 1690, 1600, 1040 cm^{-1}; ^1H NMR δ 7.56 (d, J = 7.5 Hz, 2 H, ortho H), 7.4–7.6 (m, 3 H, para and meta H), 6.44 (s, 1 H, =CH), 6.20 (s, 1 H, $=CH_2$), 5.37 (s, 1 H, $=CH_2$), 1.31 (s, 3 H, CH_3), 1.02 (d, J = 7.1 Hz, 3 H,

CH_3), 1.00 (s, 3 H, CH_3), 1.1–2.5 (m, 9 H); ^{13}C NMR δ 207.6, 151.7, 148.8, 143.3, 138.4, 130.7, 129.0, 125.0, 120.1, 48.3, 43.2, 36.1, 30.0, 29.8, 28.0, 27.0, 25.7, 22.0, 20.4; MS, m/z 342 (M^+). Anal. Calcd for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65; S, 9.36. Found: C, 73.47; H, 7.91; S, 9.11.

(3*S*,6*S*,*SS*,1′*R*,3′*R*)-3,6-Dimethyl-3-(3-hydroxy-1-methyl-2-methylenecyclopentyl)-1-(phenylsulfinyl)cyclohexene (2) and (3*S*,6*S*,-*SS*,1′*R*,3′*S*)-3,6-Dimethyl-3-(3-hydroxy-1-methyl-2-methylenecyclopentyl)-1-(phenylsulfinyl)cyclohexene (28). To a cold solution (−10 °C) of 0.066 g (0.19 mmol) of enone **27** in 1 mL of methanol was added 72 mg (0.19 mmol) of $CeCl_3 \cdot 7H_2O$ followed by 7.3 mg (0.19 mmol) of sodium borohydride. The mixture was stirred at −10 °C for 1 h, diluted with aqueous NH_4Cl, and extracted three times with ether. The combined ether layers were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 61 mg (92% yield) of mixture of alcohols **2** and **28** (9:1). For **2**: ^1H NMR δ 7.4–7.7 (m, 5 H, Ar H), 6.54 (s, 1 H, =CH), 5.25 (s, 1 H, $=CH_2$), 5.06 (s, 1 H, $=CH_2$), 4.35 (m, 1 H, CHO), 1.19 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 0.9–2.4 (m, 12 H); ^{13}C NMR δ 160.29, 147.97, 143.67, 140.17, 130.47, 128.96, 124.93, 107.24, 76.56, 48.61, 42.61, 32.68, 30.82, 29.69, 29.02, 27.04, 25.25, 21.49, 20.72. For **28** (pure **28** was obtained from the next reaction): IR (neat) 3400, 3040, 1620, 1600, 1040 cm^{-1}; ^1H NMR δ 7.4-7.7 (m, 5 H, Ar H), 6.65 (s, 1 H, =CH), 5.32 (s, 1 H, $=CH_2$), 5.17 (s, 1 H, $=CH_2$), 4.45 (m, 1 H, CHO), 1.15 (s, 3 H, CH_3), 1.11 (d, J = 6.9 Hz, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 0.9–2.4 (m, 9 H); ^{13}C NMR δ 161.12, 141.66, 130.38, 129.17, 128.96, 126.45, 124.92, 112.56, 78.35, 42.53, 34.81, 31.46, 29.73, 28.27, 26.98, 26.15, 25.28, 22.33, 20.68; MS, m/z 344 (M^+). Anal. Calcd for $C_{21}H_{28}O_2S$: C, 73.21; H, 8.19. Found: C, 73.03; H, 8.33. For the ketone resulted from the 1,4-reduction with Dibal-H in toluene at −78 °C: $[\alpha]^{22}_D$ −151.8° (c 0.11, $CHCl_3$); IR (neat) 1710, 1600, 1035 cm^{-1}; ^1H NMR δ 7.4–7.6 (m, 5 H, Ar H), 6.48 (s, 1 H, =CH), 1.12 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.09 (d, J = 7.1 Hz, 3 H, $CHCH_3$), 1.06 (s, 3 H, CCH_3), 0.92 (s, 3 H, CCH_3), 1.1–2.4 (m, 10 H); ^{13}C NMR δ 219.1, 148.5, 143.7, 139.4, 130.6, 129.0, 124.9, 51.0, 47.4, 42.3, 34.0, 29.1, 28.2, 27.0, 25.7, 21.5, 20.8, 15.8, 10.6; MS, m/z 344 (M^+).

(9*S*,10*R*,*SS*)-12,13-Deoxy-9,10-dihydro-10-(phenylsulfinyl)trichothecene (29a) and (9*S*,10*S*,*SS*)-12,13-Deoxy-9,10-dihydro-10-(phenylsulfinyl)trichothecene (29b). To a solution of 0.45 g (1.3 mmol) of mixture of alcohols **2** and **28** (9:1) in 40 mL of *t*-BuOH was added 0.73 g (13 mmol) of powdered KOH, and the mixture was stirred at 83 °C for 3 h. The mixture was diluted with water and ether, and 13 mL of 1 N HCl was added. The organic layer was separated, and the aqueous layer was again extracted with ether three times. The combined ether layers were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.255 g (63% yield) of **29a**, 85 mg (21% yield) of **29b**, and 0.041 g (90% recovery) of alcohol **28**. For **29a**: $[\alpha]^{22}_D$ +114.4° (c 0.09, $CHCl_3$); IR (neat) 1650, 1050 cm^{-1}; ^1H NMR δ 7.78 (d, J = 7.8 Hz, 2 H, ortho H), 7.5–7.6 (m, 3 H, meta and para H), 4.98 (s, 1 H, =CH), 4.61 (s, 1 H, =CH), 4.28 (d, J = 4.9 Hz, 1 H, OCHC=), 2.8 (br s, 1 H, CHO), 2.76 (m, 1 H, CHS), 1.36 (d, J = 7.2 Hz, 3 H, CH_3), 0 .92 (s, 3 H, CH_3), 0.62 (s, 3 H, CH_3), 1.0–2.7 (m, 9 H); ^{13}C NMR δ 154.85, 142.4, 131.6, 128.9, 126.13, 103.2, 80.1, 72.2, 70.54, 48.65, 42.2, 31.4, 28.40, 26.43, 26.14, 21.78, 19.21, 17.16, 16.0; MS, m/z 344 (M^+). Anal. calcd for $C_{21}H_{28}O_2S$: C, 73.21; H, 8.19. Found: C, 72.87; H, 8.11. For **29b**: $[\alpha]^{22}_D$ +12.0° (c 0.15, $CHCl_3$); ^1H NMR δ 7.72 (d, J = 7.8 Hz, 2 H, ortho H), 7.4–7.6 (m, 3 H, meta and para H), 4.93 (s, 1 H, =CH), 4.60 (s, 1 H, =CH), 4.19 (d, J = 4.8 Hz, 1 H, OCHC=), 4.14 (s, 1 H, CHO), 2.70 (s, 1 H, CHS), 1.16 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.92 (d, J = 7.1 Hz, 3 H, CH_3), 0.8–2.3 (m, 9 H); ^{13}C NMR δ 134.0, 131.39, 129.05, 125.81, 118.0, 102.59, 80.11, 71.2, 69.8, 48.8, 42.2, 31.6, 26.91, 26.02, 25.62, 22.99, 20.91, 18.51, 15.97; MS, m/z 344 (M^+).

(+)-12,13-Deoxytrichothec-9-ene [(+)-30]. A solution of 0.15 g (0.436 mmol) of tricyclic sulfoxide **29a** (or **29b**, or a mixture of **29a** and **29b**) and 50 mg (0.44 mmol) of Dabco (1,4-diazabicyclo[2.2.2]octane) in 20 mL of 1,3,5-trimethylbenzene was heated in a sealed tube at 250 °C for 36 h. The mixture was diluted with water and extracted three times with ether. The combined ether layers were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 67 mg (70% yield) of diene **30**: $[\alpha]^{22}_D$ +12.5° (c 0.04, $CHCl_3$); IR (neat) 1670, 1047 cm^{-1}; ^1H NMR δ 5.35–5.45 (m, 1 H, =CH), 4.94 (s, 1 H, $=CH_2$), 4.59 (s, 1 H, $=CH_2$), 4.30 (d, J = 5.0 Hz, 1 H, CHO), 3.72 (d, J = 5.5 Hz, 1 H, CHO), 1.68 (s, 3 H, $=CCH_3$), 1.01 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.8–2.2 (m, 8 H); ^{13}C NMR δ 155.7, 139.2, 119.9, 102.4, 80.0, 70.7, 47.9, 40.0, 32.1, 28.5, 27.5, 23.9, 23.2, 16.1, 16.0; MS, m/z 218 (M^+). Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.37; H, 10.23.

Sulfoxide **29b** eliminated at 150 °C with 1 equiv of Dabco in 1,3,5-trimethylbenzene to **30** in 89% yield.

(+)-12,13-Epoxytrichothec-9-ene [(+)-1]. To a solution of 0.1 g (0.46 mmol) of diene **30** in 8 mL of CH_2Cl_2 were added 65 mg (0.46 mmol) of Na_2HPO_4 and 90 mg (0.46 mmol) of MCPBA, and the solution was stirred at 25 °C for 1 h. The mixture was diluted with water and extracted with ether three times. The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 54 mg (50% yield) of (+)-**1**, 33 mg (30% yield) of isomeric 9,10-epoxide **31**, 12 mg (10% yield) of the diepoxide, and 8 mg (8% recovery) of starting diene **30**. For (+)-**1**: $[\alpha]^{22}_D$ +16.7° (c 0.03, $CHCl_3$); IR (neat) 1670, 1050 cm^{-1}; ^1H NMR, 5.4–5.48 (m, 1 H, =CH), 3.73 (d, J = 5 Hz, 1 H, CHO), 3.71 (d, J = 5.7 Hz, 1 H, CHO), 3.16 (d, J = 4.1 Hz, 1 H, CH_2O), 2.89 (d, J = 4.1 Hz, 1 H, CH_2O), 1.71 (s, 3 H, $=CCH_3$), 0.81 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 1.3–2.2 (m, 8 H); ^{13}C NMR δ 139.5, 119.51, 80.19, 70.61, 49.46, 45.36, 40.04, 31.41, 28.43, 26.32, 24.59, 23.23, 21.12, 16.0, 11.07; MS, m/z 234 (M^+). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.55; H, 9.62. For **31**: $[\alpha]^{24}_D$ −23.3° (c 0.03, $CHCl_3$); ^1H NMR δ 4.97 (s, 1 H, $=CH_2$), 4.58 (s, 1 H, $=CH_2$), 4.42 (d, J = 4.9 Hz, 1 H, OCHC=), 3.72 (dd, J = 5.6 Hz, 2.2 Hz, 1 H, CHO), 3.03 (d, J = 5.2 Hz, 1 H, CHO), 1.33 (s, 3 H, $OCCH_3$), 0.96 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3), 1.2–2.2 (m, 8 H); ^{13}C NMR δ 154.1, 103.17, 79.61, 70.42, 57.96, 47.32, 39.61, 32.0, 27.32, 26.9, 22.62, 21.3, 20.89, 16.87, 16.21; MS, m/z 234 (M^+). For the diepoxide: ^1H NMR δ 3.80 (d, J = 5 Hz, 1 H, CHO), 3.70 (dd, J = 5 Hz, 3 Hz, 1 H, C-2 H), 3.20 (d, J = 4 Hz, 1 H, CHO), 3.07 (d, J = 5 Hz, 1 H, CHO), 2.83 (d, J = 4 Hz, 1 H, CHO), 2.15–1.1 (m, 8 H), 1.35 (s, 3 H, Me), 0.77 (s, 3 H, Me), 0.71 (s, 3 H, Me); MS, m/z 250 (M^+).

The antipode (−)-**1** are synthesized from **20a** by following the same procedure for the synthesis of (+)-**1** from **19a**.

(3*R*,6*S*,*SR*,1′*R*,2′*S*,3′*S*)-3,6-Dimethyl-3-[3-hydroxy-2-(hydroxymethyl)-1-methylcyclopentyl]-1-(phenylsulfinyl)cyclohexene (32): $[\alpha]^{22}_D$ −96.1° (c 0.595, CH_2Cl_2); IR (neat) 3400, 1620, 1030 cm^{-1}; ^1H NMR δ 7.65–7.62 (m, 2 H, Ar H), 7.5–7.48 (m, 3 H, Ar H), 6.59 (s, 1 H, =CH), 4.48 (m, 1 H, CHO), 3.91 (t, J = 11 Hz, 1 H, CH_2O), 3.68 (dd, J = 11 Hz, 3 Hz, 1 H, CH_2O), 2.6 (m, 2 H, OH), 2.03–1.4 (m, 10 H), 1.06 (d, J = 7 Hz, 3 H, Me), 1.04 (s, 3 H, Me), 0.99 (s, 3 H, Me); ^{13}C NMR δ 145.71, 142.94, 134.01, 131.62, 129.45, 126.11, 75.42, 61.74, 48.94, 48.82, 42.52, 34.28, 32.99, 30.42, 30.13, 29.95, 19.30, 19.03; MS, m/z 362 (M^+). Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.57; H, 8.34. Found: C, 69.41; H, 8.42.

(3*S*,6*S*,*SR*,1′*S*,2′*R*,3′*R*)-3-[2-[(Benzoyloxy)methyl]-3-hydroxy-1-methylcyclopentyl]-3,6-dimethyl-1-(phenylsulfinyl)cyclohexene (33): $[\alpha]^{22}_D$ −67.4° (c 1.455, CH_2Cl_2); IR (neat) 3400, 1700, 1595, 1030 cm^{-1}; ^1H NMR δ 8.00 (d, J = 7.3 Hz, 2 H, ortho H), 7.7–7.2 (m, 8 H, Ar H), 6.63 (s, 1 H, =CH), 4.73 (dd, J = 11 Hz, 10 Hz, 1 H, CH_2O), 4.42 (dd, J = 11 Hz, 3.5 Hz, 1 H, CH_2O), 4.3 (m, 1 H, CHO), 2.2–1.3 (m, 10 H), 1.14 (s, 6 H, 2 Me), 1.10 (d, J = 7 Hz, 3 H, Me); ^{13}C NMR δ 166.99 (C=O), 147.35, 144.03, 133.82, 133.12, 131.15, 130.25, 129.74, 129.17, 128.38, 125.52, 74.62, 64.10, 49.26, 49.17, 43.32, 35.79, 34.18, 30.40, 30.35, 30.16, 22.66, 20.34, 19.44; MS, m/z, 466 (M^+). Anal. Calcd for $C_{28}H_{34}O_4S$: C, 72.07; H, 7.34. Found: C, 71.82; H, 7.57.

(3*S*,6*S*,*SR*,*1′S*,2′*R*)-3-[2-[(Benzoyloxy)methyl]-1-methyl-3-oxocyclopentyl]-3,6-dimethyl-1-(phenylsulfinyl)cyclohexene (34): $[\alpha]^{22}_D$ −160.2° (c 1.56, CH_2Cl_2); IR (neat) 1750, 1730, 1600, 1040 cm^{-1}; ^1H NMR δ 7.97 (d, J = 7.2 Hz, 2 H, ortho H), 7.65–7.3 (m, 8 H, Ar H), 6.72 (s, 1 H, =CH), 4.60 (dd, J = 11.9 Hz, 4 Hz, 1 H, CH_2O), 4.48 (dd, J = 11.9 Hz, 5 Hz, 1 H, CH_2O), 2.7–1.3 (m, 10 H), 1.18 (s, 3 H, Me), 1.12 (s, 3 H, Me), 1.10 (d, J = 7 Hz, 3 H, Me); ^{13}C NMR δ 215.98, 166.36, 146.72, 143.24, 132.73, 132.25, 129.87, 129.59, 128.77, 128.54, 127.74, 125.02, 61.89, 54.95, 48.18, 41.18, 34.63, 30.36, 29.66, 29.33, 29.05, 23.2, 22.0, 16.5; MS, m/z 464 (M^+).

(3*S*,6*S*,*SR*,1′*S*)-3,6-Dimethyl-3-(1-methyl-2-methylene-3-oxocyclopentyl)-1-(phenylsulfinyl)cyclohexene (35): $[\alpha]^{22}_D$ −52.5° (c 0.2, CH_2Cl_2); IR (neat) 1690, 1600, 1040 cm^{-1}; ^1H NMR δ 7.6 (m, 2 H, Ar H), 7.4–7.5 (m, 3 H, Ar H), 6.65 (s, 1 H, =CH), 6.16 (s, 1 H, $=CH_2$), 5.4 (s, 1 H, $=CH_2$), 2.5–1.4 (m, 9 H), 1.29 (s, 3 H, Me), 1.12 (s, 3 H, Me), 1.07 (d, J = 6.8 Hz, 3 H, Me); ^{13}C NMR δ 207.49 (C=O), 151.69, 146.87, 143.62, 132.80, 131.43, 129.39, 129.30, 126.05, 120.02, 48.95, 42.14, 36.08, 30.05, 29.90, 29.68, 25.0, 22.53, 19.36; MS, m/z 342 (M^+). Anal. Calcd for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65. Found: C, 73.59; H, 7.71.

(3*R*,6*S*,*SR*,1′*S*,3′*S*)-3,6-Dimethyl-3-(3-hydroxy-1-methyl-2-methylenecyclopentyl)-1-(phenylsulfinyl)cyclohexene (36) and (3*R*,6*S*,-*SR*,1′*S*,3′*R*)-3,6-Dimethyl-3-(3-hydroxy-1-methyl-2-methylenecyclopentyl)-1-(phenylsulfinyl)cyclohexene (37). Reduction of **35** with $CeCl_3 \cdot 7H_2O$ and $NaBH_4$ in MeOH at −10 °C gave 92% yield of **36** and **37** (1:9). When **35** was reduced with 1.2 equiv of Dibal-H in toluene at −78 °C, 76% yield of **36** and **37** (1.1:1) and 20% yield of the 1,4-reduction product were obtained. For **36**: $[\alpha]^{22}_D$ −63.3° (c 0.365, CH_2Cl_2); IR (neat) 3400, 1620 cm^{-1}; ^1H NMR δ 7.7 (m, 2 H, Ar H), 7.5 (m, 3 H,

Ar H), 6.75 (s, 1 H, CH=), 5.33 (s, 1 H, =CH), 5.21 (s, 1 H, =CH), 4.42 (m, 1 H, CHO), 2.1-1.2 (m, 9 H), 1.26 (s, 3 H, Me), 1.17 (s, 3 H, Me), 1.04 (d, J = 6.7 Hz, 3 H, Me); ^{13}C NMR δ 161.27, 144.49, 134.94, 131.42, 129.20, 129.12, 126.5, 109.61, 76.45, 50.38, 43.17, 34.92, 32.73, 30.81, 30.17, 29.69, 25.09, 22.48, 19.38. For **37**: $[\alpha]^{22}_D$ -16.52° (c 0.115, CH_2Cl_2); ^{1}H NMR δ 7.64 (m, 2 H, Ar H), 7.48 (m, 3 H, Ar H), 6.68 (s, 1 H, CH=), 5.22 (s, 1 H, =CH), 5.13 (s, 1 H, =CH), 4.40 (m, 1 H, CHO), 2.2-1.2 (m, 9 H), 1.19 (s, 3 H, Me), 1.08 (s, 3 H, Me), 1.03 (d, J = 6.6 Hz, 3 H, Me); ^{13}C NMR δ 160.47, 145.64, 143.73, 133.89, 131.36, 129.25, 126.42, 107.18, 76.52, 49.15, 41.77, 32.80, 31.11, 30.24, 29.87, 29.7, 25.0, 21.78, 19.31; MS, m/z 344 (M^+). Anal. Calcd for $C_{21}H_{28}O_2S$: C, 73.21; H, 8.19. Found: C, 73.10; H, 8.38. For the 1,4-reduction product: IR (neat) 1710, 1610 cm^{-1}; ^{1}H NMR δ 7.6 (m, 2 H, Ar H), 7.48 (m, 3 H, Ar H), 6.69 (s, 1 H, CH=), 2.4-1.2 (m, 10 H), 1.13 (s, 3 H, Me), 1.11 (d, J = 7 Hz, 3 H, Me), 1.02 (d, J = 7 Hz, 3 H, Me), 0.88 (s, 3 H, Me); MS, m/z 344 (M^+).

(9*S*,10*S*,S*R*)-12,13-Deoxy-9,10-dihydro-10-(phenylsulfinyl)trichothecene (29c) and (9*S*,10*R*,S*R*)-12,13-Deoxy-9,10-dihydro-10-(phenylsulfinyl)trichothecene (29d). For **29d**: $[\alpha]^{22}_D$ +8.15° (c 0.135, CH_2Cl_2); IR (neat) 1650, 1050 cm^{-1}; ^{1}H NMR δ 7.76 (m, 2 H, Ar H), 7.51 (m, 3 H, Ar H), 4.92 (s, 1 H, =CH), 4.55 (s, 1 H, =CH), 4.15 (d, J = 5 Hz, 1 H, CHO), 3.16 (s, 1 H, CHO), 2.57 (dd, J = 12 Hz, 3 Hz, 1 H, CHS), 1.9-1.1 (m, 9 H), 1.25 (d, J = 6.5 Hz, 3 H, Me), 0.89 (s, 3 H, Me), 0.74 (s, 3 H, Me); ^{13}C NMR δ 154.83, 145.0, 131.16, 128.71, 126.75, 103.12, 80.0, 73.23, 48.8, 42.0, 32.65, 31.51, 30.37, 29.7, 27.02, 25.97, 20.79, 16.79, 15.79; MS, m/z 344 (M^+). Anal. Calcd for $C_{21}H_{28}O_2S$: C, 73.21; H, 8.19. Found: C, 73.03; H, 8.48. For **29c**: $[\alpha]^{22}_D$ +22° (c 0.11, CH_2Cl_2); IR (neat) 1652, 1051 cm^{-1}; ^{1}H NMR δ 7.7 (m, 2 H, Ar H), 7.5 (m, 3 H, Ar H), 4.94 (s, 1 H, =CH), 4.57 (s, 1 H, =CH), 4.37 (d, J = 5 Hz, 1 H, CHO), 3.78 (s, 1 H, CHO), 2.70 (dd, J = 12 Hz, 2.7 Hz, 1 H, CHS), 2.3-1.2 (m, 9 H), 1.25 (d, J = 6.5 Hz, 3 H, Me), 0.94 (s, 3 H, Me), 0.82 (s, 3 H, Me); ^{13}C NMR δ 155.27, 143.4, 130.52, 128.7, 126.33, 103.0, 73.29, 71.68, 69.61, 48.9, 42.07, 32.39, 30.37, 28.03, 26.84, 26.7, 20.02, 18.0, 16.03; MS, m/z 344 (M^+).

Sulfoxides **29c** and **29d** underwent dehydrosulfenylation with 1 equiv of Dabco at 150 °C in 1,3,5-trimethylbenzene in a sealed tube to give 87% yield of (-)-**30**: $[\alpha]^{22}_D$ -13.0° (c 0.07, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.31, H, 10.29. (-)-**1**: $[\alpha]^{22}_D$ -16.9° (c 0.06, $CHCl_3$).

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Gas-Phase Determination of the Geometric Requirements of the Silicon β-Effect. Photoelectron and Penning Ionization Electron Spectroscopic Study of Silylthiiranes and -oxiranes. Synthesis and Chemistry of *trans*-2,3-Bis(trimethylsilyl)thiirane[†,1]

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Abstract: *trans*-2,3-Bis(trimethylsilyl)thiirane (**1**) has been synthesized in two steps from *trans*-1,2-bis(trimethylsilyl)ethene by addition of thiocyanogen followed by treatment of the adduct with sodium borohydride or lithium aluminum hydride. In the latter case minor products include *meso*-1,2-bis(trimethylsilyl)ethane-1,2-dithiol and 1,2-bis(trimethylsilyl)ethanethiol. Oxidation of thiirane **1** gives *trans*-2,3-bis(trimethylsilyl)thiirane *S*-oxide (**11**). The latter compound is remarkably stable for a sulfoxide containing a silyl group syn to oxygen. Heating **11** in the presence of dimethyl acetylenedicarboxylate affords 2,3-bis(carbomethoxy)thiophene and 2,3-dicarbomethoxy-4-(trimethylsilyl)thiophene by a novel mechanism. In order to obtain information on the magnitude and geometric dependence of the silicon β-effect in radical cations, the ultraviolet photoelectron spectrum of **1** has been determined and compared with those of a related series of silylated or *tert*-butyl-substituted thiiranes and oxiranes and their acyclic analogues. It is concluded that a trimethylsilyl group adjacent to the half-filled oxygen p-π orbital of an oxirane radical cation provides a stabilization of 20.8 kcal/mol compared to hydrogen and 3.0 kcal/mol compared to a *tert*-butyl group. These values are considerably smaller than those obtained by calculations on the stabilizing effect of silicon in the 3-silapropyl cation.

I. Introduction

The striking stabilization of carbocation and free-radical centers by β-situated silyl groups (the "β-effect") is of considerable theoretical interest[2a] as well as synthetic utility.[2b] Recent ab initio calculations by Jorgensen and co-workers[2a] indicate that the 3-silapropyl cation in the conformation in which the Si-C bond and vacant p orbital are orthogonal (A, Scheme I) is only 5 kcal/mol more stable than the analogous conformation of the *n*-propyl cation (B, Scheme I) while the 3-silapropyl cation in the optimal conformation for Si-C hyperconjunction with the p-π orbital (A′, Scheme I) is 25.1 kcal/mol more stable than the analogous conformation of the *n*-propyl cation (B′, Scheme I).[2a] The latter value is considerably larger than values of the silicon β-effect on

[†] Dedicated to Professor E. J. Corey on the occasion of his 60th birthday.

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