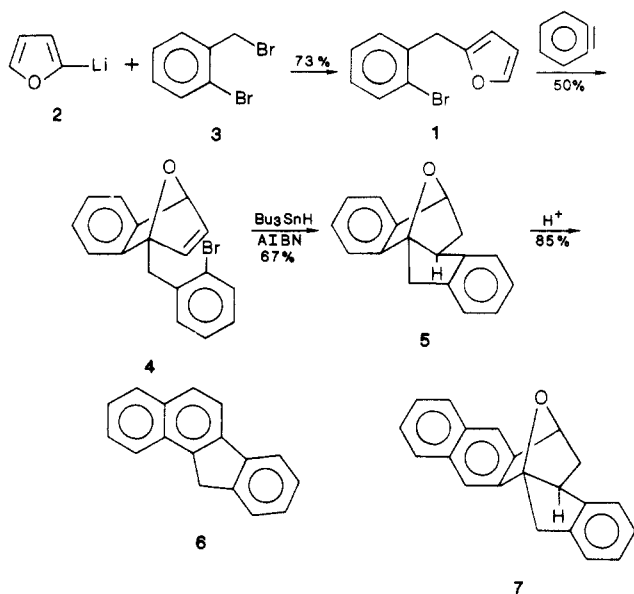


Scheme I



endoxide or nitrogen bridges by standard methods can, however, lead to variously functionalized known ring systems present in natural products.

Whereas the conversion of 4 to 5 and entries 2, 3, and 6 in Table I involve construction of a five-membered ring in the radical cyclization step, entries 1, 4, 5, and 7 show that six-membered rings are formed with equal effectiveness. The stereochemistry created in this step is assigned for 11-13, 15, and 17 by similarity of their proton NMR spectra to that of 7 and for 19, 20, 22, and 24 by the structure of the precursor. Entry 1 illustrates application of the methodology to heterocycles, by including a heteroatom in the tether between the diene moiety and radical site in the starting diene.¹⁰ Entries 2 and 6 demonstrate the use of vinyl halides in place of aryl halides at the radical-generating site. Entry 3 is an application using a carbocyclic diene.

Entries 4-6 illustrate some results with unsymmetric 1,3-dipoles. The regioisomer shown predominated by a large factor,¹¹ and in the case of styrene (entry 4) only the endo adduct 19 was obtained; with 20 and 22, however, exo/endo mixtures were obtained.

We are extending the scope of these studies to include acyclic dienes, radical cyclizations that are not terminated by hydride, tandem sequences in which both steps are intramolecular, and to examples where the radical site is attached to the dienophile instead of the diene.

Acknowledgment. We are indebted to the National Institutes of Health (GM 15997) for financial support.

(9) Structures related to 11 and 12 were recently synthesized by using intramolecular Diels-Alder methodology: Tsuge, O.; Ueno, K.; Kanemasa, S. *Heterocycles* 1986, 24, 629.

(10) The sulfide could be obtained from 13 by lithium aluminum hydride reduction; it could not be obtained directly from 10 (X = S) due to competing reactions of the sulfur with benzyne. Details will appear in a full account.

(11) With 20 and 22, in the cycloaddition step the corresponding regioisomer was formed (less than 15% of the total yield of cycloadducts).

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2-Phenylsulfonyl 1,3-Dienes as Versatile Synthons in Organic Transformations. Functionalizations via Epoxidation Reactions

Summary: 2-Phenylsulfonyl 1,3-dienes were regioselectively epoxidized at either of the double bonds in high selectivity. These epoxides are useful synthons and react with nucleophiles with complete regio- and stereospecificity. By changing the order of epoxidation and nucleophilic addition a complementary stereocontrol was obtained.

Sir: Conjugated dienes with electron-donating or electron-withdrawing substituents within the diene unit have attracted considerable attention during recent years.¹⁻⁴ Such dienes are useful reagents in cycloadditions as well as other reactions. We have recently shown that 2-phenylsulfonyl 1,3-dienes are versatile synthons that can be used as multicoupling reagents and Diels-Alder dienes with a dual electron demand.⁴ We have now studied selective epoxidation reactions of these sulfonyl dienes and their derivatives.

2-Phenylsulfonyl 1,3-dienes have two double bonds of very different reactivity. One of the double bonds is fairly electron rich whereas the other is electron deficient. Regioselective epoxidation to give either epoxide therefore seemed possible (Scheme I). Such epoxides are important classes of synthetic intermediates.⁵

Reaction of 2-(phenylsulfonyl)-1,3-cyclohexadiene (1) with *m*-chloroperbenzoic acid (*m*-CPBA) in methylene chloride resulted in a selective epoxidation to give the expected epoxide 5 (Table I, entry 1). The selectivity for epoxidation at the electron-rich double bond was ~95% as determined on the crude product. The epoxide 5 was isolated after workup⁶ in 80% yield completely free from the isomeric epoxide. When the epoxidation procedure was carried out by using alkaline hydrogen peroxide,^{7,8} epoxide 6 was formed exclusively (Table I, entry 2). In this case analysis of the crude product indicated a 100% selectivity for epoxidation at the electron-deficient double bond.

The selective epoxidations also worked fine for acyclic 2-phenylsulfonyl 1,3-dienes (entries 3-8, Table I). Thus, 2 was transformed to 7 by the use of *m*-CPBA and to 8 by the use of H₂O₂/OH⁻. Analogously, sulfonyl dienes 3 and 4 were transformed to either epoxide in high selectivity. For the acyclic dienes it was necessary to run the alkaline hydrogen peroxide epoxidation in acetone⁸ since the use

(1) (a) Danishefsky, S. *Acc. Chem. Res.* 1981, 14, 400. (b) Grayson, J. I.; Petrzilka, M. *Synthesis* 1981, 753. (c) Hickmott, P. W. *Tetrahedron* 1984, 40, 2989.

(2) (a) Evans, D. A.; Bryan, C. A.; Sims, C. L. *J. Am. Chem. Soc.* 1972, 94, 2891. (b) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* 1980, 102, 3554. (c) Cohen, T.; Kosarych, Z. *J. Org. Chem.* 1982, 47, 4005.

(3) (a) Halazy, S.; Magnus, P. *Tetrahedron Lett.* 1984, 25, 1421. (b) Åkermark, B.; Nyström, J. E.; Rein, T.; Bäckvall, J. E.; Helquist, P.; Aslanian, R. *Ibid.* 1984, 25, 5719. (c) Bloom, A. J.; Mellor, J. M. *Ibid.* 1986, 27, 873. (d) Posner, G. H.; Wettlauffer, D. G. *J. Am. Chem. Soc.* 1986, 108, 7373. (e) Posner, G. H.; Harrison, W. *J. Chem. Soc., Chem. Commun.* 1985, 1786.

(4) Bäckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* 1987, 109, 6396.

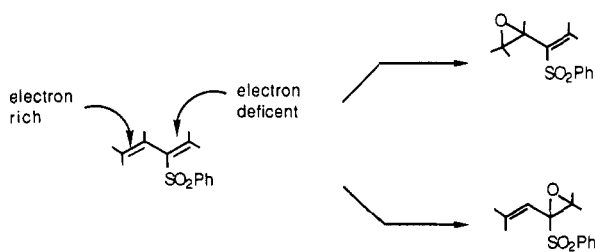
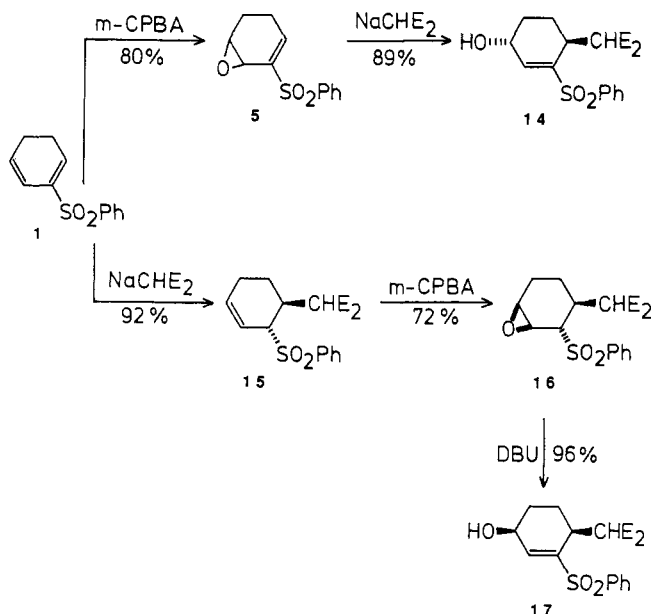
(5) (a) Saddler, J. C.; Donaldson, R. E.; Fuchs, P. L. *J. Am. Chem. Soc.* 1981, 103, 2110. (b) Saddler, J. C.; Fuchs, P. L. *Ibid.* 1981, 103, 2112. (c) Hardinger, S. A.; Fuchs, P. L. *J. Org. Chem.* 1987, 52, 2739.

(6) The precipitate formed was filtered off and the organic phase was washed with aqueous solutions of Na₂SO₃, Na₂CO₃, and brine. The crude product was purified by flash chromatography (silica, EtOAc/hexane = 10/90 and 20/80).

(7) Wasson, R. L.; House, H. O. *Org. Synth.* 1957, 37, 58. Wasson, R. L.; House, H. O. *Organic Syntheses*; Wiley: New York, 1963; *Collect. Vol. IV*, p 552.

(8) Zwanenburg, B.; ter Weil, J. *Tetrahedron Lett.* 1970, 935.

Scheme I

Scheme II. Stereoselective 1,4-Functionalization of 1 (E = CO₂Me)

of methanol afforded considerable amounts of Michael adducts.⁹

The epoxides obtained in Table I are powerful synthons for further transformations. For example, 11 and 12 should be useful in natural product synthesis. Fuchs et al.⁵ have demonstrated the use of 5 and analogous 3,4-epoxy-2-(phenylsulfonyl)-1-alkenes in selective transformations. For example it was shown that 5 can serve as a synthon for 13.^{5b} The previous synthesis of 5 involved five steps



from 1,3-cyclohexadiene in an overall yield of 40–45%.^{5a,5b,10} With our method^{4,11} 5 is obtained in three steps in 74% yield from 1,3-cyclohexadiene.

Some further demonstrations of the use of epoxidation reactions in functionalizations of the sulfonyl dienes are given in Scheme II. By changing the order of epoxidation

(9) (a) About 30–40% of addition of methanol and water occurred for the acyclic dienes. An alternative procedure would be to use *t*-BuOOH in toluene,^{9b} but for the cases tested the alkaline H₂O₂-acetone procedure⁸ worked satisfactorily. (b) Clark, C.; Hermans, P.; Meth-Cohn, O.; Moore, C.; Taljaard, H. C.; van Vuuren, G. *J. Chem. Soc., Chem. Commun.* 1986, 1378.

(10) In ref 5a (footnote 8) it was reported that compound 5 was prepared in 74% yield from 2-(phenylthio)-3-cyclohexen-1-ol (via the oxygen directed epoxidation route). Since the latter compound is obtained from 1,3-cyclohexadiene in ~60% yield, the overall yield of 5 based on 1,3-cyclohexadiene will be 40–45%.

(11) Bäckvall, J. E.; Juntunen, S. K.; Andell, O. S. *Organic Syntheses*; submitted for publication. Andell, O. S.; Bäckvall, J. E. *Tetrahedron Lett.* 1985, 26, 4555.

Table I. Selective Epoxidation of 2-Phenylsulfonyl 1,3-Dienes

entry	sulfonyl diene	conditions ^a	product	yield, % ^b
1		A		80
2	1	B		97 ^c
3		A		73
4	2	B		71
5		A		76
6	3	B		80
7		A		82
8	4	B		51

^a Method A: *m*-chloroperbenzoic acid, CH₂Cl₂, 20 °C. Method B: H₂O₂/NaOH in methanol (entry 2), ether-acetone (entry 4) or acetone (entries 6 and 8), 20 °C. ^b Isolated yield after flash chromatography (on silica except entry 7, where neutral alumina was used). ^c Chromatographic purification not needed.

and nucleophilic addition a useful stereocontrol in the 1,4-functionalization of 1 was obtained. Thus, selective epoxidation of 1 and subsequent reaction of vinyl epoxide 5 with sodium dimethyl malonate in an S_N2' manner afforded 14 as the sole product.^{12a} On the other hand, if the dimethyl malonate anion was added prior to the epoxidation, 16 was selectively formed,^{12b} which on treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded 17.¹³

When epoxide 6 was ring-opened by sodium dimethyl malonate in the presence of catalytic amounts of Pd(dba)₂

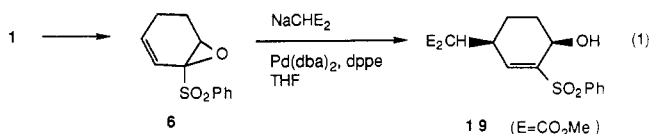
(12) (a) >99% *trans* in the crude product. (b) The crude product showed a ratio of 85/15 between *syn* and *anti* epoxide. A 72% yield of pure *syn* epoxide 16 was obtained after flash chromatography (silica, hexane/EtOAc = 80/20).

(13) (a) Compounds 14 and 17 show different ¹H NMR spectra (and also ¹³C NMR spectra) which allows an analysis of the stereoisomeric purity. The assignment of 14 and 17 was confirmed by transforming 14 to the alcohol 18 by reduction with sodium dithionite.^{13b} Authentic



samples of the alcohol 18 and its *cis* isomer were obtained by hydrolysis (MeO⁻, MeOH) of the corresponding known^{13c} acetates *trans*- and *cis*-1-acetoxy-4-(dicarbomethoxymethyl)-2-cyclohexene. (b) Bremner, J.; Julia, M.; Launay, M.; Stacino, J. P. *Tetrahedron Lett.* 1982, 23, 3265. (c) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* 1985, 107, 3676.

and dppe (1,2-bis(diphenylphosphino)ethane), **19** was formed in 85% yield (eq 1).¹⁴ Thus, three of the four



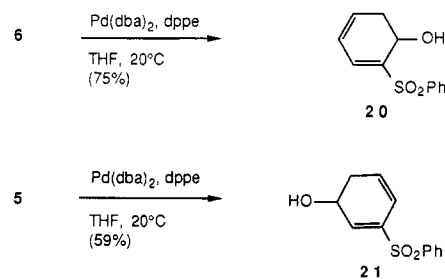
possible stereo- and regioisomers from 1,4-functionalization of **1** with OH and CH(CO₂Me)₂ can be prepared by this methodology (i.e., **14**, **17**, and **19**). The palladium-catalyzed reaction of vinyl epoxides usually works under neutral reaction conditions without added base.¹⁵ However, in the palladium-catalyzed reaction of **6** it was necessary to use 1.2 equiv of NaCH(CO₂Me)₂ to override the competing β-hydride elimination in the (π-allyl)palladium intermediate to give **20**.¹⁶ A selective formation of **20** from **6** occurred on treatment with a Pd(0) catalyst in the absence of nucleophile. An analogous Pd(0)-catalyzed rearrangement of **5** afforded **21**. Compounds **20** and **21**¹⁷ contain

(14) It is known that the palladium-catalyzed 1,4-opening of cyclic vinyl epoxides by dialkyl malonates occurs syn.^{15a} The cis stereochemistry was confirmed by ¹H NMR analysis of **19**. Thus, both of the vicinal coupling constants of CHO are <4 Hz and the two corresponding vicinal coupling constants of the other allylic proton are 9.8 and 6.9 Hz. This shows that the OH group is pseudoaxial and the CH(CO₂Me)₂ group is pseudoequatorial.

(15) (a) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969. (b) Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22*, 2575.

(16) For diene formation via (π-allyl)palladium complexes, see ref 3b and: Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.* **1978**, 2075. Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Ibid.* **1979**, 2301.

important functionalities and should be useful synthetic intermediates.



Acknowledgment. Financial support from the Swedish Natural Science Research Council and the Swedish Board of Technical Development is gratefully acknowledged.

Supplementary Material Available: Experimental details and NMR, IR, and analytical data for **5–12**, **14**, **16**, **16'**, **17**, and **19–21** (6 pages). Ordering information is given on any current masthead page.

(17) Compound **21** has previously been prepared in 50% yield by treatment of **5** with LDA in THF at -78 °C.^{5b}

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Additions and Corrections

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David K. Ho, Ann T. McKenzie, Stephen R. Byrn, and John M. Cassidy*. *O*⁵-Methyl-(±)-(2'*R*,3'*S*)-psorospermin.

Page 342. Some errors appear in the table of atomic coordinates for compound **7**: C3 y/b should be 0.2973 (6), C3 U11 should be

	x/a	y/b	z/c	U11	U22	U33	U23	U13	U12
C8	0.1893 (12)	-0.1411 (6)	0.4945 (5)	0.066 (6)	0.045 (5)	0.052 (5)	0.008 (4)	0.018 (4)	0.010 (4)
C8a	0.1961 (11)	-0.0428 (6)	0.4705 (5)	0.047 (5)	0.048 (5)	0.041 (4)	0.003 (4)	0.007 (4)	0.012 (4)
C9	0.0934 (12)	-0.0107 (5)	0.3839 (4)	0.055 (6)	0.041 (4)	0.040 (4)	0.002 (4)	0.008 (4)	0.011 (4)
O9	0.0079 (8)	-0.0723 (4)	0.3326 (3)	0.078 (4)	0.035 (3)	0.044 (3)	-0.002 (3)	-0.004 (3)	0.000 (3)
O10	0.3092 (7)	0.1231 (4)	0.5076 (3)	0.051 (4)	0.049 (3)	0.037 (3)	0.000 (2)	-0.003 (2)	0.003 (3)

0.059 (5), O5 z/c should be 0.6575 (3), O10 U11 should be 0.051 (4).

In addition to the above four corrections, in the original table of atomic coordinates atom C8 is missing, atom C9 except for x/a is incorrect, and atom O9 is missing. The correct data for C₈ through O₁₀ are