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Asymmetric Synthesis of Allylic Sulfones. Useful Asymmetric Building Blocks

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Abstract: Construction of sulfones in enantiomerically pure form provides a great opportunity to enhance their value as synthetic building blocks. Allylic sulfones, in particular, have great flexibility derived from sulfone-controlled additions to the double bond. Two strategies have been developed based upon the ability to effect asymmetric allylic alkylations with palladium employing ligands derived from c_2 symmetric diamines and 2-(diphenylphosphino)-benzoic acid. Desymmetrization of *meso*-2-ene-1,4-diol diesters does not involve the nucleophile in the enantiodiscriminating step and thus should, *a priori*, not depend upon the nature of the nucleophile. Indeed, such desymmetrization of such a diester in the presence of a sulfinate anion gave excellent enantioselectivity. On the other hand, conversion of both enantiomeric allylic esters to enantiomerically pure allylic sulfones requires sodium benzenesulfinate to participate in the enantiodiscriminating step. Five-, six-, and seven-membered substrates all gave excellent enantioselectivities. A catalytic phase transfer system proved most efficacious on larger scales. Propagating the asymmetry requires diastereoselective functionalization of the double bond. While epoxidation proved excellent for the five-membered ring case and satisfactory for the six-membered ring case, it was unsatisfactory in the seven-membered ring case. Osmium tetroxide-catalyzed *cis*-dihydroxylation gave excellent diastereoselectivities in the six- and seven-membered ring cases. Reductive cleavages produced enantiomerically pure allylic alcohols. Base-catalyzed elimination generated enantiomerically pure γ-hydroxy-α,β-unsaturated sulfones from which further stereogenic centers were produced by diastereoselective conjugate additions. Notably, an asymmetric cyclopentenone annulation using palladium-catalyzed cycloadditions now derives from racemic allyl alcohols.

Sulfones are exceptionally versatile intermediates in organic synthesis.[1] Such versatility stems from both the electronic and steric properties of such functionality, especially the allylsulfonyl moiety. For example, sulfones convert the adjacent carbon into both a nucleophilic and electrophilic center. Such dual reactivities lead us to dub them chemical chameleons.[1c] Vinyl sulfones are excellent Michael acceptors and participate in cross coupling reactions. The steric bulk of a sulfone offers an opportunity to direct reactions at the adjacent carbon. Furthermore, eliminations to alkenes and reductive cleavages allow the sulfone group to function as a selectivity control group. Allyl sulfones are particularly useful building blocks.[2] Their availability in enantiomerically pure form in simple fashion would greatly enhance their usefulness as synthetic intermediates.

The most direct synthesis of allylic sulfones is by direct allylation of a sulfinate anion.[3] Advances in asymmetric palladium-catalyzed allylic alkylation[4−6] encouraged us to examine this strategy. There are two approaches: (1) desymmetrization of a *meso*-2-ene-1,4-diol system[6a,b] and (2) deracemization of an allylic ester *via* a *meso*-π-allyl intermediate.[6c,d] The first strategy constitutes the more straightforward approach since asymmetric induction, to a first approximation, should be independent of the leaving group. However, complications

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(1) (a) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* **1986**, *86*, 903. (b) Roberts, D. W.; Williams, D. L. *Tetrahedron* **1987**, *43*, 1027. (c) Grossert, J. S. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rapoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons Ltd.: Chichester, 1988. (d) Trost, B. M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107. Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.

(2) Al: Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 7260. Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1986**, *108*, 1098. Adams, J. P.; Bowler, J.; Collins, M. A.; Jones, D. N.; Swallow, S. *Tetrahedron Lett.* **1990**, *31*, 4355. Trost, B. M.; Ghadiri, M. R. *Bull. Soc. Chim. Fr.* **1993**, *130*, 433. Cu: Julia, M.; Righini, A.; Verpeaux, J. N. *Tetrahedron Lett.* **1979**, 2393. Masaki, Y.; Sakuma, K.; Kaji, K. *J. Chem. Soc., Chem. Commun.* **1980**, 434. Julia, M.; Righini-Tapie, A.; Verpeaux, J. N. *Tetrahedron* **1983**, *39*, 3283. Julia, M.; Verpeaux, J. N. *Tetrahedron* **1983**, *39*, 3289. Masaki, Y.; Sakumi, K.; Kaji, K. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1171. Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 5216. Fe: Fabre, J. L.; Julia, M.; Verpeaux, J. N. *Bull. Soc. Chim. Fr.* **1985**, 772. Ni: Cuvigny, T.; Julia, M. *J. Organomet. Chem.* **1983**, *250*, C21; **1986**, *317*, 383. Pd: Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5979. Mo: Trost, B. M.; Merlic, C. A. *J. Org. Chem.* **1990**, *55*, 1127. Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.

(3) Trost, B. M.; Schmuff, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 396. Julia, M.; Lave, D.; Mulhauser, M.; Ramirez-Munoz, M.; Uguen, D. *Tetrahedron Lett.* **1983**, *24*, 1783. Inomata, K.; Yamamoto, T.; Kotake, H. *Chem. Lett.* **1981**, 1357.

(4) For reviews, see: Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339. Hayashi, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed; VCH Publishers: New York, 1993; pp 325−365. Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089. Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257.

(5) For some examples, see: (a) Andersson, P. G.; Harden, A.; Tanner, D.; Norrby, P. *Chem. Eur. J.* **1995**, *1*, 12. (b) Wimmer, P.; Widhalm, M. *Tetrahedron: Asymmetry* **1995**, *6*, 657. (c) von Matt, P.; Lloyd-Jones, G. L.; Minidis, A. B. E.; Pfaltz, A.; Macko, L.; Neuburger, M.; Zehnder, M.; Rüegger, H.; Pregosin, P. S. *Helv. Chim. Acta* **1995**, *78*, 265. (d) Gamez, P.; Dunjic, B.; Fache, F.; Lemaire, M. *Chem. Commun.* **1994**, 1417. (e) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493. (f) Kang, J.; Cho, W. O.; Cho, H. G. *Tetrahedron: Asymmetry* **1994**, *5*, 1347. (g) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062. (h) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y.; Miki, M.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 775. (i) Pregosin, P. S.; Rüegger, H.; Salzmann, R.; Albinati, A.; Lianza, F.; Kunz, R. W. *Organomet.* **1994**, *13*, 83. (j) Sprinz, J.; Kiefer, M.; Helmchen, G.; Reggelin, M.; Huttner, G.; Walter, O.; Zsolnai, L. *Tetrahedron Lett.* **1994**, *35*, 1523. (k) Allen, J. V.; Coote, S. J.; Dawson, G. J.; Frost, C. G.; Martin, C. J.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2065. (l) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566. (m) Hayashi, T.; Yamamoto, A.; Hagihara, T.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 191.

(6) (a) Trost, B. M.; Van Vranken, D. L. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 228. (b) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327. (c) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089. (d) Trost, B. M.; Organ, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 10320.

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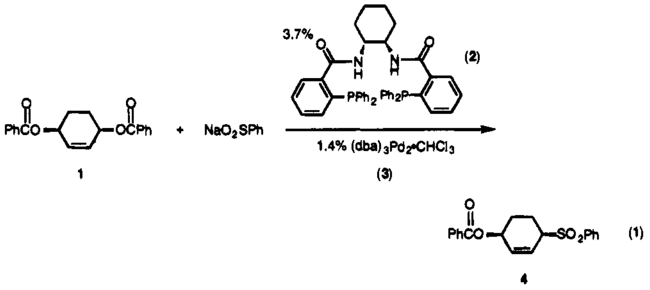
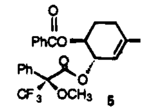
arising from coordination of the nucleophile to palladium may occur. The second strategy potentially is more general but, since it involves the nucleophile in the enantiodiscriminating step, becomes more questionable. In this paper, we examine both strategies and the utility of the resultant adducts in further synthetic transformations.[7]

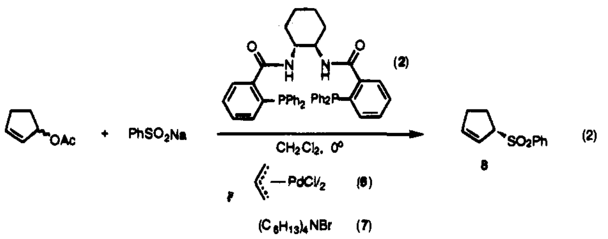
Results

Desymmetrization of *meso*-2-Ene-1,4-diol Esters. The reaction of *cis*-1,4-bis(benzoyloxy)-2-cyclohexene (**1**)[6b] with sodium benzenesulfinate catalyzed by a complex generated *in situ* by mixing our recently disclosed chiral ligand **2** with (dba)$_3$Pd$_2$·CHCl$_3$ (**3**) led to smooth reaction in 3:1 THF–water at 0 °C (eq 1).[6] Chromatography gave an 85% yield of crystalline sulfone **4**, mp 134 °C. A better set of conditions employs a two-phase methylene chloride–water system with tetra-*n*-hexylammonium bromide as the phase transfer catalyst in which the yield increased to 88%. Attempts to assess the enantioselectivity by hydrolysis of **4** to its corresponding alcohol in order to form mandelate esters failed because of its propensity to undergo elimination. Indeed, the excellent yield for the initial alkylation without being plagued by elimination is somewhat surprising considering how facile the elimination is. The reaction was performed on as large as a 9 g scale with no diminishment in either yield or er (enantiomeric ratio). Ultimately (*vide infra*), we converted the sulfone to the Mosher ester **5**[8] and assessed the dr (diastereomeric ratio) of **5** to be >98:<2 (i.e., none of the diastereomer detected by ^{1}H NMR spectroscopy) which translates to an er for **4** of >98:<2 (>96% ee).

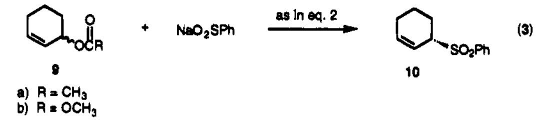


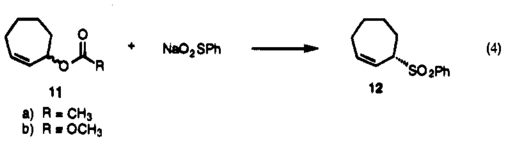


Enantioconvergency. Reaction of 3-acetoxycyclopentene with sodium benzenesulfinate in methylene chloride with a catalyst derived from the diamide ligand **2**[6b] and π-allylpalladium chloride dimer **6** in the presence of tetra-*n*-hexylammonium bromide (**7**)[6c] gave within 20 min at 0 °C a nearly quantitative yield of the alkylation product **8** (eq 2) as a low melting (mp 42– 3 °C) white solid. A chiral shift study using Eu(hfc)$_3$ in deuteriochloroform indicated an er of 99:1 (98% ee). The absolute configuration is based upon our previously established mnemonic[6b] and subsequent transformations (*vide infra*). Using the chiral ligand derived from (*R*,*R*)-1,2-diamino-1,2-diphenylethane, the reaction required 1 day for completion. Thus, we adopted the cyclohexyl-based ligand **2** as the preferred one.

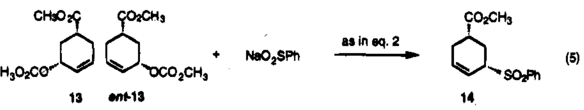


Examination of the six-membered ring substrate proved most interesting. Subjecting racemic 3-acetoxycyclohexene (**9a**) to the same reaction conditions as above also at 0 °C gave a 78% yield of sulfone **10** as a thick oil, which solidifies in the freezer (eq 3). Addition of Eu(hfc)$_3$ in deuteriochloroform separates the proximal vinyl proton into two doublets, allowing easy assay of the er as 90:10 (80% ee). Switching to the carbonate leaving group as in **9b** unexpectedly saw the er increase to 99:1 (98% ee, 87% yield). Performing the reaction in a two-phase methylene chloride–water system with **3** as the palladium(0) source produced allyl sulfone **10** of the same er in a yield of 95%. On a 20 g scale under these latter conditions, 0.28 mol % **3**, 0.60 mol % **2**, and 1 mol % **7** were employed—a set of conditions that gave complete reaction after 2 h at 0 °C. The absolute configuration is established by our mnenomic as well as by further transformations. A similar effect, although less pronounced, was observed in the seven-membered ring system (eq 4). The allyl acetate **11a** gave sulfone **12** with a 97:3 er (94% ee) in 66% yield which increased to 99:1 er (98% ee) in 95% yield for the carbonate **11b**, all at 0 °C. While the enhanced yield is not unexpected due to the carbonate being a better leaving group, the notion that the leaving group should play no role in the enantiodiscriminating step is challenged.





Substitution on a saturated carbon of the ring as in **13**[9] gave excellent results (eq 5). Chiral shift studies in which one of the vinylic protons clearly resolves into two baseline-resolved signals indicated an er of 99:1 (98% ee) in 98% yield. On the other hand, placement of a methyl group on the double bond at C-4 as in the carbonate from carveol under identical conditions led to a very sluggish reaction requiring several days at reflux to see conversion and thus almost no asymmetric induction.



Synthetic Applications. Propagation of the asymmetry introduced in the allylic alkylation requires diastereoselective functionalization of the double bond. The steric bulk of the allylic phenylsulfonyl moiety may direct the stereochemistry of addition to the adjacent double bond. In the case of **4**, the

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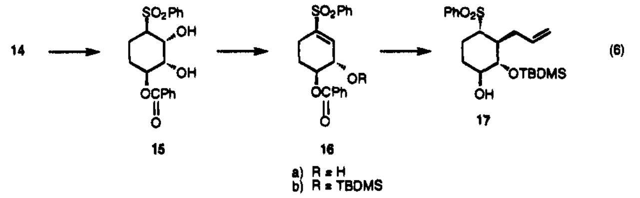
(7) (a) Cf. Hiroi, K.; Yamamoto, M.; Kurihara, Y.; Yonezawa, H. *Tetrahedron Lett.* **1990**, *31*, 2619. Hiroi, K.; Kurihara, Y. *Chem. Commun.* **1989**, 1778. Hiroi, K.; Makino, K. *Chem. Pharm. Bull.* **1988**, *36*, 1749. Hiroi, K.; Kitayama, R.; Sato, S. *Chem. Pharm. Bull.* **1984**, *32*, 2628. (b) For independent work with the 1,3-diphenylallyl system and the Helmchen–Pfaltz–Williams system, see: Eichelmann, H.; Gais, H.-J. *Tetrahedron: Asymmetry* **1995**, *6*, 643.

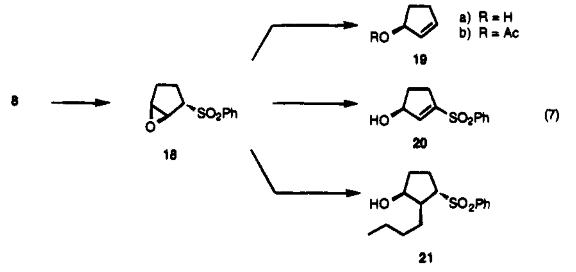
(8) For a recent reference, see: Latypov, S. K.; Seco, J. M.; Quiñoá, E.; Riguera, R. *J. Org. Chem.* **1995**, *60*, 504.

(9) (a) Trost, B. M.; Kondo, Y. *Tetrahedron Lett.* **1991**, *32*, 1613. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

two substituents would be expected to exert a synergistic effect. Thus, it was not surprising that catalytic *cis*-dihydroxylation[10] gave a single diol, **15**, in 95% yield (eq 6) using our modified conditions of methylene chloride containing a small amount of water.[11] Elimination to the vinyl sulfone **16a** was best accomplished by conversion to the cyclic carbonate ($COCl_2$, $PhCH_3$, 0 °C) followed by triethylamine in methylene chloride (95% overall yield). This allylic alcohol served as the precursor of the Mosher ester **5**. Formation of the silyl ether **16b** followed by conjugate addition gave an adduct tentatively assigned as **17** wherein the alkyl group was introduced *trans* to the allylic oxygen substituent on the basis of ample analogy.[12] Thus, the palladium-catalyzed desymmetrization of the *meso*-enediol system ultimately led to creation of three stereogenic centers of defined absolute configuration.

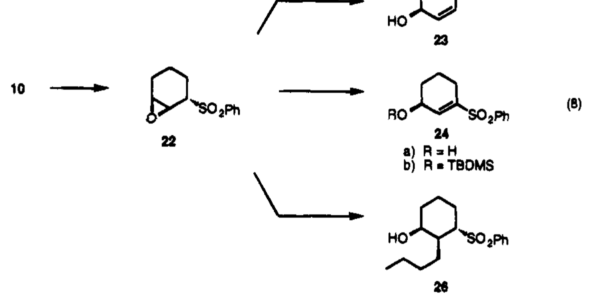


The sulfone itself may be sufficient to direct the stereochemistry of addition to the double bond. Epoxidation with *m*-chloroperoxybenzoic acid (MCPBA) of **8** led to a single epoxide (as determined by NMR spectroscopy of the crude mixture), mp 59.5–60.5 °C, in 66% yield. Since a sulfone is a rather noncoordinating functionality, the stereochemistry was assigned as *trans* as depicted in **18** (eq 7). Previously, this epoxidation with peracetic acid has been reported to be nonselective.[12f] A chiral shift study confirmed the diastero- and enantiomeric purity of the epoxide. Reductive cleavage with 5% sodium amalgam in methanol[13] provided an asymmetric synthesis of the enantiomerically pure 3-hydroxycyclopentene (**19a**) which was characterized as its acetate **19b**.[14] The negative observed rotation confirmed the absolute configuration as *S*, which independently established the absolute configuration of **8**. The volatility of **19a** and **19b** led to substantial mechanical losses such that the overall yield of **19b** was only 35%. This correlation also supports the assigned absolute and relative stereochemistry of the sulfone and epoxysulfone.

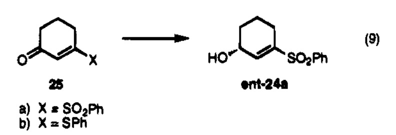


Base opening (lithium diisopropylamide (LDA), THF, −78 °C) of the epoxide gave the vinyl sulfone **20** in 81% yield. This compound had previously been used for diastereocontrolled Michael additions in which the stereochemistry depended upon the nature of the oxygen substituent.[12] For example, opening the epoxide with 2.4 equiv of *n*-butyllithium led directly to the Michael adduct **21** as a single diastereomer, mp 76–77 °C, in 74% yield. In this case, coordination to the *γ*-lithium alkoxide directed addition *syn* to this substituent.[12]

In the six-membered ring series, the diastereoselectivity of the epoxidation was diminished to a 5.3:1 ratio of the *trans* to *cis* isomers (70% yield, eq 8) from which the pure *trans*-**22** was readily separable by chromatography. Chiral shift studies with $Eu(hfc)_3$ in deuteriobenzene established diastereo- and enantiohomogeneity of the latter. Previously, an undefined ratio of diastereomers had been reported.[12f] Reductive cleavage with sodium naphthalenide gave a 58% yield of allyl alcohol **23**. Again, the yield undoubtedly reflected the volatility of the product with mechanical losses during workup which would be minimized if the reactions were performed on larger scales. Comparison of its rotation ($[\alpha]^{25}_{D}$ −117.1° (*c* 0.13, dry $CHCl_3$)) to the literature[14] established both its enantiopurity and absolute configuration. This correlation also supported the stereochemical assignments of the allylic alkylation and epoxidation reactions.



Base-catalyzed opening as before gave a quantitative yield of the alcohol **24a**.[14] Previously, we prepared *ent*-**24a** by asymmetric reduction of the sulfone **25a** in an er of 82:18 (64% ee), which could be raised to 89.5:10.5 (79% ee) by reduction of the sulfide **25b** followed by oxidation (eq 9).[15] From the rotation of *ent*-**24a** prepared by this latter method ($[\alpha]^{25}_{D}$ +41.1° (*c* 0.01, $CHCl_3$)), our observed rotation of $[\alpha]^{25}_{D}$ −51.6° (*c* 3.49, CH_2Cl_2) indicates it has the stereochemistry depicted in **24a** and an er of >99:1 (>98% ee). Elimination–Michael addition occurred as before upon treatment with 2.2 equiv of *n*-butyllithium to give a 64% yield of adduct **26** as a single diastereo- and enantiomer in addition to 21% of the vinyl sulfone **24a**, which could be converted to the same adduct by further treatment with *n*-butyllithium.[12]



To improve the diastereoselectivity of the oxidation of the double bond, we turned to dihydroxylation catalyzed by osmium tetroxide. In this case, only a single diastereomer assigned as **27** was obtained in 95% yield (eq 10). Formation of the carbonate followed by triethylamine gave vinyl sulfone **24a**, which was silylated to its *tert*-butyldimethylsilyl (TBDMS) ether in standard fashion. Its rotation of $[\alpha]^{25}_{D}$ −54.8° (*c* 3.3, $CHCl_3$)

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(10) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

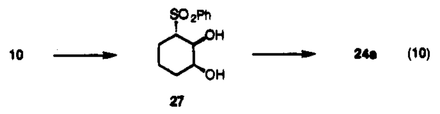
(11) Higuchi, R. Unpublished observations in these laboratories. Cf. Iwasawa, N.; Kato, T.; Narasaka, K. *Chem. Lett.* **1988**, 1721.

(12) (a) Jin, Z.; Fuchs, P. L. *J. Am. Chem. Soc.* **1995**, *117*, 3022. (b) Ranasinghe, M. G.; Fuchs, P. L. *J. Am. Chem. Soc.* **1989**, *111*, 779. (c) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4755. (d) Ponton, J.; Helquist, P.; Conrad, P. C.; Fuchs, P. L. *J. Org. Chem.* **1981**, *46*, 118. (e) Conrad, P. C.; Fuchs, P. L. *J. Am. Chem. Soc.* **1978**, *100*, 346. (f) Saddler, J. C.; Conrad, P. C.; Fuchs, P. L. *Tetrahedron Lett.* **1978**, 5079.

(13) Cf. Julia olefination; see: Kocienski, P. J. *Chem. Ind. (London)* **1981**, 548. Julia, M.; Paris, J.-M. *Tetrahedron Lett.* **1973**, 4833. Also see: Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477.

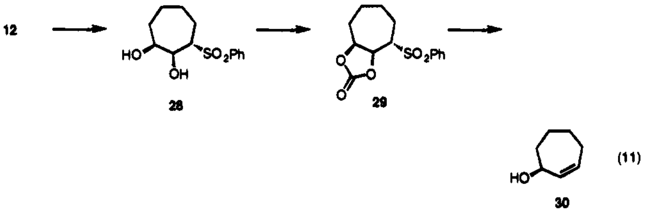
(14) Asami, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 721.

(15) Trost, B. M.; Seoane, P.; Mignani, S.; Acemoglu, M. *J. Am. Chem. Soc.* **1989**, *111*, 7487.



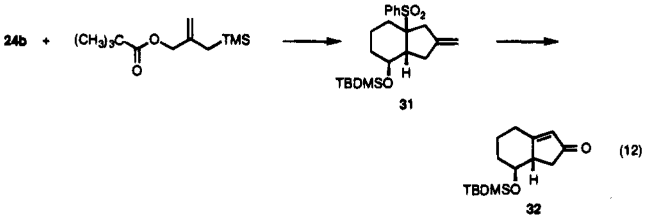
compared to a rotation of $[\alpha]^{25}_D$ +51.9° (c 0.01, $CHCl_3$) for material having an er of 96.5:3.5 (93% ee) reported previously[15] also establishes the absolute configuration as depicted and the er as being >98:2 (>96% ee).

Proceeding to the seven-membered ring allylic sulfone **12** led to an even poorer diastereoselectivity of epoxidation (approximately 2:1) compared to the above. On the other hand, the dihydroxylation gave a single diastereomeric diol, **28**, which was isolated in 96% yield as a white solid, mp 161−2 °C (eq 11). Stirring with sodium naphthalenide in THF at 0 °C gave



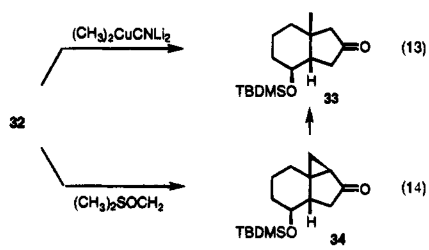
the known allyl alcohol **30** (57% yield) which, by comparison of its rotation to the literature,[14] has the absolute configuration depicted and an er of 96:4 (92% ee). This er is in excellent agreement with the er of 97:3 (94% ee) determined for the precursor allylic sulfone.

One of the uses of the γ-hydroxy-α,β-unsaturated sulfones that interested us in conjunction with a projected synthesis of pseudolarolide E[16] was a cyclopentenone annulation.[15] We therefore subjected vinyl sulfone **24b** to palladium-catalyzed trimethylenemethane (TMM) cycloaddition. Using a catalyst generated from palladium acetate and triisopropyl phosphite, 2-[(trimethylsilyl)methyl]allyl pivalate, a total of 2.7 equiv added in three portions, in toluene at 80 °C gave an approximately 8:1 mixture of the two diastereomeric adducts from which the major adduct **31** was isolated in 83% yield (eq 12). Using the



acetate of the trimethylenemethane precursor gave the adduct **31** in a slightly lower 75% yield. This compound was identical to a previously prepared sample but opposite in the sign of rotation, indicating it has the mirror image stereochemistry as depicted in **31**.[15] Ozonolysis and *in situ* elimination of the elements of benzenesulfinic acid by addition of triethylamine gave **32** in 94% yield.

The subsequent transformations of enone **32** further progagate the stereochemistry originating from the sulfone. Addition of dilithium dimethylcyanocuprate in ether at 0 °C gave a single isomer as determined by both chromatographic and spectroscopic analysis. On the basis of the assumption of least hindered addition, attack from the convex face is anticipated to give Michael adduct **33** (eq 13). Using dimethyloxysulfonium methylide, conjugate addition rather than carbonyl addition occurred to give a single cyclopropane tentatively assigned as



depicted in **34** again on the basis of approach of the ylide from the convex face. In neither case was elimination of the siloxide a problem.

The stereochemical assignment of the cyclopropane was supported by proton nuclear Overhauser effect (NOE) studies. The *endo* cyclopropyl hydrogen showed positive NOEs to both the bridgehead proton (2.0%) and the β-methylene proton adjacent to the carbonyl group (4.7%). Reductive cleavage of the cyclopropane with lithium 4,4′-di-*tert*-butylbiphenylide gave the identical product obtained from the cuprate addition, thereby supporting the stereochemical assignment of **33** as well.

Discussion

The synthetic flexibility of sulfones has established them as important building blocks in organic synthesis. The ability of a phenylsulfonyl group to function as an enantioselectivity control element depends upon the accessibility of the sulfones in enantiomercially pure form. The absence of simple protocols to obtain them in such fashion has restricted such applications. Earlier efforts in these laboratories focused on asymmetric reduction of 3-(phenylthio)- or 3-(phenylsulfonyl)cycloalkenones, but the er values were disappointing.[15] Two developments now change this picture: (1) the availability of allylic sulfones by palladium-catalyzed alkylation chemistry[3] and (2) asymmetric induction of a high order in palladium-catalyzed allylic alkylations.[5,6] The difficulty of developing ligands for asymmetric induction in transition metal reactions wherein the enantiodiscriminating step involves bond formation and/or bond cleavage outside the coordination sphere of the metal[9b] has hampered the development of asymmetric induction in this field. Recently, there has been an explosion of ligands that catalyze this reaction with excellent enantioselectivities for the case of the 1,3-diphenylallyl system,[5] a substrate we introduced as a test system for ligand design.[17] However, we began to question the validity of this test system when extrapolations to cyclic substrates led to significantly lower enantioselectivities.[17,18] It appeared that this test system was not terribly demanding since high enantioselectivities could be achieved even with BINAP.[19] Of these ligands, the chiral phosphinooxazoline series developed independently by the groups of Helmchen,[5j] Pfaltz,[5l] and Williams[5k] and the ferrocene series developed mainly by Hayashi[5m] have proven especially interesting although their scope appears to be limited. Thus, while they perform outstandingly with the 1,3-diphenyl- and 1,3-diisopropyl-substituted allyl systems, extension to other acyclic or cyclic derivatives has not been as successful to date.[18] Since the nucleophile is involved in the enantiodiscriminating step, the question of its effect on the chiral recognition must be addressed. The evidence to date suggests that while the substrate may be limited, the choice of nucleophile is less restrictive. Pertinent to this study is a report that appeared after our work was complete that sodium *p*-toluenesulfinate as a nucleophile shows

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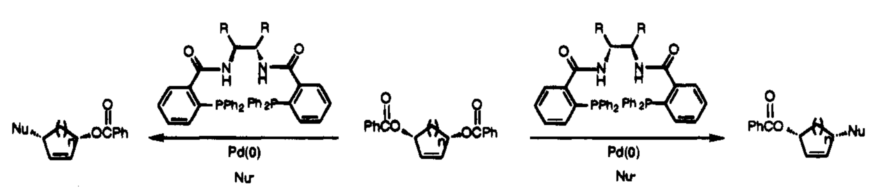
(16) Chen, G. F.; Li, Z.-L.; Chen, K.; Tang, C.-M.; He, X.; Pan, D.-J.; Hu, C. Q.; McPhail, D. R.; McPhail, A. T.; Lee, K. H. *Chem. Commun.* **1990**, 113.

(17) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.

(18) Also see ref 5e,m and Sennhenn, P.; Gabler, B.; Helmchen, G. *Tetrahedron Lett.* **1994**, *35*, 8595.

(19) Singleton, D. Unpublished work in these laboratories. For a recent independent report, see ref 5i.

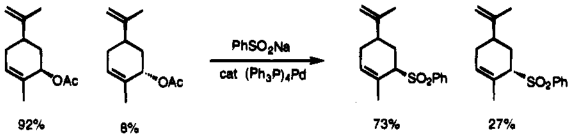


(15)

(16)

the same selectivities as established for malonate anion with this class of ligands.[7b]

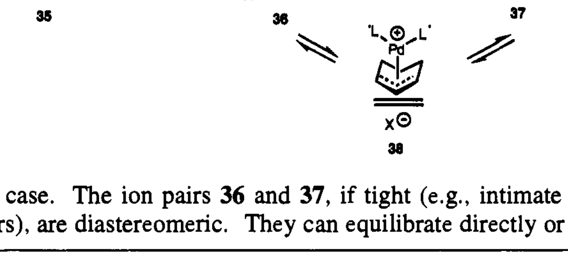
Our development of a new class of chiral ligands derived from chiral diols or diamines and 2-(diphenylphosphino)benzoic acid led to two types of reactions with excellent enantioselectivities as shown in eqs 15 and 16.[6] None of the other asymmetric ligands have been reported to be effective in either of these cases.[18,20] Of these two types, the former should not, *a priori*, involve the nucleophile. However, to the extent that the nucleophile may be a ligand to the metal, this assumption may not be valid. Concern that such coordination may occur stemmed from the diminished diastereoselectivity observed in palladium-catalyzed substitutions of allyl acetates (eq 17).[3] This



(17)

result may be explained by some leakage of the reaction whereby a sulfinate attached to palladium undergoes reductive elimination to give the product of net inversion of configuration, the *E* isomer. Furthermore, sulfinate has been shown to coordinate to Pd^{2+} in Heck reactions.[21] However, such fears proved unwarranted. The excellent enantioselectivity observed indicates either (1) such coordination does not occur during the enantiodiscriminating step or (2) such coordination does not affect the chiral discrimination. If such coordination was accompanied by reductive elimination, the diastereomeric product would have been observed but was not.

The more challenging case is the enantioconvergency of racemic allylic esters. Fundamental to this strategy is the assumption that, upon ionization of the leaving group, the resulting ion pair is achiral with achiral ligands as in **35** and the π-allyl unit remains fully symmetrical in the ion pair **38** with respect to the external anion. However, that need not be



the case. The ion pairs **36** and **37**, if tight (e.g., intimate ion pairs), are diastereomeric. They can equilibrate directly or *via* a looser ion pair such as a solvent-separated ion pair like **38**. If reaction occurs *via* the latter, asymmetric induction should be independent of the leaving group. To the extent that reaction occurs *via* the former, there can be a dependence on the leaving group in one of two ways. Since these ion pairs are diastereomeric, even with rapid equilibration, they will react at different rates. Alternatively, if interconversion between themselves or between themselves and **38** is slow, any kinetic bias that **36** or **37** exhibits with respect to the regioselectivity of attack of the nucleophile will be observed.

This scenario can account for the unexpected dependence upon the leaving group observed in the six- and seven-membered ring cases. With acetate as a leaving group, reaction may be occurring to some extent *via* a tight ion pair which compromises the chiral recognition imposed by the ligands. With a better leaving group which more likely will lead to solvent separation, the full impact of the chiral recognition imposed by the ligands may be felt. While other explanations may be brought forth (e.g., formation of σ- rather than π-allyl complexes), the importance of ion pairs in non-metal-catalyzed allylic substitution[22] suggests they should at least be considered in metal-catalyzed reactions. Since the typical solvents employed in metal-catalyzed substitutions like THF and methylene chloride favor formation of ion pairs, their involvement in all palladium-catalyzed substitutions is likely. It is interesting to note that the different ring sizes showed a dependence on the leaving group in the order six > seven > five, the five-membered ring showing no dependence. Thus, the structure of the allyl unit as well as the leaving group is important. Practically, use of the carbonate obviates this complication.

The ability of sulfones to serve as nucleophiles with high enantioselectivity in the presence of tetrahexylammonium bromide is a significant expansion of palladium-catalyzed asymmetric alkylations. It reinforces the concept that, for these alkylations, the structure of the anion of the nucleophile is less important than the structure of the cation—a most surprising dependence given the fact that it is the anion that ultimately bonds and not the cation. The success of these alkylations expands the domain of applicability of this family of catalysts in organic synthesis. To date, they prove to have the broadest range of applications. In the previously reported examples,[7] sulfinate esters arising from O alkylation competing with S alkylation as well as sulfone were frequently encountered. In our alkylations, we have not detected the presence of such products. Whether they were formed but reversibly under our conditions such that the allylic sulfinate was converted into allylic sulfone or our catalysts direct reaction more selectively to S alkylation cannot be differentiated at the present time.

Access to allylic sulfones asymmetrically now provides an opportunity to extend the use of sulfones as building blocks. Among the various possibilities, their ability to control the diastereoselectivity of addition to the double bond to ultimately create γ-alkoxy-α,β-unsaturated sulfones enantiomerically pure is one of the most valuable. For the five-membered ring, excellent diastereoselectivity is seen even with a rather non-

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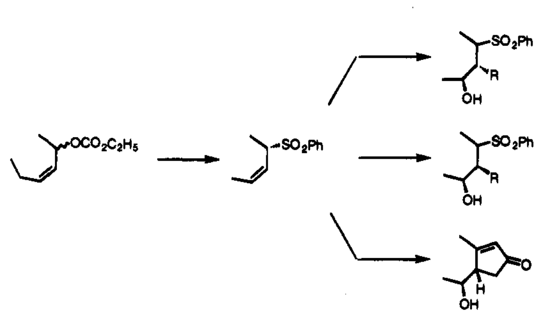
(20) Mori, M.; Nukui, S.; Shibasaki, M. *Chem. Lett.* **1991**, 1797. In the case of substrates from (*E*)-2-butene-1,4-diol, it cannot be discerned whether the enantiodiscriminating step is the ionization or nucleophilic addition. See: Uozumi, Y.; Tanahashi, A.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 6826. Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1988**, *29*, 99, 669. Also see: Massacret, M.; Goux, C.; Lhoste, P.; Sinou, D. *Tetrahedron Lett.* **1994**, *35*, 6093.

(21) Tamaru, Y.; Yoshida, Z. *Tetrahedron Lett.* **1978**, 4527. Chiswell, B.; Venanzi, L. M. *J. Chem. Soc. A* **1966**, 1246. Garves, K. *J. Org. Chem.* **1970**, *35*, 3273. Selke, R.; Thieli, W. *J. Prakt. Chem.* **1971**, *313*, 875.

(22) Sneen, R. A. *Acc. Chem. Res.* **1973**, *6*, 46. Kantner, S. S.; Humski, K.; Goering, H. L. *J. Am. Chem. Soc.* **1982**, *104*, 1693.

discriminating epoxidizing agent. In the six-membered ring, reaction *via* the equatorial sulfone conformer **39** would show a lower diastereoselectivity than *via* **40**. Thus, while a satisfactory level of diastereoselectivity was observed in the epoxidation, better results are obtained with the more discriminating osmium-catalyzed dihydroxylation. The seven-membered ring gave unsatisfactory results in the former but excellent selectivity in the latter. The resultant diol has virtue in and of itself or can function as the equivalent of the epoxide. For elimination, the cyclic carbonate is sufficient activation, leading either to an allyl alcohol under reductive conditions or a γ-alkoxy-α,β-unsaturated sulfone under basic conditions. Diastereoselective addition to such Michael acceptors may occur either *syn* or *anti* to the allylic oxygen,[12] thus providing a diastereo- and enantioselective synthesis of vicinal systems as illustrated in eq 18. Since the sulfone still may serve to facilitate further C−C bond formation, the single stereogenic center of the sulfone-bearing carbon may propagate into more than two stereogenic centers. Also, access to an asymmetric cyclopentenone annulation allowed the Michael system to extend the creation of additional stereogenic centers ultimately having their origin in the carbon bearing sulfone. The desymmetrization of the enediol system extends each of these reactions to one more center. This also serves as a viable approach for the synthesis of the very difficultly accessible enantiomerically pure 1-cycloalken-3-ols[23] although not as efficiently as our recently developed deracemization protocol.[6d] Thus, by combining the ability of palladium-catalyzed allylic alkylations to be performed asymmetrically with the use of sulfones as versatile building blocks, a powerful approach for asymmetric synthesis from readily available precursors emerges.

39 **40**



(18)

Experimental Section

Reactions were generally conducted under a postive pressure of dry nitrogen within glassware which had been flame-dried under a stream of dry nitrogen. Reaction flasks were sealed with red rubber septa and were, unless otherwise mentioned, magnetically stirred. Anhydrous solvents and reaction mixtures were transferred by an oven-dried syringe or cannula. Flash chromatography employed E. Merck silica gel (Kiesselgel 60, 230−400 mesh). Analytical TLC was performed with 0.2 mm coated commercial silica gel plates (E. Merck, DC-Plastikfolien, Kiesselgel 60 F_{254}). ^{1}H NMR spectra were obtained and recorded from a Gemini GEM-200 (200 MHz), Nicolet NT-300 (300 MHz), or Varian XL-400 (400 MHz), instrument, with TMS as the internal standard. ^{13}C NMR spectra were recorded on a Nicolet NT-300 (75 MHz) or a Varian XL-400 (100 MHz) instrument. Chemical shifts are reported in δ units, parts per million from the central peak of $CDCl_3$ (δ 77.0) as an internal reference. IR spectra were performed by the NIH Mass Spectral Facility at the School of Pharmacy, University of California−San Francisco on a Kratos MS-90 instrument with an ionizing current of 98 mA and an ionizing voltage of 70 eV. Microanalyses were performed by M-H-W Laboratories, Phoenix, AZ.

Enantioselectivities were determined by a combination of shift studies, derivatizations to mandelates, and rotations. Rotation data are employed only by comparisons to such data obtained under the same conditions in these laboratories. When rotation data are employed, such data for one of the compounds in a sequence are checked by at least one additional method for verification.

Preparation of 1(*S*)-(Benzoyloxy)-4(*R*)-(phenylsulfonyl)cyclohex-2-ene (4). Method A. A premixed orange solution of catalyst generated from $(dba)_3Pd{\cdot}CHCl_3$ (200 mg, 0.218 mmol) and ligand **2**[6b] (400 mg, 0.579 mmol) in 3 mL of THF was added to a solution of sodium benzenesulfinate (3.20 g, 19.5 mmol) and dibenzoate **1** (5.00 g, 15.5 mmol) in 50 mL of THF and 10 mL of water at 0 °C. After 10−15 min, the mixture turned yellow. It was stirred at 0 °C until TLC indicated complete consumption of starting material (10 h), at which point aqueous sodium bicarbonate and methylene chloride were added. The organic layer was separated and washed with sodium bicarbonate and brine. After drying (Na_2SO_4), column chromatography of the residue (30% ether in hexane) gave 4.5 g (75% yield) of product as a white solid, mp 134 °C, $[\alpha]^{25}_{D}$ +22.5° (*c* 1.1, $CHCl_3$), R_f = 0.8 (ether). IR (neat): 3080, 2960, 1675, 1480, 1335, 1080 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (d, *J* = 7.1 Hz, 2 H), 7.82 (d, *J* = 7.1 Hz, 2 H), 7.5−7.7 (m, 4 H), 7.40 (t, *J* = 7.7 Hz, 2 H), 6.21 (ddd, *J* = 3.9, 2.0, 1.9 Hz, 1 H), 6.15 (dd, *J* = 10.2, 2.5, Hz, 1H), 5.40 (dd, *J* = 3.0, 1.2 Hz, 1 H), 3.82 (m, 1 H), 2.2−1.9 (m, 3 H), 1.9−1.8 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 165.7, 136.6, 133.4, 133.1, 132.3, 129.9, 129.6, 129.3, 129.0, 128.3, 124.3, 65.8, 61.5, 25.5, 19.0. HRMS: calcd for $C_{12}H_{12}O_2S$ (M^+ − $PhCO_2H$) 220.0558, found 220.0557.

Method B. A premixed orange solution of catalyst generated from **3** (400 mg, 0.436 mmol) and ligand **2** (800 mg, 1.16 mmol) in 5 mL of methylene chloride was added to a two-phase mixture of sodium benzenesulfinate (5.0 g, 30.5 mmol), dibenzoate **1** (9.00g, 30.2 mmol), and tetra-*n*-hexylammonium bromide (3.20 g, 7.36 mmol) in 100 mL of methylene chloride and 50 mL of water. After 8 h, aqueous ammonium chloride and methylene chloride were added, and the reaction was worked up as above to give 8.4 g (88% yield) of **4**.

3(*S*)-(Phenylsulfonyl)cyclopent-1-ene (8). A mixture of sodium benzenesulfinate (98 mg, 0.60 mmol), tetrahexylammonium bromide (**7**) (258 mg, 0.60 mmol), π-allylpalladium chloride dimer (**6**) (1.8 mg, 0.005 mmol), and ligand **2** (10.3 mg, 0.015 mmol) was diluted with 4 mL of methylene chloride. After 15 min at room temperature (rt), the temperature was lowered to 0 °C, at which point 3-acetoxycyclopent-1-ene (25 mg, 0.20 mmol) was added all at once. Reaction was complete in 20 min as judged by TLC, at which point it was absorbed on 800 mg of silica gel. This plug of silica gel was added to the top of a prepacked column and the product eluted (10% ethyl acetate in hexanes) to give 40 mg (98% yield) of a white solid, mp 42−3 °C, R_f = 0.15, $[\alpha]^{25}_{D}$ −216.6° (*c* 1.56, CH_2Cl_2). Performing the reaction with 4.0 g (24.4 mmol) of sodium benzenesulfinate, 2.05 g (16.3 mmol) of 3-acetoxycyclopentene, 7.5 mg (0.02 mmol) of **6**, and 48 mg (0.06 mmol) of **2** (approximately halfway the reaction appeared to slow, so a second portion of catalyst was added) in 100 mL of methylene chloride gave 3.39 g (89% yield) of product with an identical er. IR (neat): 1660, 1600, 1585, 1445, 1144, 1083 cm^{-1}. ^{1}H NMR ($CDCl_3$ 300 MHz): δ 7.88 (d, *J* = 7.0 Hz, 2H), 7.67 (br t, *J* = 1.2 Hz, 1H), 7.65 (br t, *J* = 2.0 Hz, 2H), 6.11 (m, 1H), 5.66 (m, 1H), 4.28 (br d, *J* = 8.8 Hz, 1H), 2.39−2.12 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 140.1 (−), 137.2 (+), 133.4 (−), 128.8, 128.7 (−), 123.5 (−), 72.1 (−), 31.6 (+), 24.2. Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81; MW, 208.0558. Found: C, 63.21; H, 5.80; MW, 208.0556.

Preparation of 3(*S*)-(Phenylsulfonyl)cyclohex-1-ene (10). Method A. Following the above protocol, sodium benzenesulfinate (631 mg, 3.84 mmol), cyclohex-1-en-3-yl methylcarbonate (**9b**; 300 mg, 1.92 mmol), **7** (1.67 g, 3.84 mmol), **6** (17.6 mg, 0.048 mmol followed by 8.8 mg, 0.024 mmol), and **2** (100 mg, 0.144 mmol followed by 50 mg, 0.072 mmol) in 25 mL of methylene chloride gave after 3 h using the same workup and purification procedure 426 mg (99% yield) of a viscous oil which solidifies in the freezer, R_f = 0.15, $[\alpha]^{25}_{D}$ −136.8° (*c* 3.84, CH_2Cl_2). IR (neat): 1650, 1590, 1447, 1148, 1086 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.69−7.51 (m,

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[23] Takano, S.; Yamada, O.; Iida, H.; Ogasawara, K. *Synthesis* **1994**, 592.

3H), 6.08 (m, 1H), 5.77 (dd, J = 10.3, 2.4 Hz, 1H), 3.76 (m, 1H), 2.00−1.70 (m, 5H), 1.51 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−): δ 137.2 (+), 135.3 (−), 133.6 (−), 129.1 (−), 128.9 (−), 118.4 (−), 61.7 (−), 24.3 (+), 22.6 (+), 19.4 (+). HRMS: calcd for $C_{12}H_{15}O_2S$ (M + H$^+$) 223.0792, found 223.0787. Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.84; H, 6.35. Found: C, 64.71; H, 6.25.

Method B. A premixed orange solution of **3** (332 mg, 0.362 mmol) and **2** (530 mg, 0.76 mmol) in 10 mL of methylene chloride was added to a two-phase mixture of sodium benzenesulfinate (32.0 g, 195 mmol), **7** (560 mg, 1.29 mmol), and **9b** (20.0 g, 128 mmol) in 150 mL of methylene chloride and 45 mL of water at 0 °C. When monitoring by TLC indicated complete consumption of starting material (2 h), aqueous ammonium chloride (100 mL) and methylene chloride (100 mL) were added. The organic layer was washed with an aqueous sodium bicarbonate solution (3 × 100 mL) and brine (100 mL), dried (Na$_2$SO$_4$), and evaporated *in vacuo* and the residue chromatographed (30% ether in hexanes) to give 45 g (95% yield) of the above product.

Preparation of 3(*S*)-(Phenylsulfonyl)-1-cycloheptene (12). Following the procedure for the preparation of **4**, sodium benzenesulfinate (154 mg, 0.94 mmol), **11b** (80 mg, 0.47 mmol), **7** (409 mg, 0.94 mmol), **6** (4.3 mg, 0.012 mmol), and **2** (24.4 mg, 0.035 mmol) gave, after 4 h at rt and direct flash chromatography (10% ethyl acetate in hexanes, R_f = 0.15), 108 mg (97% yield) of product as a white solid, mp 87−8 °C, $[\alpha]^{25}_D$ −89.6° (c 3.94, CH$_2$Cl$_2$). IR (neat): 1650, 1590, 1447, 1305, 1145, 1089 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.90 (dd, J = 8.1, 1.3 Hz, 2H), 7.70−7.52 (m, 3H), 6.01 (m, 1H), 5.80 (dd, J = 12.5, 4.4 Hz, 1H), 3.85 (m, 1H), 2.28−1.88 (m, 4H), 1.74−1.43 (m, 4H). ^{13}C NMR (CDCl$_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 137.7 (+), 136.8 (−), 128.0 (−), 128.0 (−), 123.8 (−), 66.2 (−), 28.0 (+), 27.9 (+), 26.8 (+), 26.0 (+). HRMS: calcd for $C_{13}H_{17}O_2S$ (M$^+$ + 1) 237.0949, found 237.0952. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 65.88; H, 6.59.

Preparation of Methyl 3(*R*)-(Phenylsulfonyl)cyclohex-4-ene-1(*S*)-carboxylate (14). Following the procedure for the preparation of **4**, sodium benzenesulfinate (66 mg, 0.40 mmol), **13** and *ent*-**13** (43 mg, 0.20 mmol), **7** (174 mg, 0.40 mmol), **6** (1.8 Mg, 0.005 mmol), and **2** (10.3 mg, 0.015 mmol) gave, after 8.5 h at rt and direct flash chromatography (20% ethyl acetate in hexanes, R_f = 0.15), 54 mg (98% yield) of product as a viscous oil, $[\alpha]^{25}_D$ −56.2° (c 4.1, CH$_2$Cl$_2$). IR (neat): 1733, 1655, 1580, 1448, 1305, 1148, 1084 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.86 (d, J = 7.3 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.55 (t, J = 7.6 Hz, 2H), 6.02 (m, 1H), 5.88 (d, J = 10.1 Hz, 1H), 3.89 (1, H), 3.66 (s, 3H), 2.54 (m, 1H), 2.40−2.25 (m, 2H), 2.07 (m, 1H), 1.70 (q, J = 11.6 Hz, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 174.2 (+), 136.4 (+); 133.9 (−), 132.6 (−), 129.2 (−), 129.0 (−), 119.0 (−), 62.6 (−), 52.0 (−), 38.1 (−), 27.2 (+), 25.5. HRMS: calcd for $C_{13}H_{13}O_3S$ (M$^+$ − OCH$_3$) 249.0580, found 249.0592. Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 60.19; H, 5.68.

Preparation of 1(*S*)-(Benzoyloxy)-4(*R*)-(phenylsulfonyl)cyclohexane-2(*R*),3(*R*)-diol (15). To a methylene chloride solution (10 mL) of sulfone **14** (4.5 g, 13.1 mmol) at 0 °C were added osmium tetroxide (5 mg, 0.02 mmol) and *N*-methylmorpholine *N*-oxide (NMO) monohydrate (6.0 g, 44.4 mmol). Upon completion of reaction as monitored by TLC (1.4 h), aqueous sodium bicarbonate (100 mL) and methylene chloride (100 mL) were added. The organic layer was washed with sodium bicarbonate (2 × 100 mL) and brine (100 mL), dried (Na$_2$SO$_4$), and evaporated *in vacuo* and the residue chromatographed (30% ether in hexanes) to give 4.72 g (95% yield) of **15** as a white solid, mp 160−2 °C (resolidifies and melts again at 180 °C), R_f = 0.49 (5% ethyl acetate in ether), $[\alpha]^{25}_D$ +17.4° (c 0.35, CHCl$_3$). IR (neat): 3520, 1720, 1450, 1130 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.95 (d, J = 7.2 Hz, 2 H), 7.77 (d, J = 7.2 Hz, 2 H), 7.75 (m, 1 H), 7.7−7.5 (m, 3H), 7.39 (t, J = 7.8 Hz, 2 H), 5.34 (d, J = 3.0 Hz, 1H), 4.50 (s, 1 H) 4.25 (dd, J = 10.0, 2.9 Hz, 1 H), 4.14 (dd, J = 3.2, 3.1 Hz, 1H), 3.47 (ddd, J = 7.8, 7.5, 4.1 Hz, 1 H), 3.09 (s, 1 H), 2.10−1.60 (m, 4 H). ^{13}C NMR (75 MHz, CDCl$_3$, ppm): δ 164.9, 136.2, 134.2, 133.3, 129.6, 129.4, 129.3, 129.2, 128.4, 70.6, 69.4, 67.1, 63.1, 23.0, 19.8. HRMS: calcd for $C_{19}H_{21}O_6S$ (M$^+$ + H) 377.1059, found 377.1059.

Preparation of 4(*S*)-(Benzoyloxy)-3(*S*)-hydroxy-1-(phenylsulfonyl)cyclohexene (16a) and Its *tert*-Butyldimethylsilyl Ether 16b. A toluene solution of phosgene (10 mL, 1.93 M, 19.3 mmol) was added to a methylene chloride solution (20 mL) of diol **15** (4.5 g, 1.2 mmol) at 0 °C. After 3 h at 0 °C, the reaction mixture was poured into 1 M aqueous hydrochloric acid (100 mL) and extracted with methylene chloride (2 × 50 mL). The organic solution was washed with aqueous sodium bicarbonate (2 × 100 mL) and brine (100 mL), dried (Na$_2$SO$_4$), and evaporated *in vacuo* to give after flash chromatography (30% ether in hexanes) 4.8 g (100% yield) of cyclic carbonate, R_f = 0.49 (5% ethyl acetate in petroleum ether), mp 180−2 °C $[\alpha]^{25}_D$ −17.0 (c 0.76, CHCl$_3$). IR (neat): 1820, 1720, 1450, 1310, 1150, 1070 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 8.03 (dd, J = 8.3, 1.4 Hz, 2 H), 7.95 (d, J = 7.1, 1.4 Hz, 2 H), 7.76 (td, J = 7.5, 1.5 Hz, 1 H), 7.7−7.55 (m, 3H), 7.51 (d, J = 7.9 Hz, 1 H), 7.47 (d, J = 7.4 Hz, 1 H), 5.49 (d, J = 4.5 Hz, 1H), 5.24 (dd, J = 6.6, 6.6 Hz, 1H) 4.90 (dd, J = 6.3, 4.5 Hz, 1 H), 3.43 (dd, J = 12.0, 8.0 Hz, 1H), 2.30−2.15 (m, 3 H), 2.10−1.90 (m, 1 H). ^{13}C NMR (75 MHz, C$_6$D$_6$, ppm): δ 164.9, 152.2, 137.3, 134.7, 133.8, 129.8, 129.7, 128.8, 128.7, 128.6, 75.9, 73.1, 68.1, 63.0, 23.4, 16.6. HRMS: calcd for $C_{19}H_{18}O_2S$ (M$^+$ − CO$_2$) 358.0875, found 358.0860.

Triethylamine (253 mg, 2.5 mmol) was added to a rt solution of the above carbonate (1.00 g, 2.5 mmol) at rt. After 6 h, the reaction was poured into 1 M aqueous hydrochloric acid (100 mL) and extracted with methylene chloride (2 × 50 mL). The organic phase was washed with aqueous hydrochloric acid (2 × 50 mL), aqueous sodium bicarbonate (2 × 50 mL), and brine (100 mL) and dried (Na$_2$SO$_4$) to give, after flash chromatography (30% ether in hexane), 850 mg (95% yield) of **16a**, mp 180 °C, $[\alpha]^{25}_D$ −6.8° (c 1.3, CHCl$_3$). IR (neat): 3500, 1720, 1450, 1320, 1150 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.83 (d, J = 7.1 Hz, 2 H), 7.62 (t, J = 7.4 Hz, 1 H), 7.59−7.50 (m, 2 H), 4.21 (s, 1 H), 4.18 (d, J = 5.3 Hz, 1 H), 3.90 (s, 1 H), 3.59 (m, 1H), 2.27 (m, 1 H), 1.95 (dd, J = 8.4, 4.3 Hz, 1 H), 1.60 (m, 1 H), 1.95 (m, 1 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 166.4, 142.0, 138.4, 135.8, 133.7, 133.4, 129.6, 129.4, 129.3, 128.4, 128.2, 73.8, 68.6, 24.5, 21.4. HRMS: calcd for $C_{19}H_{18}O_5S$ 358.0875, found 358.0875.

Pyridine (158 mg, 2.0 mmol) and TBDMS(Cl) (300 mg, 2.0 mmol) were added to a solution of the above alcohol **16a** (500 mg, 1.4 mmol) in 2 mL of DMF at 0 °C. After 6 h, the reaction mixture was poured into 1 M aqueous hydrochloric acid (50 mL) and extracted with methylene chloride (50 mL). The organic phase was washed with 1 M aqueous hydrochloric acid (50 mL), aqueous sodium bicarbonate (2 × 100 mL), and brine (100 mL) and dried (Na$_2$SO$_4$) to give 591 mg (92% yield) of **16b**, mp 110−3 °C, $[\alpha]^{25}_D$ −31.6° (c 0.54, CHCl$_3$). IR (neat): 1720, 1450, 1300, 1150, 1090 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.89 (d, J = 7.1 Hz, 2 H), 7.83 (d, J = 7.2 Hz, 2 H), 7.66 (t, J = 7.4 Hz, 1 H), 7.55 (m, 3H), 7.37 (m, 2 H) 6.86 (d, J = 1.9 Hz, 1H), 5.10 (m, 1H) 4.43 (dd, J = 4.9, 3.7 Hz, 1 H), 2.36 (m, 2H), 2.07 (m, 1 H), 1.94 (m, 1 H), 0.86 (s, 9 H), 0.14 (s, 3 H), 0.09 (s, 3 H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 165.4, 144.5, 138.6, 135.9, 133.5, 133.1, 129.7, 129.4, 129.1, 128.3, 128.1, 72.2, 67.2, 25.6, 25.5, 23.2, 20.6, 17.8, −4.7, −4.9. HRMS: calcd for $C_{20}H_{23}O_5SSi$ (M$^+$ − C$_4$H$_9$) 415.1035, found 415.1046.

Preparation of 2(*S*)-(*tert*-Butyldimethylsiloxy)-3(*S*)-allyl-4(*R*)-(phenylsulfonyl)cyclohexan-1(*S*)-ol (17). A solution of excess allylmagnesium bromide (2.0 mL, 2.0 M, 4.0 mmol) in ether was added to a solution of the vinyl sulfone **16b** (50 mg, 0.11 mmol) at −78 °C. After 4 h, a saturated aqueous ammonium chloride solution (10 mL) and ether (100 mL) were added. The organic phase was washed with brine (2 × 100 mL) and dried (Na$_2$SO$_4$) to give, after flash chromatography (30% ether in hexane), 20 mg (36% yield) of **17**, R_f = 0.49 (5% ethyl acetate in ether). IR (neat): 3500, 1450, 1370, 1150 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.83 (dd, J = 7.2, 1.6 Hz, 2 H), 7.64 (dt, J = 7.4, 1.5 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 2 H), 5.84 (m, 1H), 5.26 (d, J = 17.1 Hz, 1H), 5.20 (d, J = 10.2 Hz, 1H), 3.38 (m, 2 H), 3.07 (dt, J = 11.6, 4.1 Hz, 1 H), 2.90 (m, 1H), 2.78 (m, 1 H), 2.10 (m, 2 H), 1.85 (m, 1 H), 1.62 (m, 1 H), 1.48 (ddd, J = 9.0, 8.3, 4.2 Hz, 1 H), 1.20 (m, 1 H), 0.89 (s, 9H), 0.13 (s, 6 H). ^{13}C NMR (75 MHz, CDCl$_3$, ppm): δ 138.3, 133.6, 133.0, 129.1, 128.6, 119.6, 77.4, 73.6, 62.0, 41.1, 30.6, 29.5, 26.0, 24.7, 18.5, −3.5, −4.2. HRMS: calcd for $C_{17}H_{25}O_4SSi$ 353.1242, found 353.1248.

Preparation of 1(*S*)-(Phenylsulfonyl)-2(*S*),3(*S*)-epoxycyclopentane (18). A solution of MCPBA (50%, 780 mg, 2.26 mmol) in methylene chloride (10 mL) was added to sulfone **8** (393 mg, 1.88 mmol) in 10 mL of methylene chloride at 0 °C. After 36 h, the reaction was diluted with ether. The organic phase was washed with saturated aqueous sodium bicarbonate and brine, dried ($MgSO_4$), and evaporated *in vacuo* to give, after flash chromatography, 278 mg (66% yield) of **18** as a white solid, mp 59.5−60.5 °C, $[\alpha]^{25}_{D}$ −44.4° (*c* 2.18, CH_2Cl_2). IR (neat): 1450, 1310, 1144, 1084 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.93 (d, J = 7.2 Hz, 2H), 7.70 (br t, J = 5.4 Hz, 1H), 7.61 (br t, J = 7.8 Hz, 2H), 3.73 (m, 2H), 3.57 (d, J = 1.7 Hz, 1H), 2.12 (m, 1H), 2.00 (m, 1H), 1.78−1.62 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 138.0 (+), 134.1 (−), 129.4 (−), 128.5 (−), 65.0 (−), 57.6 (−), 55.8 (−), 6.1 (+), 21.1 (+). HRMS: calcd for $C_{11}H_{13}O_3S$ (M^+ + H) 225.0585, found 225.0595. Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.91; H, 5.39. Found: C, 59.18; H; 5.22.

Preparation of 3(*S*)-Acetoxycyclopentene (19b). Cold (0 °C) dry methanol (150 mL) was added to a neat mixture of 5% sodium amalgam (8.2 g, 17.8 mmol) and epoxide **18** (1.0 g, 4.5 mmol) at 0 °C. After 2 h, the solution was decanted from the mercury and acidified to pH 6 with aqueous 10% hydrochloric acid. The majority of the methanol was removed *in vacuo* at 0 °C (*caution*: loss of material due to volatility). The residue was diluted with ether, dried ($MgSO_4$), and concentrated *in vacuo*. Pyridine (334 mg, 4.23 mmol) and 4-(dimethylamino)pyridine (DMAP) (13 mg, 0.1 mmol) followed by acetyl chloride (345 mg, 4.23 mmol) were added to the crude alcohol dissolved in dry methylene chloride (25 mL) at 0 °C. After 6 h, the mixture was diluted with ether. The organic phase was washed with 10% aqueous hydrochloric acid and saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and evaporated *in vacuo* (*caution*: volatility of product) to give, after flash chromatography (1% ether in pentane), 209 mg (37% yield) of colorless oil, $[\alpha]^{25}_{D}$ −169.4° (*c* 5.96, CH_2Cl_2). Spectral data agreed with those recorded in the literature. The rotation is lower than expected on the basis of a literature value of $[\alpha]^{25}_{D}$ −83.8° (*c* 1.09, CH_2Cl_2)[14] for material claimed to have a 41% ee, but our ee of 98% derives from a NMR chiral shift study with $Eu(hfc)_3$ in deuteriobenzene and not rotation.

Preparation of 3(*S*)-Hydroxy-1-(phenylsulfonyl)cyclopentene (20). A solution of **18** (20 mg, 0.09 mmol) in 1 mL of dry THF was added to a −78 °C solution of LDA in 1 mL of THF prepared from diisopropylamine (10 mg, 0.98 mmol) and *n*-butyllithium (59 μL, 1.6 M, 0.094 mmol). After 1 h, saturated aqueous ammonium chloride (1 mL) was added and the reaction was allowed to reach rt. After dilution with ether, the organic phase was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo* to give, after flash chromatography, 16 mg (81% yield) of **20** as a white solid, mp 65.0−65.5 °C, $[\alpha]^{25}_{D}$ −65.8° (*c* 2.16, CH_2Cl_2). IR (neat): 3413, 1619, 1587, 1447, 1149, 1098, 1066 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.89 (dd, J = 7.1, 1.5 Hz, 2H), 7.63 (m, 1H), 7.54 (m, 2H), 6.64 (d, J = 2.0 Hz, 1H), 4.93 (m, 1H), 2.95 (br s, 1H (−OH)), 2.60 (m, 1H), 2.47−2.34 (m, 2H), 2.40 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 146.9 (+), 142.5 (−), 138.5 (+), 133.7 (−), 129.2 (−), 128.0 (−), 76.1 (−), 33.8 (+), 29.1 (+). Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.91; H, 5.39; MW, 224.0507. Found: C, 59.05; H, 5.41; MW, 224.0515.

Preparation of 2(*S*)-*n*-Butyl-3(*S*)-(phenylsulfonyl)cyclopentan-1(*S*)-ol (21). A solution of *n*-butyllithium (268 μL, 1.53 M in hexanes, 0.428 mmol) was added to a −78 °C solution of epoxide **18** (40 mg, 0.178 mmol) in 5 mL of dry ether. After 16 h, saturated aqueous ammonium chloride and ether were added. The organic phase was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo* to give 37.2 mg (74% yield) of **21** as a white solid, mp 76−7 °C, $[\alpha]^{25}_{D}$ +28.8° (*c* 1.00, CH_2Cl_2). IR (neat): 3515, 1305, 1285, 1143, 1083 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.89 (dd, J = 7.2, 1.5 Hz, 2H), 7.64 (m, 1H), 7.56 (br t, J = 7.7 Hz, 2H), 4.36 (br s, 1H), 3.28 (q, J = 5.8 Hz, 1H), 2.32 (m, 1H), 2.10 (m, 2H), 1.82−1.70 (m, 2H), 1.57 (br s, 1H (−OH)), 1.45 (m, 1H), 1.40−1.12 (m, 5H), 0.83 (t, J = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 139.0 (+), 133.5 (−), 129.2 (−), 128.5 (−), 73.6 (−), 67.3 (−), 46.4 (−), 33.8 (+), 30.2 (+), 28.2 (+), 24.9 (+), 22.7 (+), 13.9 (−). HRMS: calcd for $C_{15}H_{22}O_3S$ 282.1290, found 282.1301.

Preparation of 1(*S*)-(Phenylsulfonyl)-2(*S*),3(*S*)-epoxycyclohexane (22). Following the protocol for the preparation of **18**, MCPBA (50%, 1.2 g, 3.45 mmol) and sulfone **10** (426 mg, 1.92 mmol) in a total of 20 mL of methylene chloride gave, after purification by flash chromatography (30% ethyl acetate in hexanes), 320 mg (70% yield) of the *trans*-epoxide **22** as a white solid, mp 68−9 °C, $[\alpha]^{25}_{D}$ −8.6° (*c* 6.92, CH_2Cl_2). The minor isomer was easily separated during the above purification and was not isolated. IR (neat): 1448, 1308, 1144, 1084 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.94 (dd, J = 7.0, 1.5 Hz, 2H), 7.70 (m, 1H), 7.63−7.57 (m, 2H), 3.49 (d, J = 3.6 Hz, 1H), 3.35 (dd, J = 11.2, 6.3 Hz, 1H), 3.26 (t, J = 1.8 Hz, 1H), 2.09 (dt, J = 15.3, 1.6 Hz, 1H), 1.88−1.69 (m, 2H), 1.63−1.50 (m, 2H), 1.35 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 137.5 (+), 134.1 (−), 129.4 (−), 128.8 (−), 60.1 (−), 52.5 (−), 49.5 (−), 23.6 (+), 20.9 (+), 15.8 (+). HRMS: calcd for $C_{12}H_{15}O_3S$ (M^+ + H) 239.0741, found 239.0739. Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92. Found: C, 60.80; H, 6.04.

Preparation of 3(*S*)-Hydroxy-1-cyclohexene (23). A solution of sodium naphthalenide (1.17 mL, 0.43 M in THF, 0.50 mmol) was added to a 0 °C solution of epoxide **22** (20 mg, 0.084 mmol) in 1 mL of THF. The naphthalenide solution was added until the green color persisted, at which point water (2 mL) was added. After dilution with methylene chloride, the organic phase was dried ($MgSO_4$), evaporated *in vacuo* at 0 °C, and flash chromatographed (30% ether in pentane) to give 24 mg (58% yield) of allyl alcohol **23**, $[\alpha]^{25}_{D}$ −117.1 (*c* 0.13, dry $CHCl_3$), whose spectral properties are identical to those reported.[14]

Preparation of 2(*S*)-Hydroxy-3(*S*)-(phenylsulfonyl)cyclohexan-1(*S*)-ol (27). Following the protocol for the preparation of **15**, sulfone **10** (9.5 g, 36 mmol), NMO hydrate (10 g, 74 mmol) and osmium tetroxide (10 mg, 0.04 mmol) in methylene chloride (300 mL) and water (5 mL) gave, after flash chromatography (30% ether in hexanes), 9.7 g (90% yield) of diol **27**, $[\alpha]^{25}_{D}$ +2.9° (*c* 2.5, $CHCl_3$). IR (neat): 3520, 1450, 1370, 1035 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.90 (d, J = 8.2 Hz, 2 H), 7.71 (t, J = 7.4 Hz, 1 H), 7.51 (dd, J = 8.5, 7.4 Hz, 2 H), 4.54 (s, 1 H), 4.15 (dd, J = 10.2, 2.5, Hz, 1H), 4.06 (d, J = 2.2 Hz, 1 H), 3.89 (dd, J = 10.1, 2.9, 1 H), 3.38 (ddd, J = 10.1, 9.8, 2.9, 1 H), 2.78 (s, 1 H), 1.93 (d, J = 12.0 Hz, 1 H), 1.87 (d, J = 12.8 Hz, 1 H), 1.8−1.1 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 136.4, 134.2, 129.3, 129.0, 69.9, 68.6, 63.7, 29.2, 25.1, 17.9. HRMS: calcd for $C_{12}H_{16}O_4S$ 256.0769, found 256.0778.

Preparation of 3(*S*)-Hydroxy-1-(phenylsulfonyl)cyclohexene (24a) and Its *tert*-Butyldimethylsilyl Ether 24b. Method A (from Epoxide 22). Following the protocol for the preparation of **20**, epoxide **22** (40 mg, 0.17 mmol) and LDA (from 20.4 mg, 0.20 mmol, of diisopropylamine and 115 μL, 1.6 M in hexanes, 0.185 mmol, of *n*-butyllithium) in a total of 3 mL of THF gave, after purification by flash chromatography (30% ethyl acetate in hexanes), 39.5 mg (99% yield) of the product as a viscous oil, $[\alpha]^{25}_{D}$ −51.6° (*c* 3.49, CH_2Cl_2). IR (neat): 3500, 1444, 1303, 1150 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.86 (dd, J = 7.1, 1.4 Hz, 2H), 7.63 (m, 1H), 7.56 (br t, J = 7.7 Hz, 2H), 6.98 (s, 1H), 4.38 (m, 1H), 2.48 (br s, 1H (−OH)), 2.17−2.13 (m, 2H), 1.94−1.76 (m, 2H), 1.64−1.47 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 142.0 (+), 138.7 (−), 138.6 (+), 133.5 (−), 129.2 (−), 128.2 (−), 65.6 (−), 30.4 (+), 22.9 (+), 19.2 (+). Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; MW, 238.0664. Found: C, 60.24; H, 5.76; MW, 238.0663.

Method B (from Diol 27). Following the protocol for the preparation of **16a**, diol **27** (8.4 g, 28.4 mmol), phosgene (32 mL, 1.93 M in toluene, 61.8 mmol) in methylene chloride (200 mL), and pyridine (10 mL) gave, after flash chromatography (30% ether in hexane), 9.1 g (99% yield) of the cyclic carbonate, mp 162−3 °C $[\alpha]^{25}_{D}$ +41.6° (*c* 2.6, $CHCl_3$). IR (neat): 1795, 1450, 1310, 1285, 1150 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J = 7.0 Hz, 2 H), 7.72 (t, J = 7.3 Hz, 1 H), 7.62 (d, J = 7.8 Hz, 2 H), 5.01 (dd, J = 7.8, 6.6 Hz, 1 H), 4.85 (dd, J = 6.4, 3.7 Hz, 1H), 3.26 (m, 1 H), 2.28 (m, 1 H), 2.22 (m, 1 H), 1.9−1.5 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 153.3, 137.8, 134.4, 129.5, 128.7, 75.9, 73.3, 64.5, 25.9, 21.0, 17.3. HRMS: calcd for $C_{13}H_{14}O_5S$ 282.0562, found 282.0564.

The carbonate (1.65 g, 5.1 mmol) and triethylamine (639 mg, 6.32 mmol) in methylene chloride (10 mL) for 6 h gave, after flash chromatography (30% ether in hexanes), 1.47 g (97% % yield) of the above alcohol **24a** with the same properties.

Silylation of alcohol **24a** (500 mg, 1.7 mmol) using the same protocol as for the preparation of **16b** with *tert*-butyldimethylsilyl chloride (300 mg, 2.0 mmol) and pyridine (316 mg, 4 mmol) in DMF (2 mL) for 6 h gave, after flash chromatography (25% ether in hexane), 591 mg (92% yield) of the silyl ether **24b**, $[\alpha]^{25}_{D}$ −54.8° (*c* 3.3, $CHCl_3$), spectroscopically identical with the sample previously prepared.[15]

Preparation of 2(*S*)-*n*-Butyl-3(*S*)-(phenylsulfonyl)cyclohexan-1(*S*)-ol (26). A solution of epoxide **22** (40 mg, 0.17 mmol) in 1 mL of THF was added to a −78 °C solution of LDA (prepared from 20.4 mg, 0.201 mmol, of diisopropylamine and 0.115 μL, 1.6 M in hexanes, 0.185 mmol, of *n*-butyllithium) in 2 mL of THF. After 1 h, saturated aqueous ammonium chloride and ether were added. The organic phase was washed with brine, dried ($MgSO_4$), evaporated *in vacuo*, and resuspended in 2 mL of THF. This mixture was added to a solution of *n*-butyllithium (210 μL, 1.6 M in hexanes, 0.356 mmol) in 2 mL of THF at −78 °C. After 16 h, during which time the mixture was allowed to come to rt, a saturated aqueous ammonium chloride solution and ether were added. The organic phase was washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*. Flash chromatography (30% ethyl acetate in hexanes) of the resultant oil provided 32 mg (64% yield) of the product, $[\alpha]^{25}_D$ +32.2° (*c* 0.74, CH_2Cl_2), as a viscous oil and 8.5 mg (21% recovery) of **21a**. IR (neat): 3515, 1450, 1303, 1284, 1138, 1085 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.87 (dd, *J* = 7.0, 1.5 Hz, 2H), 7.64 (m, 1H), 7.56 (br t, *J* = 7.6 Hz, 2H), 4.28 (m, 1H), 3.25 (q, *J* = 7.1 Hz, 1H), 2.01 (m, 1H), 1.88 (m, 1H), 1.73−1.47 (m, 8H), 1.34−1.18 (m, 4H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 139.0 (+),133.4 (−), 129.0 (−), 128.5 (−), 66.9 (−), 63.5 (−), 40.7 (−), 31.3 (+), 29.2 (+), 27.1 (+), 25.0 (+), 22.6 (+), 19.3 (+), 14.0 (−). HRMS: calcd for $C_{12}H_{15}O_3S$ ($M^+ - C_4H_9$) 239.0742, found 239.0743. Anal. Calcd for $C_{16}H_{24}O_3S$: C, 60.48; H, 5.92. Found: C, 64.89; H, 7.93.

Preparation of 2(*S*)-Hydroxy-3(*S*)-(phenylsulfonyl)cycloheptan-1(*S*)-ol (28) and Its Cyclic Carbonate 29. A solution of allyl sulfone **12** (100 mg, 0.403 mmol) in THF (6 mL) was added to a solution of NMO hydrate (66 mg, 0.645 mmol) and osmium tetroxide (3.4 mg, 0.0134 mmol) in THF (2 mL) followed by water (2.6 mL). After 16 h at rt, sodium thiosulfate pentahydrate (100 mg) was added. The reaction mixture was filtered through Celite and the latter washed with methylene chloride (50 mL). Brine (25 mL) was added to the resultant organic layers. The aqueous layer was washed with methylene chloride. The combined organic phases were dried ($MgSO_4$) and evaporated *in vacuo*. Flash chromatography (85% ethyl acetate in hexanes) gave 107 mg (95% yield) of the product as an amorphous white solid. IR (neat): 3487, 1446, 1287, 1138 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.91 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.71 (m, 1H), 7.69−7.15 (m, 2H), 4.29 (dd, *J* = 8.0, 3.3 Hz, 1H), 3.87 (dd, *J* = 9.1, 2.9 Hz, 1H), 3.20 (td, *J* = 9.1, 2.9 Hz, 1H), 2.05−1.89 (m, 2H), 1.76−1.60 (m, 2H), 1.57−0.89 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 137.0 (+), 134.1 (−), 129.3 (−), 129.0 (−), 73.4 (−), 71.2 (−), 70.3 (−), 30.7 (+), 27.0 (+), 25.2 (+), 24.6 (+). HRMS: calcd for $C_{13}H_{19}O_4S$ ($M^+ + H$) 271.1004, found 271.1016.

A solution of triphosgene (119 mg, 0.399 mmol) in methylene chloride (1 mL) was added to a −78 °C solution of diol **27** (103 mg, 0.399 mmol) and pyridine (190 mg, 2.4 mmol) in 1.5 mL of methylene chloride. The reaction was allowed to warm to rt at, which point TLC indicated it to be complete. After dilution with methylene chloride, the organic phase was washed with saturated aqueous ammonium chloride, 10% aqueous hydrochloric acid, and saturated aqueous sodium bicarbonate, dried ($MgSO_4$), and evaporated *in vacuo*. Flash chromatography (30% ethyl acetate in hexanes) gave 114 mg (96% yield) of carbonate as a white solid, mp 161−2 °C, $[\alpha]^{25}_D$ +25.6° (*c* 1.05, CH_2Cl_2). IR (neat): 1805, 1446, 1307, 1138, 1046 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.89 (dd, *J* = 7.0, 1.5 Hz, 2H), 7.73−7.54 (m, 3H), 5.05 (dd, *J* = 9.5, 7.7 Hz, 1H), 4.73 (m, 1H), 3.36 (t, *J* = 9.5 Hz, 1H), 2.64 (m, 1H), 2.08−1.91 (m, 3H), 1.71 (m, 1H), 1.48−1.25 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz, APT pulse sequence—evens up (+), odds down (−)): δ 152.7 (+), 138.1 (+), 134.3 (−), 129.2 (−), 128.8 (−), 79.8 (−), 77.2 (−), 66.2 (−), 29.7 (+), 28.4 (+), 24.8 (+), 23.6 (+). Anal. Calcd for $C_{14}H_{16}O_5S$: C, 56.74; H, 5.44; MW, 296.0719. Found: C, 56.64; H, 5.67; MW, 296.0721.

Preparation of 3(*S*)-Hydroxy-1-cycloheptene (30). A solution of sodium naphthalenide (0.354 M in THF) was added to a 0 °C solution of cyclic carbonate **29** (57.6 mg, 0.194 mmol) in THF (1 mL) until the green color persisted (3.30 mL, 1.17 mmol), at which point water (2 mL) was added. The product was extracted into methylene chloride. The organic phase was dried ($MgSO_4$) and evaporated *in vacuo* at 0 °C (*caution*: volatility of the product). Flash chromatography (30% ether in pentane) gave 12.6 mg (57% yield) of allyl alcohol **30**, $[\alpha]^{25}_D$ −32.0° (*c* 0.20, CH_2Cl_2). Spectral data agreed well with the literature.

Preparation of 2-Methylene-4(*S*)-(*tert*-butyldimethylsiloxy)-7a-(*S*)-(phenylsulfonyl)-1,2,3a(*R*),4,5,6,7,7a-octahydroindene (31) and 7(*S*)-(*tert*-Butyldimethylsiloxy)-1,4,5,6,7,7a(*S*)-hexahydroinden-2-one (32). A solution of vinyl sulfone **24b** (836 mg, 1.64 mmol), palladium acetate (17 mg, 0.076 mmol), and triisopropyl phosphite (98 mg, 0.47 mmol) in 0.5 mL of toluene was heated to 80 °C and 2-[(trimethylsilyl)methyl]allyl pivalate (580 mg, 2.54 mmol) added. After 24 and 48 h at 80 °C, additional portions of TMM precursor (230 mg, 1.00 mmol) were added. When TLC indicated complete consumption of starting material, the reaction was directly chromatographed (30% ether in hexanes) to give 800 mg (83% yield) of adduct **31** whose properties agree with those previously recorded.[15]

Ozone was bubbled through a solution of sulfone **31** (560 mg, 1.38 mmol) in methanol (20 mL) and methylene chloride (20 mL) at −78 °C until the blue color persisted, at which point the solution was purged with nitrogen and dimethyl sulfide (2 mL) added. After warming to rt, triethylamine (3 mL) was added and the mixture stirred overnight. Flash chromatography gave 334 mg (94% yield) of enone **32**, $[\alpha]^{25}_D$ −20.7° (*c* 3.3, $CHCl_3$), whose spectral properties agreed with those previously recorded.[15]

Preparation of 4(*S*)-(*tert*-Butyldimethylsiloxy)-7a(*R*)-methyl-3a-(*S*)-octahydroinden-2-one (33). A solution of enone **32** (80 mg, 0.30 mmol) in ether (4 mL) was added to a −78 °C solution of dilithium dimethylcyanocuprate generated from methyllithium (6 mL, 1.5 M in ether, 9.0 mmol) and cuprous cyanide (410 mg, 4.5 mmol) in 4 mL of ether at 0 °C. The solution was allowed to warm to 0 °C for 8 h, at which point it was recooled to −78 °C and excess trimethylchlorosilane (1.0 mL, 7.9 mmol) added. The solution was warmed to rt and saturated aqueous sodium bicarbonate added. After dilution with ether, the aqueous phase was extracted with additional ether. The combined organic phases were washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*. Flash chromatography (25% ether in hexanes) of the residue gave 50 mg (60% yield) of **33**, $R_f = 0.6$ (25% ethyl acetate in hexanes), mp 77−8 °C, $[\alpha]^{25}_D$ −9.01° (*c* 0.76, $CHCl_3$). IR (neat): 1750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.49 (dd, *J* = 6.6, 6.6 Hz, 1 H), 2.40 (dd, *J* = 9.1, 8.2 Hz, 1 H), 2.25 (d, *J* = 9.1, 1 H), 2.20 (d, *J* = 8.2, 1H), 1.9−1.8 (m, 2 H), 1.8−1.6 (m, 3 H), 1.5−1.2 (m, 3 H), 1.17 (s, 3 H), 0.87 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 219.3, 71.4, 50.8, 49.6, 41.6, 39.1, 34.2, 32.2, 29.7, 25.8, 18.7, 17.9, −4.2, −4.8. HRMS: calcd for $C_{16}H_{30}O_2Si$ 282.2016, found 282.2022.

Preparation of 7(*S*)-(*tert*-Butyldimethylsiloxy)-3(*R*),3a(*R*)-methano-7a(*S*)-octahydroinden-2-one (34). A mixture of sodium hydride (3.6 mg, 0.15 mmol) and trimethylsulfonium iodide (33 mg, 0.15 mmol) in DMSO (0.5 mL) was heated at 100 °C for 5 min and recooled to rt, at which point enone **32** (40 mg, 0.15 mmol) was added. After 3 h at rt, the reaction mixture was poured into a 1:1 ether−water two-phase system. The aqueous layer was washed with additional ether. The combined organic phases were washed with brine, dried (Na_2SO_4), and evaporated *in vacuo*. Flash chromatography (30% ether in hexanes) gave 25 mg (57% yield) of cyclopropane **14** as a white solid, $R_f = 0.3$ (30% ether in hexanes), mp 46−8 °C. IR (neat): 1730 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.15 (ddd, *J* = 10.2, 9.4, 4.2 Hz, 1 H), 2.23 (dd, *J* = 17.3, 6.7 Hz, 1 H), 2.12 (dd, *J* = 10.2, 6.7 Hz, 1 H), 2.02 (d, *J* = 17.3 Hz, 1H), 1.95−1.80 (m, 2 H), 1.8−1.6 (m, 3 H), 1.5−1.2 (m, 5 H), 1.03 (d, *J* = 5.0, 3.5 Hz, 1H), 0.87 (s, 9 H), 0.05 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 214.1, 75.3, 45.0, 37.6, 34.8, 34.5, 33.7, 30.3, 25.8, 22.6, 18.9, 17.9, −3.8, −4.7. HRMS: calcd for $C_{15}H_{25}O_2Si$ ($M^+ - CH_3$) 265.1624, found 265.1622.

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