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Stereocontrolled Synthesis of *trans*-Cyclopropyl Sulfones from Terminal Epoxides

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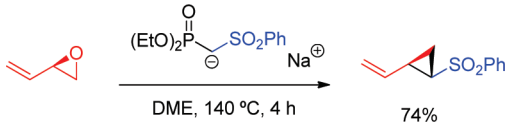

Treatment of a range of (enantiopure) epoxides with the sodium salt of diethyl (phenylsulfonyl)methylphosphonate in DME at 140 °C for 4 h gives a variety of (enantiopure) *trans*-cyclopropyl sulfones with high diastereoselectivity.

The cyclopropane moiety is ubiquitous in Nature, being found in numerous amino acids, fatty acids, polyketides, and terpenes.[1] Cyclopropanes are also regularly utilized in medicinal chemistry, including in peptidomimetic approaches, since they provide the capability to arrange pendant groups in specific and rigid three-dimensional orientations.[2] In addition, reactions involving metal-catalyzed ring-opening of cyclopropanes with subsequent cyclopentannulation are becoming ever more common.[3] Methods for the stereocontrolled synthesis of cyclopropanes are thus of vital importance, and a great deal of effort has been put into the development of a multitude of catalytic asymmetric processes that target them.[4] The basis of such reactions lies predominantly in metal-catalyzed (e.g., Rh or Cu) diazo decomposition/carbene insertion into alkenes along with asymmetric variants of the venerable Simmons−Smith[5] and Corey−Chaykovsky reactions,[6] though more recently, there has been an ever-increasing number of organocatalytic methods developed.[7] In spite of these advances, wasteful resolution processes remain popular in an industrial setting.[8] It is evident therefore, that methods to access cyclopropanes in a stereocontrolled manner, particularly via conceptually different approaches, are still of significant interest.

In 1961, Wadsworth and Emmons reported the direct conversion of epoxides to cyclopropanes.[9] Though potentially very powerful, this method has not found widespread appeal, and at present, this process is limited to the formation of cyclopropyl esters using phosphonate esters,[10] e.g., **1a**, and to spirocyclic cyclopropyl ketones using keto-stabilized phosphonates.[11−13] In the case of the former examples, the reaction pathway involves ring-opening of epoxide **2** with anion **1b** (Scheme 1, step 1) followed by transfer of diethyl phosphite to the newly formed alkoxide of **3** (step 2) and finally stereospecific intramolecular ring-closure of the subsequently generated α-stabilized anion **4**[14] (step 3) to give *trans*-cyclopropyl ester **5**. In the synthesis of cyclopropyl esters, high *trans*-selectivity is observed. It has been proposed that this may be the result of (a) ring closure being highly diastereoselective, which may be due to chelation control,[10a,n] or (b) rapid equilibration of a mixture of cyclopropanes to

(1) For respective representative examples, see: (a) Parry, R. J.; Mafoti, R. *J. Am. Chem. Soc.* **1986**, *108*, 4681. (b) MacMillan, J. B.; Molinski, T. F. *J. Nat. Prod.* **2005**, *68*, 604. (c) Ringel, S. M.; Greenough, R. C.; Roemer, S.; Connor, D.; Gutt, A. L.; Blair, B.; Kanter, G.; von Strandtmann, M. *J. Antibiot.* **1977**, *30*, 371. (d) Zheng, G. C.; Ichikawa, A.; Ishitsuka, M. O.; Kusumi, T.; Yamamoto, H.; Kakisawa, H. *J. Org. Chem.* **1990**, *55*, 3677.

(2) Cyclopropane-containing drugs accounted for > $7 billion in sales in 2006. For a review of recent peptidomimetic approaches, see: Youla, S. T. *Acc. Chem. Res.* **2008**, *41*, 1252.

(3) (a) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051. (b) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117.

(4) (a) Goudreau, S. R.; Charette, A. B. *Angew. Chem., Int. Ed.* **2010**, *49*, 486. (b) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041. (c) McGarrigle, E. M.; Myers, E. L.; Illa, O.; Shaw, M. A.; Riches, S. L.; Aggarwal, V. K. *Chem. Rev.* **2007**, *107*, 5841. (d) Maas, G. *Chem. Soc. Rev.* **2004**, *33*, 183. (e) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977. (f) *Comprehensive Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH Inc.: New York, 2000; p 864. (g) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.

(5) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256.

(6) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(7) (a) Hansen, H. M.; Longbottom, D. A.; Ley, S. V. *Chem. Commun.* **2006**, 4838. (b) Kunz, R. K.; Macmillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 3240. (c) Papageorgious, C. D.; Cubillo de Dios, M. A.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 4641. (d) Bremeyer, N.; Smith, S. C.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 2681.

(8) For a recent example, see: Beaulieu, P. L.; Gillard, J.; Bailey, M. D.; Boucher, C.; Duceppe, J.-S.; Simoneau, B.; Wang, X.-J.; Zhang, L.; Grozinger, K.; Houpis, I.; Farina, V.; Heimroth, H.; Krueger, T.; Schnaubelt, J. *J. Org. Chem.* **2005**, *70*, 5869.

(9) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733.

(10) Examples of Wadsworth−Emmons cyclopropanation in synthesis are as follows: (a) Delhaye, L.; Merschaert, A.; Delbeke, P.; Briône, W. *Org. Process Res. Dev.* **2007**, *11*, 689. (b) Armstrong, A.; Scutt, J. N. *Chem. Commun.* **2004**, 510. (c) Armstrong, A.; Scutt, J. N. *Org. Lett.* **2003**, *5*, 2331. (d) Singh, A. K.; Rao, M. N.; Simpson, J. H.; Li, W. S.; Thornton, J. E.; Kuehner, D. E.; Kacsur, D. J. *Org. Process Res. Dev.* **2002**, *6*, 618. (e) Petter, R. C.; Banerjee, S.; Englard, S. *J. Org. Chem.* **1990**, *55*, 3088. (f) Petter, R. C. *Tetrahedron Lett.* **1989**, *30*, 399. (g) Fitzsimmons, B. J.; Fraser-Reid, B. *Tetrahedron* **1984**, *40*, 1279. (h) Izydore, R. A.; Ghiradelli, R. G. *J. Org. Chem.* **1973**, *38*, 1790. (i) Tömösközi, I. *Tetrahedron* **1966**, *22*, 179. For the analogous, but less facile, use of phosphoranylidenes, see: (j) Denney, D. B.; Vill, J. J.; Boskin, M. J. *J. Am. Chem. Soc.* **1962**, *84*, 3944. For related approaches, see: (k) Clarke, C.; Fox, D. J.; Pedersen, D. S.; Warren, S. *Org. Biomol. Chem.* **2009**, *7*, 1329. (l) Clarke, C.; Foussat, S.; Fox, D. J.; Pedersen, D. S.; Warren, S. *Org. Biomol. Chem.* **2009**, *7*, 1323. (m) Krawczyk, H.; Wąsek, K.; Kędzia, J. *Synthesis* **2009**, 1473–1476. (n) Krawczyk, H.; Wąsek, K.; Kędzia, J.; Wojciechowski, J.; Wolf, W. M. *Org. Biomol. Chem.* **2008**, *6*, 308–318. (o) Fox, D. J.; Parris, S.; Pedersen, D. J.; Tyzack, C. R.; Warren, S. *Org. Biomol. Chem.* **2006**, *4*, 3108. (p) Boesen, T.; Fox, D. J.; Galloway, W.; Pedersen, D. S.; Tyzack, C. R.; Warren, S. *Org. Biomol. Chem.* **2005**, *3*, 630–637.

(11) Jacks, T. E.; Nibbe, H.; Wiemer, D. F. *J. Org. Chem.* **1993**, *58*, 4584.

(12) Wadsworth and Emmons have reported an isolated example of the use of the diethyl cyanomethylphosphonate for the conversion of styrene oxide to the corresponding cyanocyclopropane (51% yield); see ref 9.

(13) Katritzky et al. have reported three examples of an analogous cyclopropanation using 1-(benzotriazol-1-yl)diphenylphosphine oxide; see: Katrizky, A. R.; Wu, H.; Xie, L.; Jiang, J. *J. Heterocycl. Chem.* **1995**, *32*, 595.

(14) An example of the protonated intermediate **4** has been detected by LC/MS; see ref 10d.

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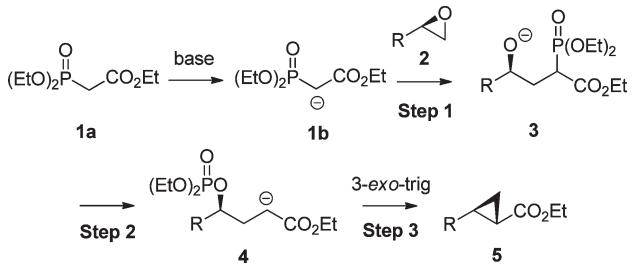
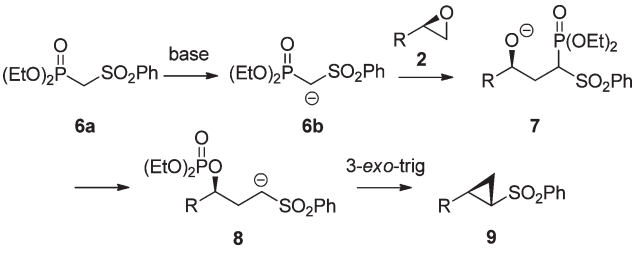
SCHEME 1. Reaction Pathway for the Direct Conversion of Epoxides to *trans*-Cyclopropyl Esters



SCHEME 2. Proposed Reaction Pathway for the Direct Conversion of Epoxides to Cyclopropyl Sulfones

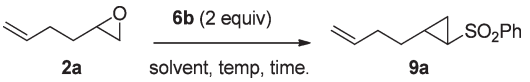


the thermodynamically favored *trans*-isomers following ring closure.[9]

Given the excellent yields and diastereoselectivities often seen with this reaction,[15] coupled with the range of anion-stabilizing groups one might employ and ready availabilty of enantiopure epoxides,[16] it is highly surprising that the scope of this reaction has not been examined further. Cyclopropyl sulfones have found a variety of uses in synthesis,[17] and since sulfones exhibit a similar anion-stabilizing ability to esters, we investigated whether we could affect the direct conversion of epoxides to cyclopropyl sulfones using sulfone phosphonate **6a**[18] (Scheme 2).

Our work began by examining the reaction between 1,2-epoxyhex-5-ene **2a** and anion **6b**. Initially, a slurry of **6b** (generated from **6a** using 1.05 equiv of NaH) was heated to reflux in PhMe with epoxide **2a** for 16 h. This gave the desired *trans*-cyclopropyl sulfone **9a** in a promising 74% yield and with high diastereocontrol (dr 97:3 (GC)) (Table 1, entry 1).[19] In order to optimize this reaction, we examined a number of solvents (entries 2−5). Yields were generally comparable, however, from a practical point of view, the insolubility of **6b** made the reactions in PhMe and dioxane less straightforward due to significant foaming during the deprotonation of **6a**. The promising yield obtained in DME prompted us to examine this solvent more closely. Attempts to use an alternate counterion were briefly investigated. Under conditions otherwise comparable to those described for entry 2, use of *n*-BuLi as base (entry 6) resulted in precipitation of the anion and a lower yield of **9a** (61%). The use of a potassium counterion (KH as base) led to an anion which remained in solution but which led to a far greater product distribution (as judged by TLC analysis). Next, we began to examine the effect of temperature. Raising the temperature to 120 °C instantly led to improvement in yield to 80% (entry 7). Further increase in temperature to 140 °C (entry 8)[20] and decreasing the reaction time to 8 h increased the yield (83%) and also the dr (98:2). In fact, reduction of the reaction time to only 4 h at this temperature led to an identical yield and dr (entry 9). An attempt to further decrease the reaction time by increasing the temperature further led to a reduction in yield (entry 10). Finally, we attempted to reduce the quantity of anion **6b** needed; however, lowering this to 1.5 equiv led to a noticeable 10% drop in yield (entry 11).

TABLE 1. Optimization of the Direct Conversion of Epoxides to Cyclopropyl Sulfones



entry	solvent	temp/°C	time/h	yield[a] (%)
1	PhMe	110	16	74[b]
2	DME	86	16	70
3	dioxane	100	16	67
4	DMF	120	16	65
5	THF	67	20	56
6	DME	86	16	61[c]
7	DME	120	16	80
8	DME	140	8	83[d]
9	DME	140	4	83[d]
10	DME	160	2	76
11	DME	140	4	73[e]

[a]Isolated yield following column chromatography (SiO_2). [b]dr 97:3. [c]*n*-BuLi used as base. [d]dr 98:2. [e]**6b** (1.5 equiv).

Under these reaction temperatures, it is remarkable that transfer of the phosphite group to the alkoxide (cf. **7**→**8**) is so selective over that of the sulfone.[21] Considerable synthetic effort utilizing the endocyclic restriction test has demonstrated

(15) Reaction between (*S*)-propylene oxide and **1a** has been reported to give up to 95% yield with dr >98:2; see ref 10a.

(16) Amatore, M.; Beeson, T. D.; Brown, S. P.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 5121. (b) Wong, O. A.; Shi, Y. *Chem. Rev.* **2008**, *108*, 3958. (c) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.

(17) Cyclopropyl sulfones can be subjected to alkylation/acylation; see: (a) Chang, Y. H.; Pinnick, H. W. *J. Org. Chem.* **1978**, *43*, 373. (b) Corey, E. J.; Weatherhead-Kloster, R. A. *Org. Lett.* **2006**, *8*, 171. (c) Tanikaga, R.; Yamada, S.; Nishikawa, T.; Matsui, A. *Tetrahedron* **1998**, *31*, 8933. (d) Tanaka, K.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2071. They can be converted to methylene cyclopropanes; see: (e) Baldwin, J. E.; Adlington, R. M.; Bebbington, D. *Tetrahedron* **1994**, *50*, 12015. (f) Lai, M. T.; Oh, E.; Shih, Y.; Liu, H. W. *J. Org. Chem.* **1992**, *57*, 2471. They can form π-allyl palladium complexes which undergo reactions with electron deficient alkenes; see: (g) Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 2871. They can undergo desulfonylation to give simple cyclopropanes; see: (h) Kazuta, Y.; Matsuda, A.; Shuto, S. *J. Org. Chem.* **2002**, *67*, 1669. They can act as synthons for 1,3-dipoles; see: (i) Trost, B. M.; Cossy, J.; Burkes, J. *J. Am. Chem. Soc.* **1983**, *105*, 1052. They can participate in Julia-type olefinations; see: (j) Bernard, A. M.; Frongia, A.; Piras, P. P.; Secci, F. *Synlett* **2004**, 1064. (k) Aïssa, C. *J. Org. Chem.* **2006**, *71*, 360. They can be regioselectively cleaved to give vinylstannanes; see: (l) Hayashi, N.; Hirokawa, Y.; Shibata, I.; Yasuda, M.; Baba, A. *J. Am. Chem. Soc.* **2008**, *130*, 2912.

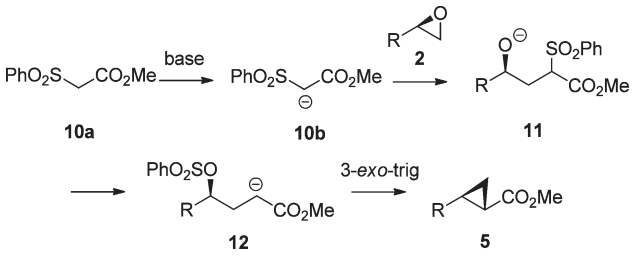
(18) Diethyl (phenylsulfonyl)methylphosphonate **6a** is readily available via an Arbusov reaction between triethyl phosphite and chloromethyl phenyl sulfide and oxidation of the resultant product with Oxone; see the Supporting Information.

(19) The *trans*-stereochemistry was assigned by ^{1}H NMR spectroscopy (NOE, coupling constant analysis and comparison with data in ref 17b) and ultimately by X-ray crystallographic analysis of **9b**,**f**; see the Supporting Information.

(20) Temperatures of up to 150 °C have been found to be beneficial in the reaction between **1b** and propylene oxide; see ref 10b.

(21) Sulfone anion **6b** has previously been used for the synthesis of vinyl sulfones. While in these cases transfer of diethyl phosphite also occurs in preference to the sulfone and competitive formation of vinyl phosphonates is not observed, such reactions are carried out at room temperature or below.

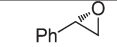
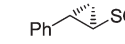
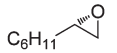
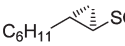
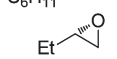
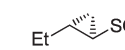
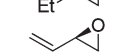
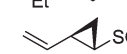
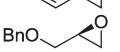
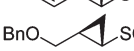
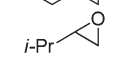
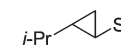
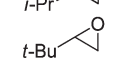
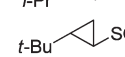
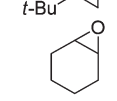
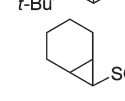
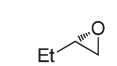
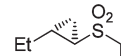
SCHEME 3. Reaction Pathway for an Unsuccessful Sulfur(VI)-Based Analogue of the Wadsworth−Emmons Cyclopropanation (Homologous-Julia) Reaction



that the favored pathway for substitution at atoms in the top right-hand corner of the periodic table including S(VI) is concerted and involves a transition-state geometry in which the nucleophile, leaving group, and reacting center are linearly disposed.[22] In contrast, it has been shown that substitution at phosphorus(V) can proceed via a non-concerted addition/Berry pseudorotation/elimination process, such that a linear arrangement is not always required for reaction to occur.[23] This may explain why the rates for transfer of sulfur(VI) and phosphorus(V) centered groups in small rings can be vastly different. To test this hypothesis, we briefly investigated the reaction between sodium methyl phenylsulfonylacetate **10a** and 1,2-epoxyhex-5-ene **2a**. Such a reaction (homologous Julia) would require transfer of the sulfone to the alkoxide of **11** in order to form cyclopropyl ester **5** (Scheme 3); however, despite repeated attempts, we could find no evidence of cyclopropane formation, even at elevated temperatures.

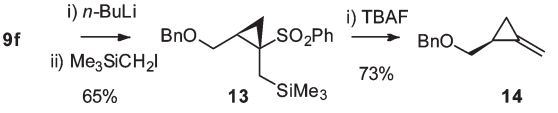
Given the utility of cyclopropyl sulfones,[17] we next examined the scope of this new cyclopropane ring-forming reaction with a variety of enantiopure epoxides (Table 2). Use of (*S*)-styrene oxide **2b** (>98% ee) under the optimal conditions developed (**6b** (2 equiv), DME, 140 °C, 4 h) gave the expected *trans*-phenyl cyclopropyl sulfone **9b** in 86% yield (entry 1) and with high diastereocontrol (dr >200:1). Analysis of **9b** revealed it to have an ee of >98% (HPLC), demonstrating that the cyclopropane ring-closing step is stereospecific. Simple alkyl-substituted enantiopure terminal epoxides (including volatile substrates) also gave good yields of *trans*-cyclopropyl sulfones (entry 2 and 3) though with marginally lower dr (98:2). We next examined substrates whose products would be more amenable to further synthetic manipulation. (*R*)-Vinyl oxirane **2e** gave good yield (74%) of the corresponding enantiopure vinyl *trans*-cyclopropyl sulfone **9e** (entry 4) as a single diastereomer upon treatment with **6b**. This result is significant since despite the utility of vinylcyclopropanes in synthesis,[3,17g,17i] this substrate has not been reported in analogous epoxide to cyclopropane conversions.[9−13] Though there is the possibility of π-allyl cation formation following loss of diethyl phosphate during the reaction pathway, there was no loss of stereointegrity (as judged by chiral HPLC) and no evidence of allylic substitution. Reaction of (*S*)-benzyl glycidyl ether **2f** with **6b** gave the benzyloxymethylene-substituted cyclopropyl sulfone **9f** in 60% yield (entry 5), again as a single diastereomer. We were intrigued by the diminished yield

TABLE 2. Examination of Substrate Scope

Entry	Epoxide		Product[a]		Yield[b]
1		**2b**		**9b**	86
2		**2c**		**9c**	85
3		**2d**		**9d**	82
4		**2e**		**9e**	74
5		**2f**		**9f**	60
6		**2g**		**9g**	31
7		**2h**		**9h**	0
8		**2i**		**9i**	5
9		**2j**		**9j**	17[c]

[a]Reactions carried out with **6b** (2 equiv) at 140 °C in DME for 4 h. [b]Isolated yield following column chromotography. [c]Diethyl (pyridin-2-yl)sulfonylmethylphosphonate used as reagent.

SCHEME 4. Expedient Synthesis of a Methylecyclopropane



for cyclopropane **9f** and so examined the effect of substitution at the γ-position. Isopropyloxirane **2g** gave the expected cyclopropyl sulfone **9g**, but in only 31% yield (entry 6), whereas reaction with *tert*-butyloxirane **2h** did not give the expected cyclopropyl sulfone **9h** (entry 7). Monitoring of this latter reaction by in situ ^{1}H NMR analysis revealed the appearance of signals characteristic of an olefin, indicating that neopentyl-like rearrangement[24] had occurred with loss of diethyl phosphate; however, it was not possible to isolate such products. We also examined whether non-terminal epoxides were substrates for this process; however, cyclohexene oxide **2i** gave the desired cyclopropyl sulfone **9i** in only 5% yield. Finally, we briefly examined the use of heteroaryl sulfones in this process, with a view that the products could be used in Julia−Kocienski olefination reactions[17k] to give methylene cyclopropanes. However, significant reduction in yield was observed (17%) when a 2-pyridylsulfone was employed (entry 9).

To further demonstrate the utility of our methodology, we deprotonated cyclopropyl sulfone **9f** with *n*-BuLi and then alkylated the resultant anion with iodomethyltrimethylsilane, which gave the corresponding trisubstituted cyclopropane **13** in 65% yield as a single diastereomer (as judged by ^{1}H NMR) (Scheme 4). Overall, this gave silyl sulfone **13** in only two steps from commercially available materials. Cyclopropane **13** has been synthesized by Liu and co-workers in four steps[17f] en route to [(methylenecyclopropyl)acetyl]-CoA, the causative agent of Jamaican vomiting sickness, which results from ingestion of the unusual amino acid hypoglycin A found in unripe ackee fruit. Silyl sulfone **13**

(22) Jarboe, S. G.; Terrazas, M. S.; Beak, P. *J. Org. Chem.* **2008**, *73*, 9627.
(23) (a) Tollefson, M. B.; Li, J. J.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 9052. (b) Westheimer, F. H. *Acc. Che,. Res.* **1968**, *1*, 70.
(24) Streitwieser, A. *Chem. Rev.* **1956**, *56*, 571.

was readily converted to methylene cyclopropane **14**[17l] on treatment with TBAF in THF, and hence, the present work should allow ready access to such compound as single enantiomers.[25]

In summary, the present method provides a very efficient and straightforward elaboration of enantiopure *trans*-cyclopropylsulfones and methylene cyclopropanes from terminal epoxides which proceeds with high diastereoselectivity. Such products are highly useful synthetic intermediates in a variety of processes.[17] This methodology should allow for a significant expansion of the Wadsworth−Emmons cyclopropanation reaction and considerably increases its synthetic appeal.

Experimental Section

General Procedure for the Direct Conversion of Epoxides to *trans*-Cyclopropylsulfones. To a vigorously stirred suspension of NaH (49 mg, 2.05 mmol) in anhydrous DME (2 mL) at 25 °C was added a solution of diethyl (phenylsulfonyl)methylphosphonate **6a** (584 mg, 2.00 mmol) in anhydrous DME (2 mL) dropwise over 5 min. The resulting clear solution was stirred for a further 5 min before the epoxide (1.00 mmol) was added dropwise over 1 min. The reaction was heated to 140 °C for 4 h. Once cooled, the reaction mixture was dry loaded onto silica (5 mL) and purified by flash column chromatography (EtOAc/petrol).

(**1*S*,2*R*)-2-Vinylcyclopropyl Phenyl Sulfone 9e.** According to the general procedure, (*R*)-vinyl oxirane (81 μL, 1.00 mmol) gave the *title compound* (154 mg, 74%) as a white solid: mp 67−68 °C; $[\alpha]_D$ +6.4 (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 3066w, 1446 m, 1302s (SO_2), 1143s (SO_2), 1058 m; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91−7.84 (m, 2H), 7.65−7.58 (m, 2H), 7.57−7.50 (m, 2H), 5.37 (ddd, J = 17.1, 10.2, 7.9 Hz, 1H), 5.15 (d, J = 17.1 Hz, 1H), 5.00 (d, J = 10.2 Hz, 1H), 2.44 (ddd, J = 8.3, 5.3, 4.4 Hz, 1H), 2.42−2.31 (m, 1), 1.62 (dt, J = 9.5 and 5.3 Hz, 1), 1.12 (dt, J = 8.3 and 5.9, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 135.6, 133.9, 129.7, 127.8, 117.1, 40.3, 23.2, 13.4; HRMS m/z ($M + NH_4^+$, 100) found 226.0892, $C_{11}H_{16}O_2NS$ requires 226.0896.

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Supporting Information Available: Spectroscopic data along with ^1H and ^{13}C NMR spectra for compounds **6a**, **9a**−**j**, and **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

(25) Chiral methylene cyclopropanes have been used in tandem rhodium-catalyzed C−H activation/cycloisomerization reactions; see: Aïssa, C.; Fürstner, A. *J. Am. Chem. Soc.* **2007**, *129*, 14836.