Synthesis of Enantiopure 2-Malonylvinyl Sulfoxides via Addition-Elimination Reactions of 2-Halo- and 2-(Mesyloxy)vinyl Sulfoxides

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Enantiomerically pure (*E*)-2-bromo- and (*E*)-2-iodovinyl sulfoxides **3a** and **3b** have been prepared in multigram quantities from (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene; enantiomerically pure (*E*)-2-(mesyloxy)vinyl sulfoxide **3c** has been synthesized by reaction of the enolate derived from condensation of 1-lithiomethyl *p*-tolyl sulfoxide and DMF with methanesulfonyl chloride. These compounds react with anions derived from diethyl alkylmalonates to produce enantiopure 2-malonylvinyl sulfoxides in good to excellent yields and with a high degree of stereoselectivity. The transformations proceed through an "addition-rotation-elimination" sequence, and the stereochemical results reinforce the concept that nucleophilic additions to vinyl sulfoxides are sterically controlled and occur predominately *syn* to the sulfinyl electron lone pair.

The utilization of enantiopure sulfoxides as chiral auxiliaries to direct asymmetric bond formation is a firmly established synthetic strategy.[2] Research activity in this area continues to be keen; some significant recent developments include diastereoselective Diels-Alder cycloadditions,[3] intramolecular ene reactions,[4] and reductions of β-keto sulfoxides,[5] each capable of proceeding with excellent diastereocontrol (>95% de).

Our own contribution in this field is represented by the enantiospecific vinylogous Pummerer reaction,[6] in which chiral, nonracemic vinyl sulfoxides are reacted with ketenes to afford enantiopure γ-(arylthio)-γ-butyrolactones. The remarkable enantiospecificity of this lactonization is believed to be a consequence of a [3,3]-sigmatropic rearrangement of the intermediate vinyl oxysulfonium enolate **1**, which proceeds from a single, thermodynamically preferred conformation (Figure 1).

In the context of a project designed to expand the synthetic utility of the sulfoxide-directed lactonization, we required an efficient route to enantiopure 2-substituted vinyl sulfoxides **2**. The 2-substituents were to be terminally functionalized in order to effect intramolecular, stereoselective replacement of the arylthio group of the derived γ-(arylthio)-γ-butyrolactones.[7] This account describes in detail the synthesis of these enantiopure vinyl sulfoxides.

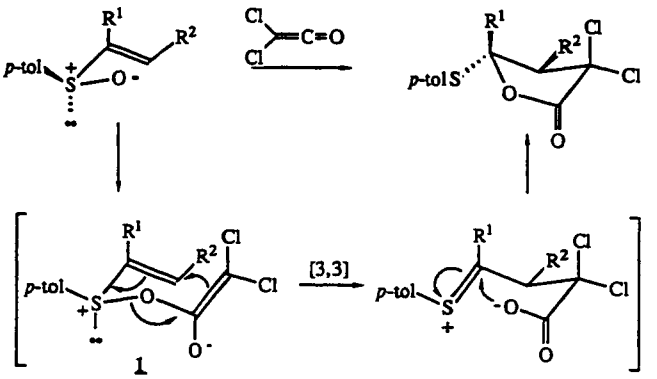
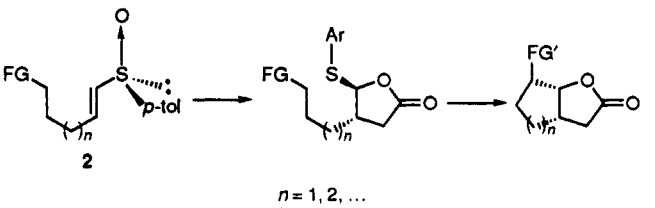


Figure 1. Presumed mechanism for the reaction of enantiomerically pure vinyl sulfoxides with dichloroketene to produce β-dichloro-γ-(arylthio)-γ-butyrolactones.



Results

Several different synthetic approaches to chiral vinyl sulfoxides have been reported in the literature. For

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(1) Taken, in part, from Ph.D. Thesis, R. S. Paley, University of Michigan, 1987.

(2) For reviews, see: (a) *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons: 1988. (b) Posner, G. H. *Acc. Chem. Res.* **1987**, *20*, 72-87. (c) Solladié, G. *Synthesis* **1981**, 185-196. (d) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961-968.

(3) Leading references: (a) Alonso, I.; Carretero, J. C.; García Ruano, J. L. *J. Org. Chem.* **1993**, *58*, 3231-3232. (b) Arai, Y.; Matusi, M.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 1983-1985. (c) Posner, G. H.; Harrison, W. *J. Chem. Soc., Chem. Commun.* **1985**, 1786-1787.

(4) Hiroi, K.; Umemura, M. *Tetrahedron Lett* **1992**, *33*, 3343-3346.

(5) An overview, along with a comprehensive list of pertinent references, can be found in a recent review article: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307-1370.

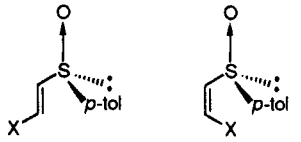
(6) (a) Marino, J. P. *Pure Appl. Chem.* **1993**, *65*, 667-674. (b) Marino, J. P.; Bogdan, S.; Kimura, K. *J. Am. Chem. Soc.* **1992**, *114*, 5566-5572. (c) Marino, J. P.; Fernández de la Pradilla, R. *Tetrahedron Lett.* **1985**, *25*, 5381-5384. (d) Marino, J. P.; Perez, A. D. *J. Am. Chem. Soc.* **1984**, *106*, 7643-7644.

(7) Marino, J. P.; Laborde, E.; Paley, R. S. *J. Am. Chem. Soc.* **1988**, 110, 966-968.

0022-3263/94/1959-3193$04.50/0

instance, simple enantiopure vinyl sulfoxides are usually prepared by the Andersen[8] method, in which vinyl Gringard or vinyllithium reagents are reacted with enantiomerically pure menthyl *p*-toluenesulfinate. This procedure, however, is limited by the availability of stereochemically homogeneous vinyl halides or vinylstannanes and by the number of other functional groups that can be incorporated into the organometallic reagent. Another approach to vinyl sulfoxides involves the stereospecific reduction of alkynyl sufoxides;[9] this methodology, however, requires strong reducing agents (LAH, DIBAL) which would also be incompatible with additional functionalization of the 2-substituent. An alternative method of vinyl sulfoxide synthesis is the Horner–Wittig reaction of the anion of dimethyl ((*R*)- or (*S*)-*p*-toluenesulfinyl)-phosphonate with aldehydes;[10] unfortunately, this reaction is usually nonstereoselective. Since our synthetic requirements precluded the utilization of these methodologies, we sought a new stereocontrolled route for the synthesis of **2**.

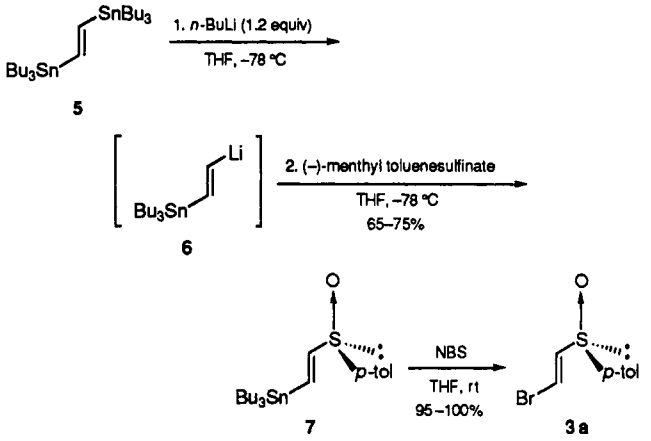
In selecting the appropriate strategy which would provide access to the desired 2-substituted vinyl sulfoxides, we recognized the earlier contribution of Hori and Oishi[11] who reported the stereospecific addition–elimination reaction of (*E*)- and (*Z*)-2-bromovinyl sulfoxides with malonate anions. Although this work involved racemic sulfoxides, the reaction conditions employed were sufficiently mild to allow for the preparation of terminally substituted enantiopure vinyl sulfoxides. The extension of this approach to our synthetic goals would therefore require the synthesis of enantiopure 2-halovinyl sulfoxides **3** and **4** (or their synthetic equivalents).



3 **4**

Our initial solution to this problem centered around the synthesis of (*E*)-2-bromovinyl sulfoxide **3a** (X = Br, Scheme 1). Starting with (*E*)-1,2-bis(tributylstannyl)-ethene[12] (**5**), we envisioned a sequential replacement of each tributylstannyl unit while retaining its *trans* stereochemistry. This was to be accomplished by an Andersen reaction using the vinyllithium species derived from **5**, followed by stereospecific conversion of the resulting 2-stannylvinyl sulfoxide to **3a**. Initial attempts to prepare 2-stannylvinyl sulfoxide **7** were only marginally successful, as treatment of the monolithiated species **6** with enantiomerically pure menthyl *p*-toluenesulfinate (THF, −78 °C) produced the desired Andersen adduct in low yield

Scheme 1



(*ca.* 20%). It was reasoned that the origin of this poor conversion was due to that fact that the vinyllithium species **6** was basic enough to deprotonate vinyl sulfoxide **7** as it was formed, thus quenching the nucleophile and, therefore, preventing the reaction from going to completion. This setback was overcome by addition of a cold (−78 °C) THF solution of vinyllithium **6** to a cold (−78 °C) THF solution of the sulfinate ester *as rapidly as possible* (see Experimental Section for details). Yields of 65–75% of 2-stannylvinyl sulfoxide **7** (10- to 20-mmol scale) were routinely obtained using this procedure. Conversion of **7** to the desired (*E*)-2-bromovinyl sulfoxide **3a** (J_t = 13.5 Hz) was accomplished by treatment with NBS.[13] Both enantiomers of **3a** were prepared by this protocol, and their enantiomeric purities (100% ee) were verified by spectroscopic and polarimetric measurements of subsequently derived products (*vide infra*). Additionally, iodo analog **3b** (X = I) was prepared by treatment of **7** with iodine.

An alternative sequence for the preparation of a 2-halovinyl sulfoxide equivalent was also undertaken. (*S*)-(−)-Methyl *p*-tolyl sulfoxide,[14] readily available by treatment of (+)-menthyl toluenesulfinate with methylmagnesium iodide, was deprotonated with LDA and reacted with dimethylformamide.[15] The resulting enolate **8** was collected by filtration, resuspended in THF, and treated with mesyl chloride to provide 2-(mesyloxy)vinyl sulfoxide **3c** (X = OMs) in 70% yield as a 6:1 mixture of (*E*) and (*Z*) isomers, respectively (Scheme 2). The major *trans* isomer (J_t = 12.1 Hz) could be easily purified by column chromatography. This sequence had the advantage of circumventing the use of toxic organostannane reagents and was more easily performed on a large scale (45 mmol).

While these investigations were underway, concurrent studies from another laboratory established a route for the preparation of the *cis* analog of **3**, (*Z*)-2-iodovinyl sulfoxide **4**.[16] Sulfoxide **4** was available from (+)-(*R*)-

(8) (a) Andersen, K. K. *Tetrahedron Lett.* **1962**, *3*, 93–95. (b) Andersen, K. K. *J. Org. Chem.* **1964**, *29*, 1953–1956. (c) Posner, G. H.; Mallamo, J. P.; Mura, K. *J. Am. Chem. Soc.* **1981**, *103*, 2886–2888. (d) Posner, G. H.; Mallamo, J. P.; Hulce, M.; Frye, L. L. *J. Am. Chem. Soc.* **1982**, *104*, 4180–4185.

(9) Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078–1082.

(10) (a) Burke, S. D.; Shankaran, K.; Helber, M. J. *Tetrahedron Lett.* **1991**, *32*, 4655–4658. (b) Reference 2c.

(11) Hori, I.; Oishi, T. *Tetrahedron Lett.* **1979**, *20*, 4087–4090.

(12) (a) Corey, E. J.; Wollenburg, R. H. *J. Org. Chem.* **1975**, *40*, 2265–2266. (b) Corey, E. J.; Wollenburg, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 5581–5583. (c) Bottaro, J. C.; Hanson, R. N.; Seitz, D. E. *J. Org. Chem.* **1981**, *46*, 5221–5222.

(13) Collins, P. W.; Jung, C. J.; Gasiecki, A.; Pappo, R. *Tetrahedron Lett.* **1978**, *19*, 3187–3190.

(14) Solladié, G.; Hutt, J.; Girardin, A. *Synthesis* **1987**, 173.

(15) Kawecki, R.; Kozerski, L. *Tetrahedron* **1986**, *42*, 1469–1473. For an analogous transformation of a vinyl sulfoximine: Paley, R. S.; Snow, S. R. *Tetrahedron Lett.* **1990**, *31*, 5853–5856. For an analogous transformation of a vinyl sulfone: Marino, J. P.; Long, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 7916–7917.

(16) Fernández de la Pradilla, R.; Morente, M.; Paley, R. S. *Tetrahedron Lett.* **1992**, *33*, 6101–6102. The experimental details for the preparation of **4** will be published elsewhere. The optical purity of **4** was 100%, as confirmed by analysis of its ^{1}H NMR spectrum in the presence of Eu(hfc)$_3$.

Scheme 2

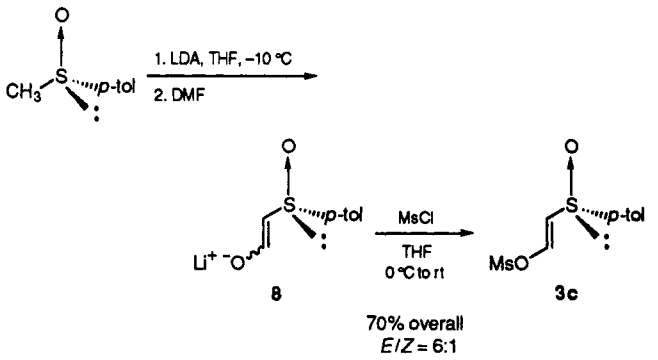
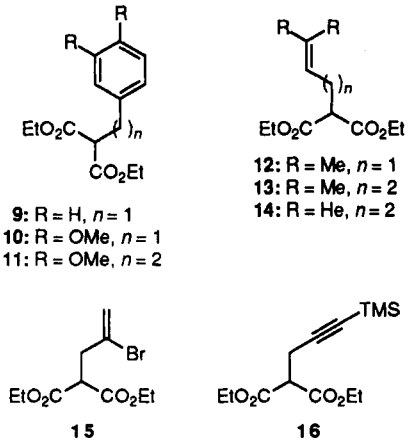
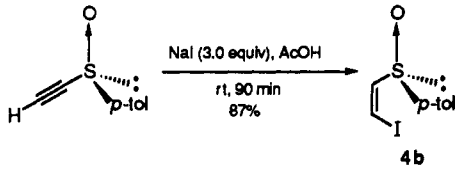


Chart 1



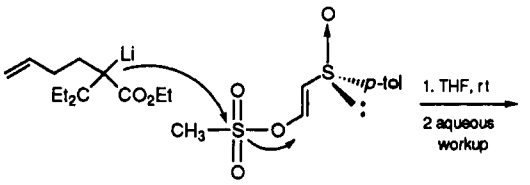
ethynyl *p*-toluenesulfoxide[9] by treatment with NaI (3.0 equiv) in acetic acid (rt, 90 min) in 87% yield.

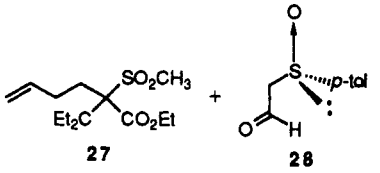


The availability of the requisite vinyl sulfoxide precursors allowed us to turn our attention toward the preparation of the terminally substituted malonate derivatives for the proposed addition–elimination reactions. All the malonate derivatives (**9**–**16**, Chart 1) were prepared by alkylation of diethyl malonate with the corresponding alkyl bromides, iodides, or mesylates using standard conditions (NaH, THF, 0 °C to rt).[17]

With the terminally substituted malonate derivatives in hand, the addition–elimination reaction with sulfoxides **3** and **4** could be explored on enantiopure substrates. On the basis of Hori and Oishi's results, it was expected that retention of the double-bond stereochemistry would take place in all cases. Surprisingly, complete retention was observed only in some cases (**9**–**11**, **16**). In order to establish general trends for this addition–elimination process, and to compare the reactivity of the novel 2-(mesyloxy)vinyl sulfoxide **3c** to its halogenated analogs, we performed the reaction under a variety of conditions. The results of this study are summarized in Tables 1 and 2.

Several trends become evident upon examination of these results. First, while the addition of benzyl- and phenylethyl-substituted malonate nucleophiles (**9**–**11**) to (*E*)-halovinyl sulfoxides **3** were stereospecific, the addition of the remaining substituted malonates were not, although the latter were still highly stereoselective (Table 1, entries 7, 9, 10, and 15–17). While it is possible that the diminished stereoselectivity in these latter cases is a result of steric effects (*vide infra*), we are unable to dismiss the possibility that electronic effects may play a role in enhancing the stereoselectivity of the aromatic-substituted malonates. Second, the additions of malonate nucleophiles to (*Z*)-iodovinyl sulfoxide **4** were stereospecific and required the use of lithio malonates (Table 2); incomplete conversions were observed when sodiomalonates were employed. Third, the yields of the products derived from the 2-(mesyloxy)vinyl sulfoxide **3c** were similar to those obtained from the halogenated analogs **3a** and **3b**, though highly dependent on the particular nucleophile used (Table 1, cf. entries 2 and 3, 10 and 11, 14 and 15). However, (*E*)/(*Z*) ratios for products derived from **3c** were consistently greater than those from **3a** and **3b**. Finally, utilization of the sodiomalonate anion as the nucleophile with **3c** was essential, since the analogous lithium anion provided sulfone **27** and α-sulfinyl aldehyde **28**, a result of attack at the sulfur atom of the mesyl group.[18]





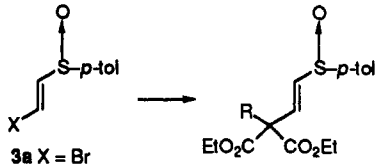
The enantiomeric purity of 2-malonylvinyl sulfoxides **17**–**26**, and therefore of their precursors **3** and **4**, was assessed to be 100% on the basis of examination of their ^{1}H NMR spectra in the presence of a chiral shift reagent. For example, using Eu(hfc)$_3$ (*ca.* 5 mg/mL), base-line separation of the *p*-tolyl methyl resonance ($\Delta\delta$ = 0.018 ppm) from each of the two enantiomers of a sample of racemic **17** was achieved; a sample of **17** derived from enantiopure **3a** revealed only one *p*-tolyl methyl resonance under similar conditions. That **17** is enantiomerically pure also implies that its immediate precursor, 2-bromovinyl sulfoxide **3a**, is enantiomerically pure.[19] That the magnitude of the optical rotation of vinyl sulfoxide **17** is the same (within experimental error) for the product derived from bromovinyl sulfoxide **3a** and its mesyl analog **3c** is strong evidence for the complete enantiopurity of the latter compound and the malonyl sulfoxides derived from it.

(17) Adams, R.; Kamm, R. M. *Organic Syntheses*; Wiley: New York, 1932; Collect. Vol. I, pp 250–251.

(18) In fact, compounds **27** and **28** were frequently formed as minor products (10–20% yield) from the reaction of sodiomalonates with β-mesylvinyl sulfoxide **3c**.

(19) The finding that **3a** is enantiomerically pure is consistent with evidence obtained elsewhere: Paley, R. S.; de Dios, A.; Fernández de la Pradilla, R. *Tetrahedron Lett.* **1993**, *34*, 2429–2432. The optical rotations of dienyl sulfoxides prepared by a Stille-type coupling of **3a** and vinylstannanes were identical to those prepared by a different method, previously reported. Furthermore, these dienyl sulfoxides derived from **3a** were judged to be enantiomerically pure after analysis by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent.

Table 1. Preparation of Enantiopure (*E*)-2-Malonylvinyl Sulfoxides



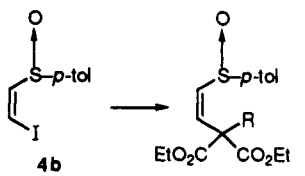
3a X = Br
b X = I
c X = OMs

17–24

entry	sulfoxide	malonate deriv	method,[a] temp (°C)	major product	*E*/*Z* ratio[b]	overall yield (%)	$[\alpha]_D$[c]
1	(*R*)-**3a**	**9**	**A**, rt	**17**	100:0	88	+86.0°
2	(*R*)-**3b**	**9**	**A**, 0 to rt	**17**	100:0	93	
3	(*R*)-**3c**	**9**	**A**, 0 to rt	**17**	100:0	64	
4	(*S*)-**3a**	**9**	**A**, 0 to rt	*ent*-**17**	100:0	86	−84.0°
5	(*R*)-**3a**	**10**	**A**, rt	**18**	100:0	98	+95.1°
6	(*R*)-**3a**	**11**	**A**, rt	**19**	100:0	78	+100°
7	(*R*)-**3a**	**12**	**A**, rt	**20**	94:6	70	+119°
8	(*S*)-**3c**	**13**	**A**, 0 to rt	**21**	90:10	71	−154° [d]
9	(*R*)-**3a**	**14**	**A**, 0 to rt	**22**	93:7	70	+128°
10	(*R*)-**3a**	**14**	**B**, rt	**22**	80:20	67	
11	(*R*)-**3c**	**14**	**A**, 0 to rt	**22**	>95:5	62	
12	(*R*)-**3c**	**14**	**B**, −60 to rt[e]	*g*	*g*	*g*	*g*
13	(*S*)-**3c**	**15**	**A**, rt	**23**	89:11	76	−75.1°
14	(*S*)-**3c**	**16**	**A**, rt	**24**	100:0	56	−158° [d]
15	(*R*)-**3b**	**16**	**A**, rt	**24**	84:16	63	
16	(*R*)-**3b**	**16**	**A**, 0 to rt	**24**	89:11	72	
17	(*R*)-**3b**	**16**	**A**, −23 to rt	**24**	91:9	*f*	

[a] Method **A**: reaction performed in THF; alkylmalonate deprotonated with NaH. Total reaction time: 12 h. Method **B**: reaction performed in THF; alkylmalonate deprotonated with *n*-BuLi. Total reaction time: 3 h. [b] (*E*)/(*Z*) ratios determined from ^{1}H NMR analysis of unpurified reaction mixture. [c] All optical rotations were measured in $CHCl_3$, unless otherwise noted. [d] Measured in acetone. [e] Identical results obtain at room temperature. [f] Yield not obtained; reaction did not proceed to completion. [g] No addition–elimination products formed (see text).

Table 2. Preparation of Enantiopure (*Z*)-2-Malonylvinyl Sulfoxides



4b

25, 26

entry	sulfoxide	malonate deriv	method,[a] temp (°C)	major product	*E*/*Z* ratio[b]	overall yield (%)	$[\alpha]_D$[c]
1	(*R*)-**4b**	**9**	**B**, −60 to rt	**25**	0:100	63	−140°
2	(*S*)-**4b**	**9**	**B**, −60 to rt	*ent*-**25**	0:100	70	+137°
3	(*R*)-**4b**	**14**	**B**, −60 to rt	**26**	0:100	73	−210°

[a] Method **B**: reaction performed in THF; alkylmalonate deprotonated with *n*-BuLi. Total reaction time: 3 h. [b] (*E*)/(*Z*) ratios determined from ^{1}H NMR analysis of unpurified reaction mixture. [c] All optical rotations were measured in $CHCl_3$.

Mechanistic Considerations

The results presented here are consistent with the mechanisms put forth by Tsuchihashi for the conjugate addition of malonate anions to vinyl sulfoxides[20] and by Rappoport for addition–elimination reactions.[21] A proposed mechanism for the reactions of the (*E*)-2-halo- and (*E*)-2-(mesyloxy)vinyl sulfoxides with malonate nucleophiles is depicted in Figure 2. The approach of the nucleophile to the vinyl sulfoxide (assumed to react from its more stable *s-cis* conformation)[22] is sterically controlled, producing a pair of diastereomeric α-sulfinyl carbanions, **A** and **B**. The stereochemistry indicated for carbanions **A** and **B**, in which the carbanion lone pair is *gauche* with respect to the sulfinyl oxygen, has been demonstrated to be preferred in THF,[23] and is in accordance with Tsuchihashi's mechanism.

Once formed, carbanions **A** and **B** must undergo internal rotation about the C_1–C_2 bond prior to expulsion of the leaving group in order to form the observed products. For the presumably more sterically encumbered malonate nucleophiles **9**–**11**, an approach *syn* to the sulfinyl lone pair is greatly preferred, leading to carbanion **B**. Two internal rotations of **B** which would lead to products are depicted in Figure 2; clearly the 60° rotation is preferred over the 120° rotation since the former would allow for an *anti* elimination whereas the latter would require an energetically less favorable *syn* elimination. Moreover, the 120° rotation pathway would result in an eclipsed conformation of the nucleophile and the sulfoxide. Thus, for nucleophiles **9**–**11**, the *trans* stereochemistry of the starting sulfoxides is retained. For the nonaromatic

(20) (a) Tsuchihashi, G.; Mitamura, S.; Ogura K. *Tetrahedron Lett.* **1976**, *17*, 855–858. (b) Tsuchihashi, G.; Mitamura, S.; Inoue, S.; Ogura K. *Tetrahedron Lett.* **1973**, *14*, 323–326.

(21) (a) Rappoport, Z. *Acc. Chem. Res.* **1992**, *25*, 474–479. (b) Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7–15.

(22) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7399–7400.

(23) Oae, S.; Uchida, Y. In ref 2a, Chapter 12 and references therein.

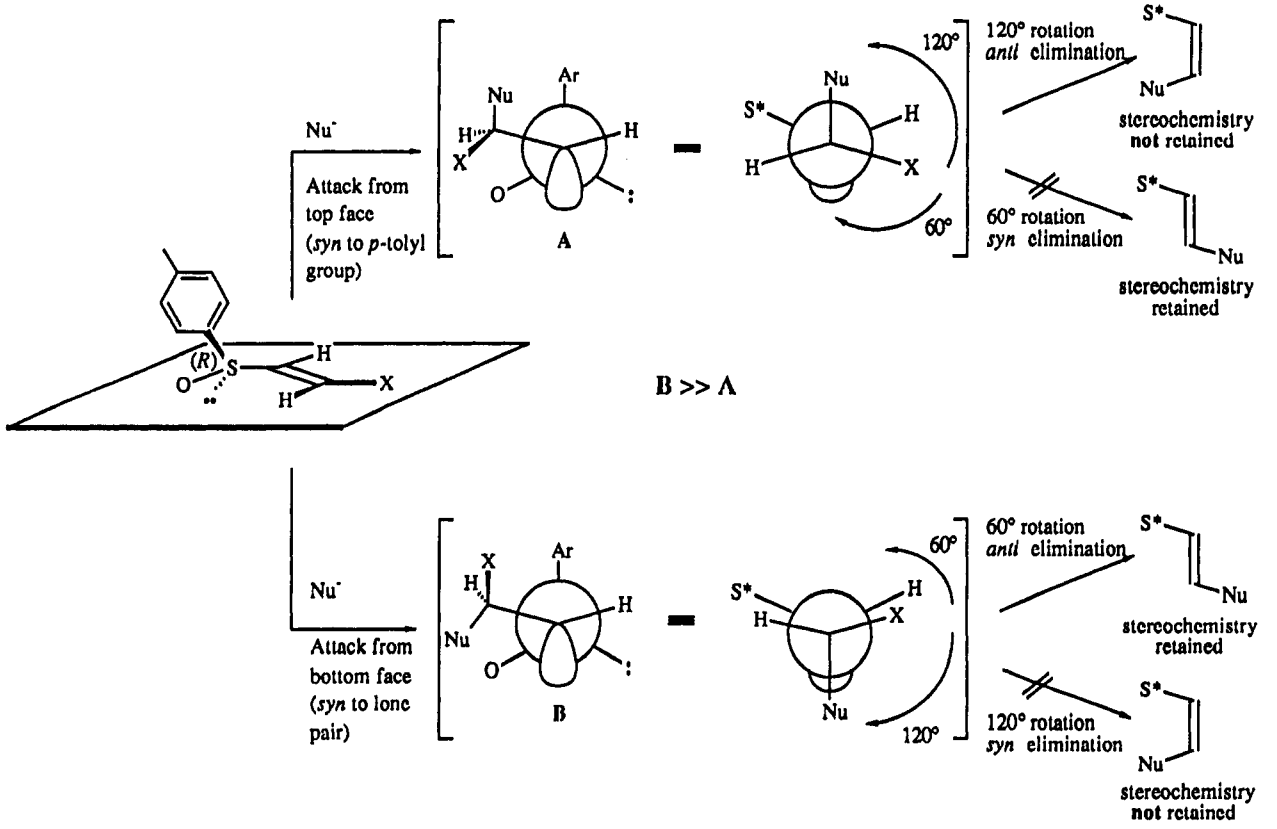


Figure 2. Possible reaction pathways for addition of malonate nucleophiles to (*E*)-2-halo- and (*E*)-2-(mesyloxy)vinyl sulfoxides **3** in THF.

substituted nucleophiles utilized in this study, an approach *syn* to the aromatic group of the sulfoxide is probably more likely, presumably due to diminished steric requirements. This *syn* approach would result in the formation of a larger relative amount of carbanion **A**. That carbanion **A** leads to the formation of the stereochemically nonretained product is readily explained: retention of stereochemistry via a 60° rotation would require a high energy *syn* elimination and does not occur. Instead, an *anti* elimination pathway is possible, via a 120° rotation; this leads to the *cis*-vinyl sulfoxide. Though this pathway would necessitate moving through an eclipsed interaction of the nucleophile and the sulfoxide, the smaller size of the nucleophile apparently diminishes its importance relative to the energy difference between the *anti* and *syn* eliminations.

Additional evidence is consistent with this mechanism. First, the (*E*)/(*Z*) ratios tend to increase as the initial reaction temperature decreases (Table 1; cf. entries 9 and 10; also 15, 16, and 17). This suggests a higher preference for the formation of **B** relative to **A**, presumably due to an increased *s-cis* conformer population resulting in a higher facial selectivity in the nucleophilic approach. Second, the (*E*)/(*Z*) ratio for vinyl sulfoxides **23** and **26** dramatically increases when 2-(mesyloxy)vinyl sulfoxide **3c** is employed instead of its halogenated analogs **3a** or **3b** (Table 1; cf. entries 9 and 11; 14 and 15). Since the facial selectivity of the nucleophilic approach would be expected to be independent of the nature of the leaving group, the **A**/**B** ratio should remain the same. However, the increased leaving group ability of the mesylate compared to the halides suggests that the barrier for *syn* elimination is low. Thus, product formation depends on which direction rotation is more likely to occur rather than on which elimination type is energetically more accessible. Therefore, the shorter 60° rotation pathway leads to stereochemically retained product, although via the minor carbanion **A**.

Finally, the stereospecific reaction of malonate nucleophiles with (*Z*)-iodovinyl sulfoxide **4** (Table 2) can also be rationalized by a similar mechanistic analysis (Figure 3). The approach of the nucleophile to vinyl sulfoxide **4** (assumed to react from its more stable *s-trans* conformation)[24] is sterically controlled and is expected to produce a pair of diastereomeric α-sulfinyl carbanions, **C** and **D**. The predominant carbanion **C** would be capable of undergoing a 60° rotation which would allow for an *anti* elimination leading to stereochemically retained product. Similarly, a 120° rotation by carbanion **D** would allow for an *anti* elimination to occur in order to provide the stereochemically nonretained product. In all cases, however, the conversion of **4** proved to be stereospecific; only the stereochemically retained (*Z*)-malonylvinyl sulfoxides were detected. This suggests that the facial selectivity of the nucleophilic approach for the (*Z*)-iodovinyl sulfoxide **4** is significantly enhanced relative to those of their (*E*)-isomers. This is most likely a consequence of the increased proximity of the bulky *p*-toluenesulfinyl group to the reactive site (at C_2) in the *s-trans* conformation when compared to the *s-cis* conformation. The enhancement of facial selectivity observed here for (*Z*)-vinyl sulfoxides is similar to that observed by Koizumi and others for Diels–Alder reactions of 3-sulfinylacrylates.[24]

(24) For example: (a) Takahashi, T.; Iyobe, A.; Arai, Y.; Koizumi, T. *Synthesis* **1989**, 189–191. (b) Takayama, H.; Hayashi, K.; Koizumi, T. *Tetrahedron Lett.* **1986**, *27*, 5509–5512. See also: de Lucchi, O.; Pasquato, L. *Tetrahedron* **1988**, *44*, 6755–6794, and references cited therein.

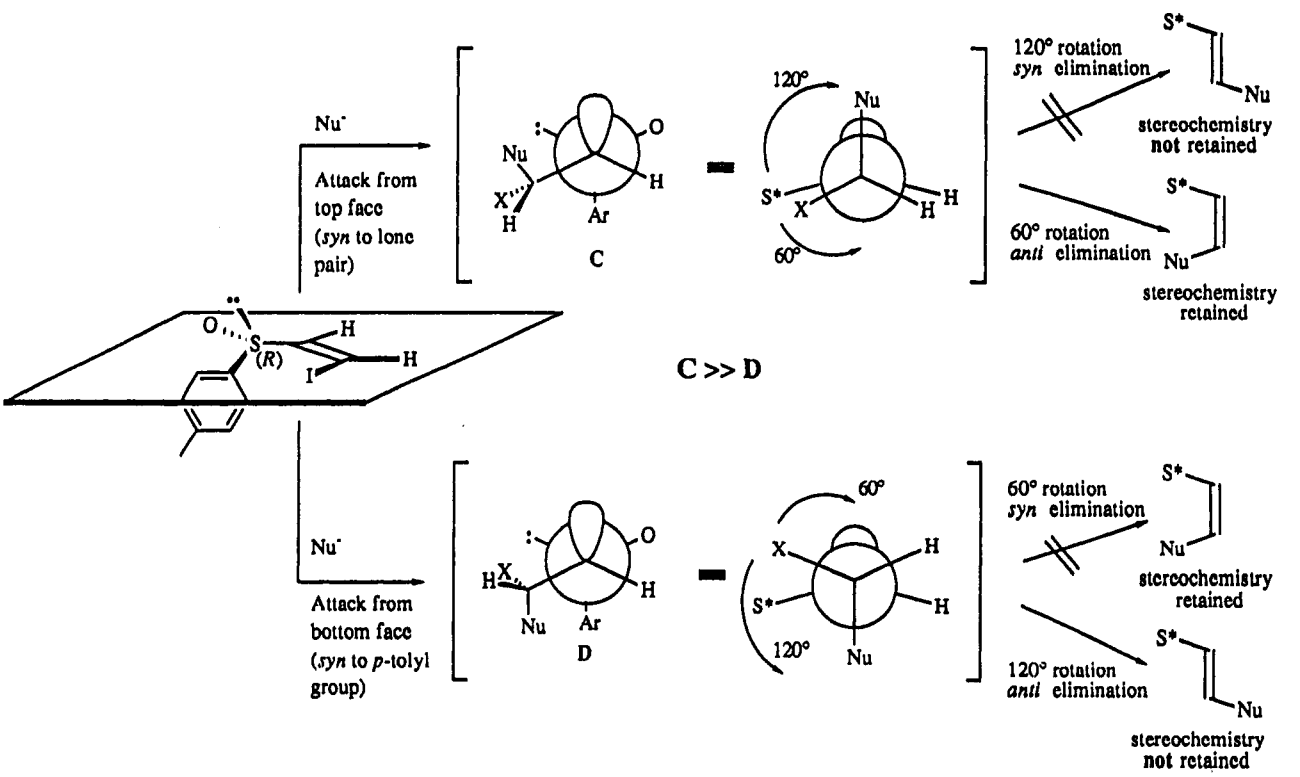


Figure 3. Possible reaction pathways for addition of malonate nucleophiles to (*Z*)-2-iodovinyl sulfoxide 4 in THF.

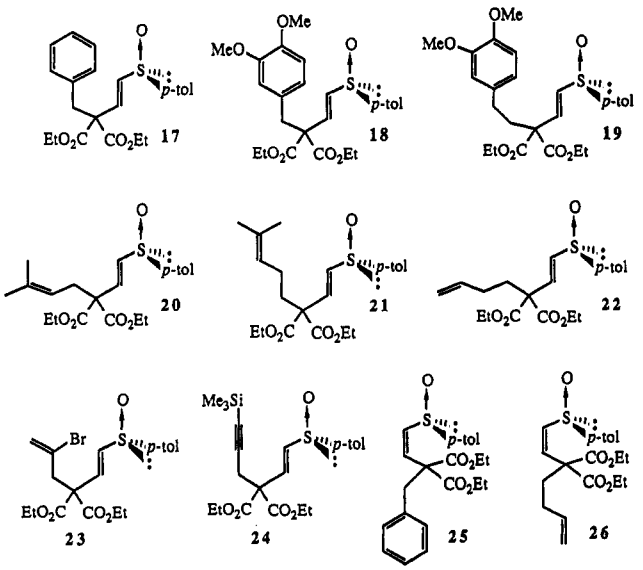


Figure 4. Enantiopure 2-malonylvinyl sulfoxides prepared from 3 and 4.

Conclusions

We have demonstrated that (*E*)-2-halo- and (*E*)-2-(mesyloxy)vinyl sulfoxides can be prepared in enantiomerically pure form on a multigram scale. These compounds, along with (*Z*)-2-iodovinyl sulfoxide, react with anions derived from diethyl alkylmalonates to produce enantiopure 2-malonylvinyl sulfoxides in good to excellent yields and with a high degree of stereoselectivity. The transformations proceed through an "addition–rotation–elimination" sequence,[21] and the stereochemical results reinforce the notion that nucleophilic additions to vinyl sulfoxides are sterically controlled and are predominately *syn* to the sulfinyl electron lone pair.

The malonylvinyl sulfoxides have been successfully elaborated into enantiopure γ-(arylthio)-γ-butyrolactones and ultimately into a series of carbocyclic, ring-fused lactones.[7] The halovinyl sulfoxides used to prepare the malonylvinyl sulfoxides have also been employed in the synthesis of enantiopure dienyl[19] and enynyl[25] sulfoxides; the details of all these transformations will be described in due course.

Experimental Section

General Methods. All reactions were carried out under a positive pressure of dry argon or nitrogen. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran (THF) was distilled from sodium and benzophenone, and dimethylformamide (DMF) from calcium hydride. Flash chromatography was performed using Merck 230–400-mesh silica gel 60. Analytical TLC was carried out on Merck silica gel 60 F-254 precoated glass plates, with detection by UV light and acidic vanillin solution in ethanol. Optical rotations were measured in $CHCl_3$ or acetone at 22 °C using a Perkin-Elmer Model 241 polarimeter. Melting points were determined in a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1600 Series FT-IR spectrophotometer or a Perkin-Elmer 727B grating IR spectrophotometer. Low-resolution mass spectra (MS) were obtained on a Finnigan 4021 GCMS/DS instrument with sample introduction *via* direct probe (dp) or through a GC column containing 5% SE 30 (gc). Mass spectra were electron-impact ionized with a beam energy of 70 eV. Masses are reported in units of mass over charge (m/z); the molecular and base peaks are indicated by (M) and (100%), respectively. High-resolution mass spectra (HRMS) were obtained on a VG 70-250-S mass spectrometer. Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI. ^1H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz using a Brüker AM-300 FT NMR spectrometer, at 360 MHz and 90 MHz using a Brüker WM-360 FT NMR, or at 200 MHz and 50

(25) Paley, R. S.; Lafontaine, J. A.; Ventura, M. P. *Tetrahedron Lett.* **1993**, *34*, 3663–3666.

MHz using an IBM/Brüker WP 200 SY instrument and $CDCl_3$ as solvent. Chemical shifts are reported as δ units from tetramethylsilane as internal standard. The following abbreviations are used to describe the peak patterns when appropiate: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

Substituted malonates **9–16** were prepared using standard procedures by alkylation of diethyl sodiomalonate with the corresponding alkyl bromide, iodide, or mesylate.[17]

(*R*)-(*E*)-*p*-Tolyl 2-(Tributylstannyl)vinyl Sulfoxide (7). A 100 mL, three-necked round bottom flask, equipped with a nitrogen inlet needle and a clamped 90° adapter tube, was charged with (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene[12] (**5**) (6.17 g, 10.2 mmol) and THF (33 mL). After the solution was cooled to −78 °C under a nitrogen atmosphere, *n*-butyllithium (5.00 mL, 2.44 M in hexanes, 12.2 mmol) was added; this mixture was stirred at −78 °C for 1 h. The solution was then added, *as rapidly as possible*, to a solution of (*S*)-(−)-menthyl *p*-toluenesulfinate (3.00 g, 10.2 mmol) in THF (100 mL) at −78 °C. [This rapid addition (less than 2 s) was accomplished by increasing the nitrogen flow over the vinyllithium species solution and through the 90° adapter tube; the solution was then emptied into the sulfinate solution by force, through the narrow bore of the adapter tube.]

The reaction mixture was stirred at −78 °C for 15 min and then the reaction was quenched with a saturated NH_4Cl solution (25 mL). After the solution was warmed to room temperature, water (10 mL) and ether (10 mL) were added and the organic layer was separated. The aqueous layer was washed with ether (2 × 75 mL); the combined organic layers were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to yield an impure yellow oil. The crude 2-stannylvinyl sulfoxide **7** was usually used without further purification.

If desired, purification was effected by column chromatography (hexanes:ethyl acetate, 15:1 to 9:1), which gave an inseparable mixture of the product and menthol. Sublimation of menthol at 0.1 mmHg and 40 °C yielded pure **7** as a yellow oil (3.02 g, 65%): $[\alpha]^{25}_D$ = +140° (*c* 1.91, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.83 (t, 9H), 0.95–1.05 (m, 6H), 1.15–1.25 (m, 6H), 1.25–1.55 (m, 6H), 2.37 (s, 3H), 6.54 (d, 1H, J = 18.1 Hz), 7.26 (d, 2H, J = 8.0 Hz), 7.32 (d, 1H, J = 18.1 Hz), 7.45 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 10.1, 13.6, 21.4, 27.2, 28.9, 125.0, 130.1, 136.0, 141.0, 141.4, 147.8; IR (neat) 2956, 1551, 1492, 1465, 1376, 1085, 1051 cm^{-1}; MS (dp) 405, 389, 325, 291, 246, 211, 177, 123, 91, 57, 41 (100%). Anal. Calcd for $C_{21}H_{27}OSSn$: C, 55.40; H, 7.92; S, 7.05. Found: C, 55.46; H 7.86; S, 7.13.

(*R*)-(*E*)-2-Bromovinyl *p*-Tolyl Sulfoxide (3a). To a solution of the unpurified 2-stannylvinyl sulfoxide **7** (from 10.2 mmol (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene[12] (**5**)) in THF (65 mL) at room temperature was added *N*-bromosuccinimide (4.36 g, 24.5 mmol). After the mixture was stirred for *ca.* 12 h, a saturated NH_4Cl solution (100 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Column chromatography (hexanes:ethyl acetate, 9:1 to 5:1) afforded 1.54 g (62% from **5**) of **3a** as a white solid: mp 58.5–60.5 °C; $[\alpha]^{25}_D$ = +246° (*c* 1.74, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.39 (s, 3H), 6.85 (d, 1H, J = 13.5 Hz), 7.14 (d, 1H, J = 13.5 Hz), 7.31 (d, 2H, J = 8.2 Hz), 7.50 (d, 2H, 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.5, 114.5, 124.8, 130.3, 139.6, 141.1, 142.4; IR ($CHCl_3$) 3075, 2940, 1575, 1565, 1495, 1262, 1045cm^{-1}; MS (dp) 247 (M + 2), 245 (M), 230, 198, 196 (100%), 139, 123, 91, 65, 39. Anal. Calcd for C_9H_9BrOS: C, 44.09; H, 3.67; Br, 32.62. Found: C, 44.27; H, 3.76; Br, 32.52. For **(*S*)-(*E*)-2-bromovinyl *p*-tolyl sulfoxide**, $[\alpha]^{25}_D$ = −246° (*c* 1.97, $CHCl_3$).

(*R*)-(*E*)-2-Iodovinyl *p*-Tolyl Sulfoxide (3b). To a solution of the unpurified 2-stannylvinyl sulfoxide **7** (from 9.9 mmol (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene[12] (**5**)) in CH_2Cl_2 (30 mL) at 0 °C was added iodine (3.77 g, 14.9 mmol). After the mixture was stirred for 4 h at 0 °C and 12 h at room temperature, a saturated $Na_2S_2O_3$ solution (15 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Column chromatography (hexanes:ethyl acetate, 9:1 to 5:1) afforded 1.85 g (64% from **5**) of **3b** as a white solid: mp 96–97 °C; $[\alpha]^{25}_D$ = +241° (*c* 0.69, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.42 (s, 3H), 7.16 (d, 1H, J = 14.3 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.40 (d, 1H, J = 14.3 Hz), 7.51 (d, 2H, 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 21.4, 88.9, 124.8, 130.3, 139.5, 142.3, 147.3; IR ($CHCl_3$) 3054, 1596, 1567, 1493, 1048 cm^{-1}; MS (dp) 292 (M), 244 (100%), 165, 139, 123, 91, 65. Anal. Calcd for C_9H_9IOS: C, 37.00; H, 3.10. Found: C, 36.84; H, 3.05.

(*S*)-(*E*)-2-(*p*-Toluenesulfinyl)vinyl Methanesulfonate (3c). To a solution of diisopropylamine (10.3 mL, 73.5 mmol) in THF (30 mL) at −10 °C was added *n*-butyllithium (1.6 M in hexanes, 45.9 mL, 73.5 mmol). After this solution was stirred for 30 min at −10 °C, a THF (20 mL) solution of (*S*)-(−)-methyl *p*-tolyl sulfoxide (11.33 g, 73.5 mmol) was added slowly via syringe; the reaction was stirred for 1 h at −10 °C. At this time, DMF (5.69 mL, 73.5 mmol) was added slowly while the reaction was allowed to warm to room temperature over 1 h. After the solution was stirred overnight, the precipitated yellow solid was filtered off and washed with several portions of diethyl ether to afford enolate **8**. This unpurified solid was suspended in THF (125 mL); the solution was cooled to 0 °C and treated with mesyl chloride (5.69 mL, 73.5 mmol). Stirring was continued for 1 h at 0 °C and 1 h at room temperature, and then the reaction was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL); the combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give a yellow oil which was purified by column chromatography (hexanes:ethyl acetate, 1:1) to afford **3c** (11.44 g, 60%) as a white solid and its (*Z*) isomer (1.89 g, 10%) as a colorless oil. **(*E*)-isomer** (major product): mp 111–112 °C; $[\alpha]^{25}_D$ = −156° (*c* 1.26, acetone); ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.18 (s, 3H), 6.32 (d, 1H, J = 12.1 Hz), 7.35 (d, 2H, J = 8.0 Hz), 7.45 (d, 1H, J = 12.1 Hz), 7.54 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 21.4, 38.6, 124.0, 124.5, 130.3, 134.0, 142.3, 142.8; IR ($CHCl_3$) 3061, 3053, 3037, 3010, 1625, 1378, 1364, 1340, 1188, 1179, 1112, 1094, 1083, 1038, 855, 785, 699, 624 cm^{-1}; MS (dp) 260 (M), 212, 165, 139, 134, 133 (100%), 123, 105, 91, 79, 65, 45; HRMS calcd for $C_{10}H_{12}O_4S_2$ 260.0177, found 260.0176. Anal. Calcd for $C_{10}H_{12}O_4S_2$: C, 46.14; H, 4.65; S 24.63. Found: C, 46.28; H, 4.62; S, 24.62. **(*Z*)-isomer** (minor product): ^1H NMR ($CDCl_3$) δ 2.42 (s, 3H), 3.24 (s, 3H), 6.00 (d, 1H, J = 5.5 Hz), 7.05 (d, 1H, J = 5.5 Hz), 7.34 (d, 2H, J = 8.0 Hz), 7.56 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 21.4, 38.6, 124.0, 124.6, 130.2, 134.0, 140.5, 142.0; MS (dp) 263 (M + 3), 262 (M + 2), 261 (M + 1), 260 (M), 212, 165, 139, 133 (100%), 123, 107, 105, 91, 79, 78, 77, 65, 63, 51; HRMS calcd for $C_{10}H_{13}O_4S_2$ (M + 1) 261.0255, found 261.0255.

General Procedure for the Preparation of 2-Malonylvinyl Sulfoxides; Method A. (*R*)-(*E*)-Diethyl 2-Benzyl-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (17). To a solution of diethyl benzylmalonate (**9**) (830 mg, 3.32 mmol) in THF (75 mL) was added NaH (79.6 mg, 3.32 mmol). After the evolution of hydrogen gas subsided, the resulting cloudy suspension was stirred at room temperature for 1 h. A solution of (*R*)-(*E*)-2-bromovinyl sulfoxide (**3a**) (813 mg, 3.32 mmol) in THF (25 mL) was then added *via* cannula. A white precipitate formed immediately, and this suspension was stirred for *ca.* 12 h. The reaction was stopped by addition of saturated NH_4Cl solution (20 mL); the organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Column chromatography of the crude material (hexanes:ethyl acetate, 3:1) afforded **17** (1.21 g, 88%) as a clear oil: $[\alpha]^{25}_D$ = +86.0° (*c* 2.59, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.22 (t, 3H, J = 7.1 Hz), 1.24 (t, 3H, J = 7.1 Hz), 2.44 (s, 3H), 3.42 (s, 2H), 4.21 (q, 2H, J = 7.1 Hz), 4.22 (q, 2H, J = 7.1 Hz), 6.47 (d, 1H, J = 15.7 Hz), 6.87 (d, 1H, J = 15.7 Hz), 7.02–7.06 (m, 2H), 7.22–7.23 (m, 3H), 7.32 (d, 2H, J = 8.2 Hz), 7.47 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.8, 21.2, 41.7, 60.8, 61.9, 61.9, 125.0, 127.2, 128.3, 128.8, 130.0, 130.2, 134.0, 135.0, 138.5, 140.9, 141.7, 168.8, 168.8; IR ($CHCl_3$) 3010, 1730, 1605, 1500, 1450, 1370, 1270, 1235, 1190, 1085, 1035, 960, 855 cm^{-1}; MS (dp) 415 (M), 397, 369, 366, 351, 291, 275, 274, 219, 201, 155, 129, 91 (100%). Anal. Calcd for $C_{23}H_{26}O_5S$: C, 66.64; H, 6.32. Found: C, 66.51, H, 6.41.

(*R*)-(*E*)-Diethyl 2-(3,4-Dimethoxybenzyl)-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (18). From diethyl (3,4-dimethoxybenzyl)malonate (**10**) (1.15 g, 3.71 mmol) in THF (60 mL), sodium hydride (89.0 mg, 3.71 mmol), and (*R*)-(+)-**3a** (909 mg, 3.71 mmol) in THF (15 mL), method A afforded **18** as a clear oil (1.73 g, 98%) after column chromatography (hexanes:ethyl acetate, 2:1): $[\alpha]^{25}_D$ = +95.1° (*c* 1.46, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.15–1.25 (m, 6H),

2.37 (s, 3H), 3.33 (s, 2H), 3.78 (s, 3H), 3.82 (s, 3H), 4.11–4.20 (m, 4H), 6.40 (d, 1H, J = 15.7 Hz), 6.55–6.69 (m, 3H), 6.82 (d, 1H, J = 15.7 Hz), 7.24 (d, 2H, J = 7.8 Hz), 7.39 (d, 2H, 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 21.3, 41.5, 56.1, 56.1, 60.3, 61.1, 62.0, 63.8, 111.9, 114.4, 122.7, 125.1, 127.7, 130.1, 134.5, 138.2, 140.9, 141.8, 148.8, 149.2, 169.0; IR ($CHCl_3$) 3010, 1730, 1595, 1515, 1465, 1445, 1370, 1030, 960, 860 cm^{-1}; MS (dp) 475 (M), 474, 335, 310, 261, 236, 215, 151 (100%). Anal. Calcd for $C_{25}H_{30}O_7S$: C, 63.27; H 6.37. Found: C, 63.05; H, 6.44.

(*R*)-(*E*)-Diethyl 2-[2-(3,4-Dimethoxyphenyl)ethyl]-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (19). From diethyl [2-(3,4-dimethoxyphenyl)ethyl]malonate (11) (798 mg, 2.46 mmol) in THF (30 mL), sodium hydride (59.0 mg, 2.46 mmol), and (*R*)-(+)-**3a** (603 mg, 2.46 mmol) in THF (30 mL), method A afforded **19** as a clear oil (933 mg, 78%) after column chromatography (hexanes:ethyl acetate, 3:1): $[\alpha]^{25}_D$ = +100.0° (*c* 4.13, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.18–1.25 (m, 6H), 2.14–2.47 (m, 4H), 2.37 (s, 3H), 3.82 (s, 6H), 4.14–4.23 (m, 4H), 6.47 (d, 1H, J = 15.7 Hz), 6.58–6.75 (m, 3H), 7.01 (d, 1H, J = 15.7 Hz), 7.28 (d, 2H, J = 8.0 Hz), 7.51 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 21.3, 30.2, 37.3, 55.8, 55.9, 59.3, 61.9, 111.4, 111.8, 120.1, 124.8, 130.0, 133.3, 133.4, 138.0, 140.3, 141.8, 147.5, 148.9, 168.8; IR ($CHCl_3$) 3000, 1730, 1595, 1515, 1465, 1420, 1370, 1260, 1155, 1080, 1025, 905, 855 cm^{-1}; MS (dp) 489 (M), 488, 443, 397, 307, 299, 230, 184, 164, 151 (100%). Anal. Calcd for $C_{26}H_{32}O_7S$: C, 63.91; H, 6.60. Found: C, 63.83; H, 6.58.

(*R*)-(*E*)-Diethyl 2-(3-methylbut-2-enyl)-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (20) was prepared from diethyl 2-(3-methylbut-2-enyl)malonate (**12**) (452 mg, 1.48 mmol) in THF (10 mL), sodium hydride (47.5 mg, 1.98 mmol), and (*R*)-(+)-**3a** (485 mg, 1.98 mmol) in THF (30 mL). Prior to purification, ^{1}H NMR indicated that a 15:1 mixture of (*E*) and (*Z*) isomers had been obtained (ratio determined by integration of the vinylic proton absorptions). Column chromatography (hexanes:ethyl acetate, 5:1) provided pure **20** as a clear oil (515 mg, 66%): $[\alpha]^{25}_D$ = +119.0° (*c* 2.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.15–1.21 (m, 6H), 1.50 (s, 3H), 1.58 (s, 3H), 2.36 (s, 3H), 2.73 (d, 2H, J = 7.3 Hz), 4.12–4.19 (m, 4H), 4.87 (br t, 1H, J = 7.3 Hz), 6.34 (d, 1H, J = 15.7 Hz), 6.89 (d, 1H, J = 15.7 Hz), 7.26 (d, 2H, J = 8.1 Hz), 7.45 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) 13.7, 17.7, 21.1, 25.5, 33.7, 59.3, 61.6, 63.5, 116.7, 124.7, 129.8, 133.8, 137.4, 140.0, 141.5, 168.7; IR ($CHCl_3$) 3010, 1710, 1420, 1360, 1090, 1040, 960, 930 cm^{-1}; MS (dp) 393 (M), 375, 307, 301, 230, 91, 69, 41 (100%). Anal. Calcd for $C_{21}H_{28}O_5S$: C, 64.26; H, 7.19. Found: C, 64.20; H, 7.13. **(*Z*)-isomer** (minor product): ^{1}H NMR ($CDCl_3$) δ 6.30 (d, 1H, J = 10.7 Hz), 6.55 (d, 1H, J = 10.7 Hz). (All other peaks were obscured by the absorptions of the major isomer; no further purification of the (*Z*)-isomer was attempted.)

(*S*)-(*E*)-Diethyl 2-(4-methylpent-3-enyl)-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (21) was prepared from diethyl 2-(4-methylpent-3-enyl)malonate (**13**) (1.20 g, 4.96 mmol) in THF (75 mL), sodium hydride (119 mg, 4.96 mmol), and (*S*)-(+)-**3c** (1.29 g, 4.96 mmol) in THF (20 mL), except that the sodiomalonate solution was recooled to 0 °C prior to addition of the THF solution of **3c**. Prior to purification, ^{1}H NMR indicated that a 8.6:1 mixture of (*E*)- and (*Z*)-isomers had been obtained (ratio determined by integration of the vinylic proton absorptions). Column chromatography (hexanes:ethyl acetate, 5:1) provided pure **21** as a light yellow oil (1.29 g, 64%): $[\alpha]^{25}_D$ = −154° (*c* 1.42, acetone); ^{1}H NMR ($CDCl_3$) δ 1.20–1.26 (m, 6H), 1.48 (s, 3H), 1.65 (s, 3H), 1.82–1.89 (m, 2H), 2.03–2.08 (m, 2H), 2.40 (s, 3H), 4.16–4.23 (m, 4H), 5.01 (br t, 1H, J = 7.1 Hz), 6.43 (d, 1H, J = 15.7 Hz), 6.99 (d, 1H, J = 15.7 Hz), 7.30 (d, 2H, J = 8.1 Hz), 7.50 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 13.7, 17.3, 21.1, 22.8, 25.3, 35.1, 59.1, 61.6, 61.6, 122.4, 124.6, 129.9, 132.6, 133.6, 137.6, 140.1, 141.6, 168.8; IR (neat) 1733, 1463, 1446, 1367, 1273, 1260, 1232, 1178, 1111, 1085, 1056, 1026, 1018, 962, 861, 810 cm^{-1}; MS (dp) 408, 407 (M), 406, 361, 315, 283, 267, 230, 209, 193, 184, 147, 119, 97, 91, 79, 69, 55, 41 (100%); HRMS calcd for $C_{22}H_{31}O_5S$ (M + 1) 407.1892, found 407.1891. **(*Z*)-isomer** (minor product; 150 mg, 7%): ^{1}H NMR ($CDCl_3$) 1.27 (t, 3H, J = 7.2 Hz), 1.31 (t, 3H, J = 7.2 Hz), 1.55 (s, 3H), 1.67 (s, 3H), 1.87–2.05 (m, 3H), 2.13–2.22 (m, 1H), 2.41 (s, 3H), 4.16–4.35 (m, 4H), 5.03–5.07 (m, 1H), 6.37 (d, 1H, J = 10.7 Hz), 6.70 (d, 1H, J = 10.7 Hz), 7.30 (d, 2H, J = 8.1 Hz), 7.56 (d, 2H, J = 8.1 Hz).

(*R*)-(*E*)-Diethyl 2-(but-3-enyl)-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (22) was prepared from diethyl 2-(but-3-enyl)-malonate (**14**) (34.9 mg, 0.163 mmol) in THF (4 mL), sodium hydride (60% dispersion in oil, 6.5 mg, 0.163 mmol), and (*R*)-(+)-**3a** (40.0 mg, 0.163 mmol) in THF (2 mL), except that the sodiomalonate solution was recooled to 0 °C prior to addition of the THF solution of **3c**. Prior to purification, ^{1}H NMR indicated that a 12.7:1 mixture of (*E*)- and (*Z*)-isomers had been obtained (ratio determined by integration of the vinylic proton absorptions). Column chromatography (petroleum ether:ethyl acetate, 9:1 to 5:1) provided pure **22** as a light yellow oil (43.6 mg, 70%): $[\alpha]^{25}_D$ = +128° (c 1.31, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 3H, J = 7.1 Hz), 1.23 (t, 3H, J = 7.0 Hz), 1.90–2.02 (m, 2H), 2.09–2.19 (m, 2H), 2.40 (s, 3H), 4.19 (q, 2H, J = 7.1 Hz), 4.20 (q, 2H, J = 7.1 Hz), 4.91–5.00 (AB of ABX system, 2H), 5.61–5.78 (X of ABX system, 1H), 6.43 (d, 1H, J = 15.6 Hz), 6.97 (d, 1H, J = 15.7 Hz), 7.30 (d, 2H, J = 8.4 Hz), 7.49 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.8, 21.3, 28.4, 34.4, 59.2, 61.9, 115.3, 124.9, 130.0, 133.6, 136.8, 137.9, 141.8, 168.9; IR (CCl_4) 2978, 2925, 2860, 1734, 1258, 1228, 1187, 1184, 1084, 1055, 785, 761 cm^{-1}. Anal Calcd for $C_{20}H_{28}O_5S$: C, 63.47; H, 6.92. Found: C, 63.09, H, 6.72.

(*S*)-(*E*)-Diethyl 2-(2-bromoprop-2-enyl)-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (23) was prepared from diethyl 2-(2-bromoprop-2-enyl)malonate (**15**) (1.36 g, 4.88 mmol) in THF (75 mL), sodium hydride (117 mg, 4.88 mmol), and (*S*)-(+)-**3c** (1.27 g, 4.88 mmol) in THF (20 mL). Prior to purification, ^{1}H NMR indicated that an 8.5:1 mixture of (*E*)- and (*Z*)-isomers had been obtained (ratio determined by integration of the vinylic proton absorptions). Column chromatography (hexanes:ethyl acetate, 5:1) provided pure **23** as a light yellow oil (1.47 g, 68%): $[\alpha]^{25}_D$ = −75.1° (*c* 2.59, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.23 (2 overlapping t, 6H, J = 7.1 Hz), 2.40 (s, 3H), 3.31 (s, 2H), 4.18–4.25 (m, 4H), 5.49 (d, 1H, J = 2.0 Hz), 5.52 (br d, 1H, J = 2.0 Hz), 6.47 (d, 1H, J = 15.7 Hz), 7.04 (d, 1H, J = 15.7 Hz), 7.30 (d, 2H, J = 8.0 Hz), 7.50 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) 13.8, 21.4, 46.2, 58.6, 62.4, 121.9, 125.0, 126.1, 130.0, 132.3, 138.7, 140.1, 141.9, 168.09; IR (neat) 1735, 1298, 1283, 1238, 1191, 1154, 1085, 1056, 620 cm^{-1}; MS (dp) 445 (M + 2), 443 (M), 399, 363, 347, 315, 275, 241, 203, 201, 173, 155, 143, 139, 123, 105, 95, 91, 77, 65 (100%); HRMS calcd for $C_{19}H_{24}{}^{79}BrO_5S$ (M + 1) 443.0528, found 443.0512. **(*Z*)-isomer** (minor product; 200 mg, light yellow oil, 8%): ^{1}H NMR ($CDCl_3$) δ 1.27 (t, 3H, J = 7.2 Hz), 1.33 (t, 3H, J = 7.2 Hz), 2.41 (s, 3H), 3.44 (dd, 1H, J = 15.1, 0.8 Hz), 3.67 (dd, 1H, J = 15.1, 0.7 Hz), 4.29–4.35 (m, 4H), 5.54 (d, 1H, J = 1.9 Hz), 5.64 (d, 1H, J = 1.9 Hz), 6.40 (d, 1H, J = 11.0 Hz), 6.83 (d, 1H, J = 11.0 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.56 (d, 2H, J = 8.2 Hz).

(*S*)-(*E*)-Diethyl 2-[2-(*p*-toluenesulfinyl)vinyl]-2-[3-(trimethylsilyl)prop-2-ynyl]malonate (24) was prepared from diethyl 2-[3-(trimethylsilyl)prop-2-ynyl]malonate (**16**) (2.29 g, 8.46 mmol) in THF (140 mL), sodium hydride (203 mg, 8.46 mmol), and (*S*)-(+)-**3c** (2.06 g, 8.46 mmol) in THF (35 mL). Column chromatography (hexanes:ethyl acetate, 5:1) provided pure **24** as a yellow oil (2.06 g, 56%): $[\alpha]^{25}_D$ = −158° (*c* 2.05, acetone); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9H), 1.23 (t, 3H, J = 7.1 Hz), 1.24 (t, 3H, J = 7.1 Hz), 2.38 (s, 3H), 2.96 (s, 2H), 4.16–4.27 (m, 4H), 6.52 (d, 1H, J = 15.6 Hz), 6.96 (d, 1H, J = 15.6 Hz), 7.28 (d, 2H, J = 7.9 Hz), 7.52 (d, 2H, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$) δ −0.3, 13.9, 21.3, 26.0, 59.0, 62.3, 62.4, 88.9, 100.2, 125.2, 130.1, 132.8, 138.2, 140.2, 141.8, 167.7, 167.8; IR (neat) 2181, 1738, 1300, 1276, 1249, 1190, 1086, 1054, 1028, 845 cm^{-1}; MS (dp) 435 (M + 1), 386, 361, 313, 275, 201, 195, 149, 123, 91, 77, 73 (100%), 65, 45; HRMS calcd for $C_{22}H_{30}O_5SiS$ 434.1583, found 434.1590.

Method B. (*R*)-(*Z*)-Diethyl 2-Benzyl-2-[2-(*p*-toluenesulfinyl)vinyl]malonate (25). To a solution of diethyl benzylmalonate (**9**) (28.1 mg, 0.113 mmol) in THF (5 mL) at −60 °C was added *n*-BuLi (1.6 M in hexanes, 0.064 mL, 0.102 mmol). After the solution was stirred for 10 min, a solution of (*R*)-(*Z*)-2-iodovinyl sulfoxide **4b** (30.0 mg, 0.102 mmol) in THF (5 mL) was added *via* cannula. The reaction mixture was allowed to warm to 0 °C and was stirred at that temperature for an additional 1.5 h. The reaction was stopped by addition of a saturated NH_4Cl solution (2 mL); the organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Column chromatography of the crude material (hexanes:ethyl acetate, 3:1) afforded **25** (20.4 mg, 63%)

as a clear oil: $[\alpha]^{25}_D = -140°$ (c 0.63, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.25 (t, 3H, J = 6.9 Hz), 1.31 (t, 3H, J = 7.0 Hz), 2.41 (s, 3H), 3.60 (AB quartet, 2H, J = 13.8 Hz), 4.17–4.32 (m, 4H), 6.35 (d, 1H, J = 11.0 Hz), 6.50 (d, 1H, J = 11.0 Hz), 7.05–7.10 (m, 2H), 7.20–7.26 (m, 3H), 7.32 (d, 2H, J = 8.2 Hz), 7.56 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.8, 13.9, 21.3, 42.8, 60.4, 62.4, 62.5, 124.7, 127.2, 128.2, 130.0, 130.1, 134.7, 136.2, 138.0, 140.6, 141.7, 169.0; IR (CCl_4) 3010, 1735, 1084, 1045, 792, 784, 759 cm^{-1}. Anal. Calcd for $C_{23}H_{26}O_5S$: C, 66.64; H, 6.32. Found: C, 66.69, H, 6.71.

(*R*)-(*Z*)-Diethyl 2-(but-3-enyl)-2-[2-(*p*-toluenesulfinyl)-vinyl]malonate (26) was prepared from diethyl 2-(but-3-enyl)-malonate (**14**) (32.1 mg, 0.150 mmol) in THF (6.5 mL), *n*-butyllithium (1.6 M in hexanes, 0.085 mL, 0.137 mmol), and (*R*)-(−)-**4b** (40.0 mg, 0.137 mmol) in THF (6.5 mL). Column chromatography (hexanes:ethyl acetate, 5:1) provided pure **26** as a light yellow oil (37.8 mg, 73%): $[\alpha]^{25}_D = -210°$ (c 1.46, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.27 (t, 3H, J = 7.1 Hz), 1.31 (t, 3H, J = 7.1 Hz), 1.96–2.17 (m, 2H), 2.19–2.54 (m, 2H), 2.40 (s, 3H), 4.22 (m, 4H), 4.96–5.08 (AB of ABX system, 2H), 5.66–5.86 (X of ABX system, 1H), 6.36 (d, 1H, J = 10.7 Hz), 6.67 (d, 1H, J = 10.7 Hz), 7.30 (d, 2H, J = 8.0 Hz), 7.56 (d, 2H, J = 8.1 Hz); ^{13}C NMR δ 13.8, 21.3, 28.6, 36.4, 59.2, 62.3, 62.4, 115.5, 124.6, 129.9, 135.7, 136.7, 138.6, 140.6, 141.5, 169.3; IR (CCl_4) 2981, 2932, 1735, 1259, 1190, 1084, 1045, 792, 761 cm^{-1}. Anal Calcd for $C_{20}H_{26}O_5S$: C, 63.47; H, 6.92. Found: C, 62.05, H, 6.64.

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