β-Sulfinyl α,*β*-Unsaturated Carbonyl Compounds from Enantiomerically Pure Sulfenic Acids

Maria C. Aversa,* Anna Barattucci, Paola Bonaccorsi,* Placido Giannetto, and Manuela Policicchio

Dipartimento di Chimica organica e biologica, Università degli Studi di Messina, Salita Sperone 31 (vill. S. Agata), 98166 Messina, Italy

aversa@imeuniv.unime.it

Received February 27, 2001

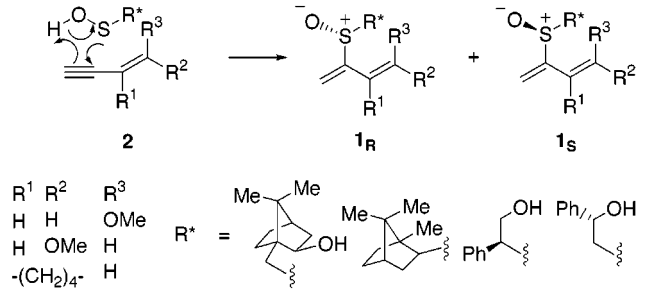
The addition of enantiopure sulfenic acids to oxoalkynes constitutes a new and efficient methodology for the synthesis of *β*-sulfinyl α,*β*-unsaturated carbonyl compounds. Sulfenic acids **3** and **4** were generated by thermolysis of suitable precursors and trapped in situ by oxoalkynes **5**, affording (R_S,*E*)- and (S_S,*E*)-3-alkylsulfinyl-1-phenyl-2-propen-1-ones, 4-alkylsulfinyl-3-buten-2-ones, and 3-[(1*S*)-isoborneol-10-sulfinyl]-2-propenoates **6** and **7** in good yields and in enantiomerically pure form after simple column chromathography. (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one (**6$_R$a**) was involved as a heterodiene in inverse-electron-demanding Diels−Alder reactions with readily available electron-rich dienophiles **14** and **15**, corroborating in each case the sulfinyl auxiliary capability in controlling the stereochemical outcome of these cycloadditions. Furthermore, the addition of methylmagnesium iodide to the carbonyl moiety of **6$_R$a** demonstrated that the chiral sulfur atom exerts a remote stereocontrol in this reaction if assisted by the hydroxy group being part of the isoborneol substituent.

Introduction

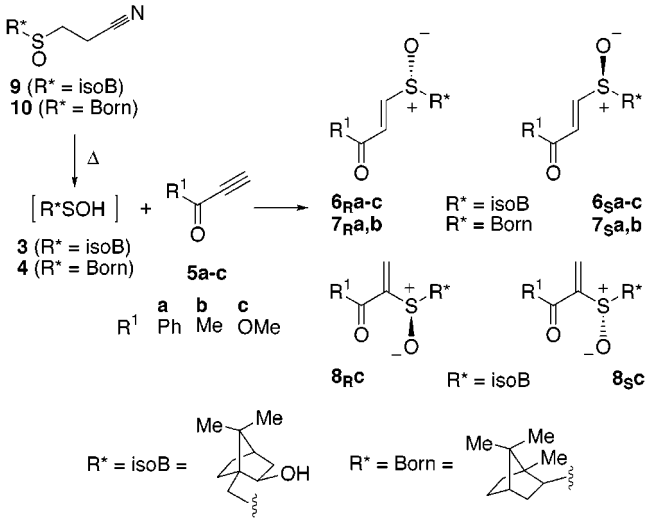
Although the addition of sulfenic acids to unsaturated bonds has been chiefly used for demonstrating the existence of such unstable species as intermediates in organic and biological processes,[1,2] some intrinsic synthetic features justify the interest devoted to this reaction; for instance, it allows easy introduction of a sulfinyl group into a suitably unsaturated substrate. The addition of sulfenic acids to alkenes or alkynes is a concerted reaction in which the nature of the unsaturated bond, on one hand, and the structural features of the sulfenic acid, on the other, play a relevant role, the former on the regioselectivity and the latter on the total yield of the addition, since stabilizing effects of the sulfenic acid structure, such as high steric demands and/or intramolecular hydrogen bonding, could prevent its self-condensation to give thiosulfinate.

Recently, we have reported the synthesis of enantiomerically pure alkylsulfinylbuta-1,3-dienes **1**, which was based on the site selective addition of chiral sulfenic acids R*SOH, generated in situ from suitable precursors, to the triple bond of enynes **2** (Scheme 1).[3] Dienes **1** have been obtained in good yield with high regio- and stereoselectivities. Accordingly, we envisaged that the addition of sulfenic acids, such as **3** and **4**, to the triple bond of compounds **5** (Scheme 2) would give an easy access to α,*β*-unsaturated carbonyl compounds bearing an enantiomerically pure *β*-sulfoxide moiety. Good stereocontrol in the formation of C−C bonds has been observed when the starting products combine the reactivity of the α,*β*-unsaturated carbonyl function with the capability of the

Scheme 1



Scheme 2



(1) Hogg, D. R. In *The chemistry of sulphenic acids and their derivatives*; Patai, S., Ed.; John Wiley & Sons: Chichester, 1990; pp 361−402.

(2) Van den Broek, L. A. G. M.; Delbressine, L. P. C.; Ottenheijm, H. C. J. In *The chemistry of sulphenic acids and their derivatives*; Patai, S., Ed.; John Wiley & Sons: Chichester, 1990; pp 701−721.

(3) (a) Aversa, M. C.; Barattucci,A.; Bonaccorsi, P.; Giannetto, P.; Jones, D. N. *J. Org. Chem.* **1997**, *62*, 4376−4384. (b) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P.; Nicolò, F. *J. Org. Chem.* **1999**, *64*, 2114−2118.

10.1021/jo015595a CCC: $20.00
Published on Web 06/19/2001

sulfinyl group as chiral auxiliary. In particular, nucleophilic additions of organometallic reagents to α-sulfinyl α,*β*-unsaturated carbonyl compounds have been extensively investigated, and it has been shown that the high level of stereocontrol observed in these reactions comes from a favored chelation of the metal atom to both the sulfinyl and carbonyl oxygen atoms.[4] α-Sulfinyl α,*β*-unsaturated carbonyl compounds have also given good stereochemical results when involved as either heterodienes[5] or dienophiles[6] in stereoselective Diels−Alder (DA) cycloadditions.

In this paper, we mainly describe a new method for the facile obtainment in high yields of enantiomerically pure *β*-sulfinyl α,*β*-unsaturated carbonyl compounds, which are potentially as useful substrates as the corresponding α-sulfinyl substituted products since they possess several reactive sites for nucleophilic and electrophilic attacks and can act as synthetic equivalents of acetylene dienophiles in DA reactions.[7] In addition, we discuss the results of reactions in which our enantiopure *β*-sulfinyl α,*β*-unsaturated ketones are involved as nucleophile acceptors and their use as heterodienes in concerted cycloadditions with electron-rich dienophiles.

Results and Discussion

Synthesis of the Enantiomerically Pure *β*-Sulfinyl α,*β*-Unsaturated Carbonyl Compounds 6−8. Sulfenic acids **3** and **4** were generated by thermolysis (toluene, 110 °C) of suitable precursors and trapped in situ by the oxoalkynes **5** (Scheme 2). Precursors of **3** and **4** were *β*-cyanosulfoxides **9** and **10**, synthesized from readily available members of the chiral pool.[3] 3-Butyn-2-one (**5b**) and methyl propiolate (**5c**) are commercially available, and 1-phenyl-2-propyn-1-one (**5a**) was easily obtained from 1-phenyl-2-propyn-1-ol.[8]

The addition of sulfenic acids **3** and **4** to oxoalkynes **5** gave sulfur epimeric mixtures of sulfinyl α,*β*-unsaturated carbonyl compounds **6**−**8**. The mixtures were separable by simple column chromatography, easily leading to enantiomerically pure compounds **6**, **7**, and $\mathbf{8_Rc}$. The ester $\mathbf{8_Sc}$ was obtained in too low yield to be isolated. Moderate to good diastereoselectivities have been observed in all the performed experiments. The sulfur configuration in the obtained products was assigned on the basis of previously observed stereochemical outcome of the sulfenic acid/enyne additions in the synthesis of alkyl sulfinyl butadienes **1**.[3,9] The obtained results are detailed in Table 1.

Table 1. Products Obtained from Addition of Sulfenic Acids 3 and 4 to Oxoalkynes 5 (Scheme 2)

R*SOH	$R^1C(O)C{\equiv}CH$	time (h)	total yield (%)	products (ratio)
3	**5a**	3	60	$\mathbf{6_Ra/6_Sa}$ (67:33)
3	**5b**	2	60	$\mathbf{6_Rb/6_Sb}$ (75:25)
3	**5c**	6.5	95	$\mathbf{6_Rc/6_Sc/8_Rc/8_Sc}$ (54:35:7:4)
4	**5a**	0.75	80	$\mathbf{7_Ra/7_Sa}$ (25:75)
4	**5b**	1	95	$\mathbf{7_Rb/7_Sb}$ (20:80)

The sterical requirements of the camphor skeleton in sulfenic acids **3** and **4** favor their addition to the triple bond of compounds **5** (see the Introduction), giving rise to the good to high yields observed in their reactions (Table 1). The isoborneol and bornyl residues, directly linked to the sulfinyl moiety, are structurally analogous: they essentially differ in the presence or absence of the hydroxy function that allows the formation of a stabilizing intramolecular hydrogen bonding with the sulfoxide oxygen atom. Some unexpected and undesired reactions of the hydroxy function previously observed[10] (see below) drove us to synthesize both isoborneol and bornyl *β*-sulfinyl α,*β*-unsaturated carbonyl compounds for studying their behavior in subsequent reactions.

The addition of intermediates **3** and **4** to the triple bond of 1-phenyl-2-propyn-1-one (**5a**) and 3-butyn-2-one (**5b**) was completely regioselective, leading to *β*-sulfinyl α,*β*-unsaturated ketones **6** or **7**. When methyl propiolate (**5c**) was involved in the reaction under study, α-sulfinyl α,*β*-unsaturated esters **8** were obtained together with *β*-sulfinyl enones **6**,[11] with the latter representing the major products of the reaction (Table 1).[12] This outcome is easily understood if one considers the regioselectivity of the addition sulfenic acid/unsaturated bond which is strictly related to the chemical nature of substituents linked to the reacting unsaturation.[13]

The results obtained (Table 1) prompted us to envisage the possibility of modulating the direction of attack of the sulfenic acid **3** to the triple bond of ynone **5a**. By transforming its carbonyl function into a dithioketal moiety showing a such reduced electron-withdrawing capacity, the formation of only α-sulfinyl α,*β*-unsaturated ketone derivatives may occur. We only partially succeeded in putting this idea into practice. When sulfenic acid **3** was reacted with the ethynyl dithioketal **11**[14] in toluene solution (Scheme 3), then equal amounts of the sulfur epimeric mixtures *of* *β*-sulfinyl and α-sulfinyl α,*β*-

(4) Posner, G. H.; Mallamo, J. P.; Hulce, M.; Frye, L. L. *J. Am. Chem. Soc.* **1982**, *104*, 4180−4185. Posner, G. H.; Switzer, C. *J. Am. Chem. Soc.* **1986**, *108*, 1239−1244. Posner, G. H.; Weitzberg, M.; Hamill, T. G.; Asirvatham, E.; Cun-Heng, H.; Clardy, J. *Tetrahedron* **1986**, *42*, 2919−2929. Posner, G. H. *Acc. Chem. Res.* **1987**, *20*, 72−78.

(5) Hayes, P.; Dujardin, G.; Maignan, C. *Tetrahedron Lett.* **1996**, *37*, 3687−3690. Hayes, P.; Maignan, C. *Tetrahedron*: *Asymmetry* **1999**, *10*, 1041−1050.

(6) García Ruano, J. L.; Carretero, J. C.; Carreño, M. C.; Martín Cabrejas, L. M.; Urbano, A. *Pure Appl. Chem.* **1996**, *68*, 925−930. Carretero, J. C.; García Ruano, J. L.; Martín Cabrejas, L. M. *Tetrahedron*: *Asymmetry* **1997**, *8*, 2215−2225.

(7) (a) Girodier, L. D.; Rouessac, F. P. *Tetrahedron*: *Asymmetry* **1994**, *5*, 1203−1206. (b) Arai, Y.; Suzuki, A.; Masuda, T.; Masaki, Y.; Shiro, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2913−2917. (c) Arai, Y.; Masuda, T.; Masaki, Y.; Shiro, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 759−762. (d) Solladié, G.; Carreño, M. C. In *Organosulphur Chemistry. Synthetic Aspects*; Page, P. C. B., Ed.; Academic Press: New York, 1995; Chapter 1, pp 1−47.

(8) Heasley, V. L.; Shellhamer, D. F.; Chappell, A. E.; Cox, J. M.; Hill, D. J.; McGovern, S. L.; Eden, C. C.; Kissel, C. L. *J. Org. Chem.* **1998**, *63*, 4433−4437.

(9) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P.; Nicolò, F.; Rizzo, S. *Tetrahedron*: *Asymmetry* **1999**, *10*, 3907−3917.

(10) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Bruno, G.; Giannetto, P.; Nicolò, F. *J. Chem. Soc., Perkin Trans. 2* **1997**, 273−277.

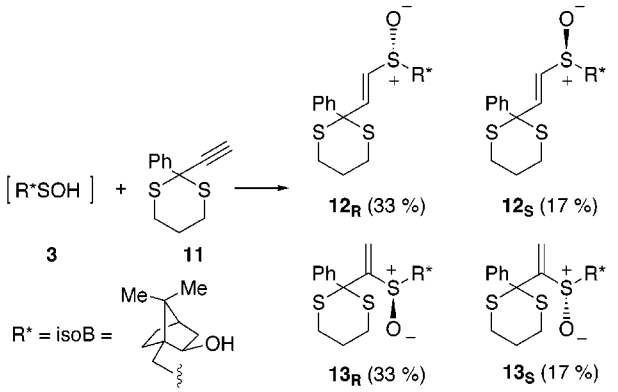
(11) (a) Davis, F. A.; Friedman, A. J.; Nadir, U.K. *J. Am. Chem. Soc.* **1978**, *100*, 2844−2852. (b) De Lucchi, O.; Lucchini, V.; Marchioro, C.; Valle, G.; Modena, G. *J. Org. Chem.* **1986**, *51*, 1457−1477, **1989**, *54*, 3245.

(12) Epimeric esters $\mathbf{6_Rc}$ and $\mathbf{6_Sc}$ had been previously synthesized (see ref 11b) by Michael addition of (1*S*)-10-mercaptoisoborneol onto methyl propiolate, followed by stereocontrolled *m*-CPBA oxidation of the sulfide. Our procedure appears to be less diastereoselective, but our yields are higher. Moreover, we obtain only (*E*)-isomers, owing to the stereospecific *cis*-addition of the sulfenic acid **3** onto the propiolate **5c**.

(13) Jones, D. N.; Cottam, P. D.; Davies, J. *Tetrahedron Lett.* **1979**, 4977−4980.

(14) We obtained in low yield the not yet known 2-ethynyl-2-phenyl-1,3-dithiane (**11**) [^{1}H NMR: δ 7.5−7.3 (m, ArH), 2.80 (m, H_2-4, 6), 2.75 (s, CH═), 2.05 (m, H_2-5)] by the reaction of commercial ethynylmagnesium bromide with in situ generated 2-chloro-2-phenyl-1,3-dithiane, following the synthetic strategy described by: Andersen, N. H.; Denniston, A. D.; McCrae, D. A. *J. Org. Chem.* **1982**, *47*, 1145−1146.

Scheme 3

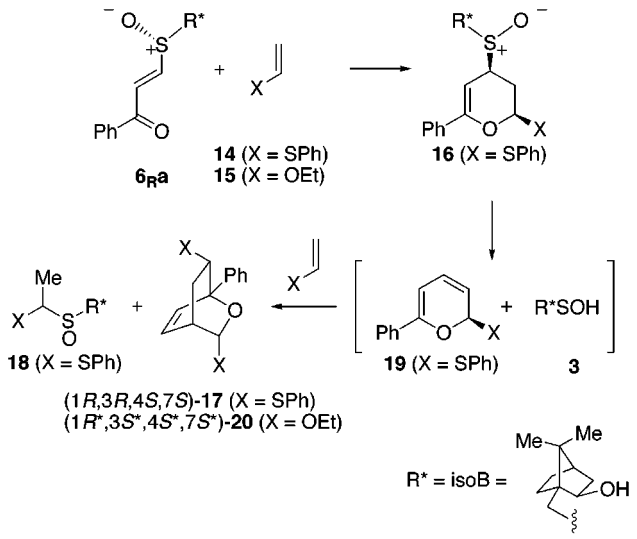


unsaturated dithioketals **12** and **13** were obtained. These could be further transformed into their corresponding α,β-unsaturated ketones. The mixture of compounds **12** and **13** was separated by column chromatography, and the products were identified by ^{1}H NMR spectroscopy[15] but were not fully characterized. This approach (Scheme 3) was of little use from a practical point of view, because α-sulfinyl **13** were formed together with β-sulfinyl derivatives **12**, and the literature reports several efficient methodologies for obtaining enantiomerically pure α-sulfinyl α,β-unsaturated ketones in moderate to good yields.[7d,16] On the contrary, to the best of our knowledge, no stereoselective syntheses of chiral acyclic β-sulfinyl α,β-unsaturated ketones such as **6** and **7** (Scheme 2) have been reported up to now.

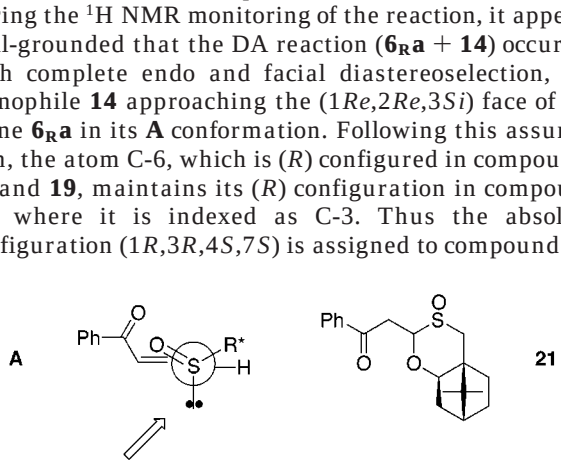
Asymmetric Diels−Alder Reactions of β-Sulfinyl α,β-Unsaturated Ketones with Electron-Rich Dienophiles. As part of our study on stereoselective DA reactions involving sulfinyl butadienes,[3,9,16b] we were interested in investigating the reactivity of enantiomerically pure β-sulfinyl α,β-unsaturated ketones in such cycloadditions. A considerable amount of work has been reported on their use as dienophiles.[7d] β-Sulfinyl α,β-unsaturated ketones can, in principle, however, act as heterodienes in inverse-electron-demanding DA reactions, giving a straightforward access to functionalized and enantiopure pyranoid systems.[17]

Readily available phenyl vinyl sulfide (**14**) and ethyl vinyl ether (**15**) were tested as electron-rich dienophiles toward (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one (**6$_R$a**) in several attempted experiments before obtaining the results depicted in Scheme 4.

Scheme 4



Reaction of **6$_R$a** with **14**, performed in refluxing 1,2-dichloroethane for 43 h, led to (4*S*,6*R*,R_S)-4-[(1*S*)-isoborneol-10-sulfinyl]-5,6-dihydro-2-phenyl-6-phenylthio-4*H*-pyran (**16**, 20% yield) as the only cycloadduct of the reaction among four possible diastereoisomers, together with (1*R*,3*R*,4*S*,7*S*)-2-oxa-1-phenyl-3,7-diphenylthiobicyclo-[2.2.2]oct-5-ene (**17**, 10% yield) and an almost 1:1 mixture of diastereomeric sulfoxides **18** (15% total yield). The fused compound **17** is the product of a second DA reaction of phenyl vinyl sulfide (**14**), used in large excess, onto the diene intermediate **19**, which was generated from **16** by elimination of (1*S*)-isoborneol-10-sulfenic acid (**3**) under the reaction conditions. The isolation of sulfoxides **18** confirmed the mechanistic pathway proposed in Scheme 4 since they are products of the trapping of sulfenic acid **3** by vinyl sulfide **14**. The structure and relative configuration of **17** are suggested on the basis of diagnostic ^{1}H NMR data, such as the resonance pattern of H_2-8, where both geminal protons are each coupled with two vicinal protons (H-4 and H-7). Moreover, the $J_{3,5}$ = 2.6 Hz is regarded as an indication of M (or W) relationship between the two protons involved. Taking into account the detection of only one cycloadduct in the reaction mixture, and its partial conversion to **17**, verified during the ^{1}H NMR monitoring of the reaction, it appears well-grounded that the DA reaction (**6$_R$a** + **14**) occurred with complete endo and facial diastereoselection, the dienophile **14** approaching the (1*Re*,2*Re*,3*Si*) face of the diene **6$_R$a** in its **A** conformation. Following this assumption, the atom C-6, which is (*R*) configured in compounds **16** and **19**, maintains its (*R*) configuration in compound **17**, where it is indexed as C-3. Thus the absolute configuration (1*R*,3*R*,4*S*,7*S*) is assigned to compound **17**.



When ethyl vinyl ether (**15**) was reacted with **6$_R$a**, only the condensed compound **20** was isolated in 15% yield.

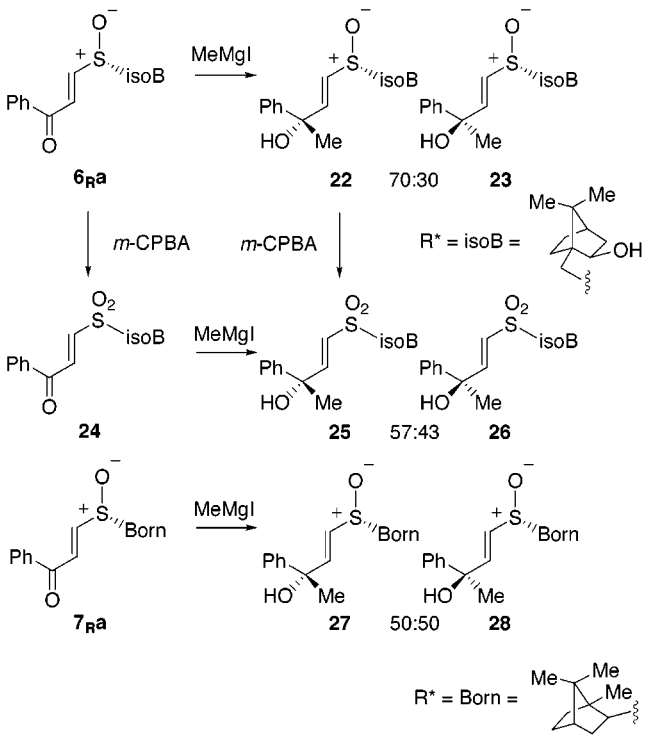
Long reaction times and moderate to low yields observed in these DA cycloadditions (Scheme 4) addressed

(15) Meaningful ^{1}H NMR parameters are as follow. (**R_S,*E*)-2-[2-[(1*S*)-isoborneol-10-sulfinyl]vinyl]-2-phenyl-1,3-dithiane (12$_R$)**: δ 7.09 (AB d, $J_{1'',2''}$ 14.7, H-2"), 6.19 (AB d, H-1′′), 4.09 (dd, $J_{2',3'}$ 7.7 and 3.1, H-2′), 3.26 and 2.42 (AB system, $J_{10'A,10'B}$ 13.2, H_2-10′), 1.10 (s, H_3-8′), 0.83 (s, H_3-9′). **(*S*$_S$,*E*)-2-[2-[(1*S*)-isoborneol-10-sulfinyl]-vinyl]-2-phenyl-1,3-dithiane (12$_S$)**: δ 7.00 (AB d, $J_{1'',2''}$ 14.7, H-2"), 6.20 (AB d, H-1′′), 4.05 (dd, $J_{2',3'}$ 7.7 and 3.5, H-2′), 3.33 and 2.52 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 1.12 (s, H_3-8′), 0.83 (s, H_3-9′). **(*R*$_S$)-2-[1-[(1*S*)-isoborneol-10-sulfinyl]vinyl]-2-phenyl-1,3-dithiane (13$_R$)**: δ 6.39 and 5.96 (split AB system, $J_{2''A,2''B}$ 1.5, H_2-2′′), 4.11 (dd, $J_{2',3'}$ 7.7 and 3.8, H-2′), 3.11 and 2.85 (AB system, $J_{10'A,10'B}$ 13.1, H_2-10′), 1.07 (s, H_3-8′), 0.84 (s, H_3-9′). **(*S*$_S$)-2-[1-[(1*S*)-isoborneol-10-sulfinyl]vinyl]-2-phenyl-1,3-dithiane (13$_S$)**: δ 6.47 and 6.03 (split AB system, $J_{2''A,2''B}$ 1.4, H_2-2′′), 4.09 (m, H-2′), 3.50 and 2.71 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 1.12 (s, H_3-8′), 0.83 (s, H_3-9′).

(16) (a) Alexandre, C.; Belkadi, O.; Maignan, C. *Synthesis* **1992**, 547−548. (b) Aranda, M. T.; Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Carreño, M. C.; Cid, M. B.; García Ruano, J. L. *Tetrahedron*: *Asymmetry* **2000**, *11*, 1217−1225.

(17) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Bruno, G.; Giannetto, P.; Panzalorto, M. *Tetrahedron*: *Asymmetry* **1997**, *8*, 2989−2995.

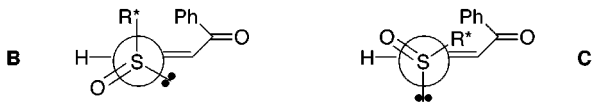
Scheme 5



our efforts toward the use of Lewis acid catalysis in the cycloaddition of (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one (**6_Ra**) with phenyl vinyl sulfide (**14**). The presence of Lewis acids ($LiClO_4$ suspended in CH_2Cl_2, $TiCl_4$, $ZnCl_2$, or $BF_3{\cdot}Et_2O$) favored in all cases polymerization of the dienophile **14**, decomposition of the *β*-sulfinyl α,*β*-unsaturated ketone **6_Ra**, and formation of diastereomeric mixtures of 2-oxa-4-thiatricycloundecane 4-oxides **21**, arising from intramolecular 1,4-conjugate addition of the isoborneol hydroxy function onto the α,*β*-unsaturated ketone moiety.[10,18] The reaction of (R_S,*E*)-3-[(1*S*-*exo*)-2-bornylsulfinyl]-1-phenyl-2-propen-1-one (**7_Ra**) with phenyl vinyl sulfide (**14**) resulted in extensive polymerization when performed in the presence of $LiClO_4$.

***β*-Sulfinyl α,*β*-Unsaturated Ketones as Nucleophile Acceptors in 1,2-Additions.** Freshly prepared methylmagnesium iodide (3.5 equiv) was added to (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one (**6_Ra**) at − 78 °C in diethyl ether. This reaction led to compounds **22** and **23** coming from the exclusive nucleophile 1,2-addition to the carbonyl moiety (Scheme 5). Epimers **22** and **23** were obtained in a 70:30 ratio and are separable by column chromatography. Although a number of reports demonstrated that a chiral sulfoxide substituent can control diastereofacial selectivity in nucleophile additions, the facial discrimination observed in our addition could not be easily explained by the presence of the sulfinyl chiral auxiliary, which was far away from the reactive site. A highly diastereoselective 1,4-conjugate addition of organoaluminum reagents to α-sulfinyl α,*β*-unsaturated carbonyl compounds was recently reported[19] where a hydroxy group in the substrate assisted the organoaluminum reagent in the nucleophile transfer. Following the idea that some kind of assistance could be analogously exerted by the hydroxy function of the isoborneol sulfinyl moiety in the ketone **6_Ra**, we decided to react methylmagnesium iodide with (R_S,*E*)-3-[(1*S*-*exo*)-2-bornylsulfinyl]-1-phenyl-2-propen-1-one (**7_Ra**) under the same conditions as the first experiment. The lack of diastereoselectivity observed in this 1,2-addition (Scheme 5) indicated that the hydroxy group in the skeleton of the chiral auxiliary was responsible for the facial diastereoselection observed when **6_Ra** underwent the nucleophilic addition. Methylmagnesium iodide was also reacted with (*E*)-3-[(1*S*)-isoborneol-10-sulfonyl]-1-phenyl-2-propen-1-one (**24**), readily prepared by *m*-CPBA oxidation of the corresponding sulfinyl propenone **6_Ra**, and the addition gave compounds **25** and **26** in almost equal amounts (Scheme 5). Thus, the stereogenic sulfur appears to be essential in the promotion of a significant facial discrimination during the nucleophilic addition onto the carbonyl moiety. Sulfone **25** was also obtained by oxidizing the sulfoxide **22**.

These results provided the basis for a tentative rationalization of the stereochemical outcome of the addition (MeMgI + **6_Ra**). The observed diastereoselection can be explained taking into account different conformations of the *β*-sulfinyl α,*β*-unsaturated ketone **6_Ra** around the C(3)−S bond. Conformations **B** and **C** can be regarded



as almost equally populated and favored among others, owing to (i) the s-trans arrangement of the SO bond with respect to the vicinal unsaturation, a feature often observed in compounds possessing the vinylsulfoxide moiety,[3b,20] (ii) the isoborneol residue in close proximity to the carbonyl function, so allowing magnesium interaction with both carbonyl and isoborneol oxygen atoms, as depicted in Figure 1 for **6_Ra** in its **B** conformation. In this chelated conformation, the nucleophile approachs the substrate from the less sterically congested *Re* face, whereas, in the **C** conformation, the position and structural features of the isoborneol group could allow magnesium/oxygen atoms interactions in both sides with respect to the sulfinyl α,*β*-unsaturated carbonyl plane, so eluding any kind of diastereotopic differentiation. Recently, Node et al.[21] described an asymmetric *tandem* Michael addition/Meerwein−Pondorf−Verley reduction

(18) $TiCl_4$ (0.4 equiv) was added to a solution of (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one (**6_Ra**) (1 equiv) and phenyl vinyl sulfide (**14**) (2 equiv) in CH_2Cl_2 at − 20 °C. After spontaneous reaching of the room temperature and stirring for 7 days under argon, the solvent was removed in a vacuum and the mixture chromatographed on silica gel (petrol/ethyl acetate 99: 1 as eluant), giving (1*R*,4*R*,6*S*,9*R*)-11,11-dimethyl-2-oxa-3-benzoylmethyl-4-thiatricyclo[6.2.1.$0^{1,6}$]undecane 4-oxides **21A** and **21B** in enantiomerically pure forms. Here, some meaningful ^{1}H NMR parameters are reported. **21A**, more mobile C-3 epimer, 15% yield: *δ* 4.80 (dd, $J_{1'A,\,3}$ 7.0, $J_{1'B,\,3}$ 5.0, H-3), 3.58 (dd, $J_{1,\,10}$ 7.8 and 3.2, H-1), 3.26 (AB dd, $J_{1'A,\,1'B}$ 13.6, H_A-1′), 3.07 (AB d, $J_{5A,\,5B}$ 14.1, H_A-5), 3.17 (AB dd, H_B-1′), 2.75 (AB d, H_B-5), 1.31 (s, H_3-12), 0.91 (s, H_3-13). **21B**, less mobile C-3 epimer, 20% yield: *δ* 5.32 (dd, $J_{1'A,\,3}$ 7.5, $J_{1'B,\,3}$ 4.4, H-3), 3.67 (dd, $J_{1,\,10}$ 7.9 and 3.3, H-1), 3.50 (AB dd, $J_{1'A,\,1'B}$ 16.5, H_A-1′), 3.18 (AB d, $J_{5A,\,5B}$ 14.2, H_A-5), 3.15 (AB dd, H_B-1′), 2.75 (AB d, H_B-5), 1.32 (s, H_3-12), 0.91 (s, H_3-13).

(19) Carreño, M. C.; Pérez González, M.; Ribagorda M. *J. Org. Chem*. **1996**, *61*, 6758−6759.

(20) Adams, H.; Bailey, N. A.; Jones, D. N.; Aversa, M. C.; Bonaccorsi, P.; Giannetto, P. *Acta Crystallogr*. **1995**, *C51*, 1357−1359. Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Bonini, B. F.; Giannetto, P.; Nicolò, F. *Tetrahedron*: *Asymmetry* **1999**, *10*, 3919−3929.

(21) Node, M.; Nishide, K.; Shigeta, Y.; Shiraki, H.; Obata, K. *J. Am. Chem. Soc.* **2000**, *122*, 1927−1936.

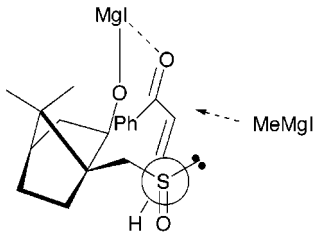
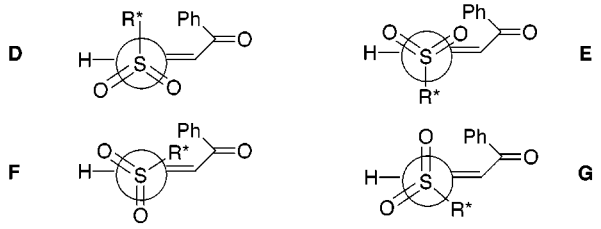


Figure 1. Nucleophilic approach of MeMgI to the chelated **B** conformation of $\mathbf{6_Ra}$.

of α,β-unsaturated ketones via the formation of a chelated adduct that highly resembles the one depicted in Figure 1. When the sulfone **24** undergoes nucleophilic attack from Grignard reagent, four conformations **D**−**G** have to be regarded as almost equally populated, that is **D** and **E** analogous to **B**, and **F** and **G** analogous to **C**. Following the previously discussed rationale, **F** and **G** allow magnesium/oxygen atom interactions in both sides with respect to the sulfinyl α,β-unsaturated carbonyl plane (no tangible diastereoselection), and if **D** offers the less sterically congested *Re* face to the nucleophilic approach, the equally populated conformation **E** suffers the attack from the *Si* face of the carbonyl plane (again no tangible diastereoselection).



Conclusions

Enantiopure alkanesulfenic acids can fulfill a relevant role in the stereoselective synthesis of usable sulfinyl substituted substrates: in this paper, we have described an easy access to β-sulfinyl α,β-unsaturated carbonyl compounds by their addition to ynones. The pericyclic mechanism of the reaction guarantees good stereochemical control. The structural nature of the sulfenic acids allows the obtainment in high yields of products easily separable by column chromatography in enantiopure form.

The synthesized β-sulfinyl α,β-unsaturated ketones have shown their low capability as heterodienes in inverse-electron-demanding DA reactions, but the sulfinyl group has appeared once again as a very good chiral auxiliary in controlling the stereochemical outcome of these cycloadditions. Moreover, the unsaturated substrates **6** and **7** have confirmed their expected value as nucleophile acceptors giving useful stereochemical results in 1,2-addition of Grignard reagents: the chiral sulfur atom exerts a remote stereocontrol if assisted by the hydroxy group being part of the isoborneol substituent. Further, β-sulfinyl α,β-unsaturated ketones with similar structural characteristics could be prepared from readily available starting products, such as enantiopure methyl mandelate (Scheme 1).[3a]

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions with TMS as internal standard; *J* values are given in Hz; the assignments are supported by attached proton test (APT) and homodecoupling experiments. Protons and carbon nuclei, marked with (′), pertain to isoborneol or bornyl moieties, but to benzoylmethyl substituent for compounds **21** only. The symbol (″) identifies aromatic nuclei in compounds **6**−**8** and vinyl nuclei in compounds **12** and **13**. Mass spectra were measured by FAB (*m*-nitrobenzyl alcohol as matrix). Optical rotations were measured in $CHCl_3$ solutions. All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254), and the products were visualized with acidic vanillin solution. Silica gel 60, 230−400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 30−40 °C. Elemental analyses were performed by REDOX, Milano, Italy.

Sulfinyl Esters and Ketones 6−8. General Procedure. A solution of the carbonyl compound **5** (4.5 mmol) and sulfoxides **9** or **10** (3 mmol) in toluene (5 mL) was maintained at reflux temperature. When the reaction appeared complete by TLC, the solvent was removed under reduced pressure and the reaction mixture was separated by column chromatography. Some experimental details are reported in Table 1. The relative amounts of the products obtained were evaluated by ^{1}H NMR.

Reaction of 1-Phenyl-2-propyn-1-one[8] (5a) with 3-[(1*S*)-Isoborneol-10-sulfinyl]propanenitriles 9.[3a] The following epimers were obtained by elution with petrol containing ethyl acetate (10−15%) and are reported in order of elution from the column.

(R_S,*E*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one ($\mathbf{6_Ra}$): oil; 40% yield; $[\alpha]^{23}_D$ −101.4 (*c* 0.015); ^{1}H NMR δ 8.10 (m, H-2″,6″), 7.83 (AB d, $J_{2,3}$ 14.5, H-3), 7.74 (AB d, $J_{2,3}$ 14.5, H-2), 7.7−7.5 (m, H-3″-5″), 4.17 (dd, $J_{2',3'}$ 7.9 and 4.2, H-2′), 3.31 and 2.67 (AB system, $J_{10'A,10'B}$ 13.3, H_2-10′), 1.9−1.6 (m, H_2-3′,5′,6′, H-4′), 1.10 (s, H_3-8′), 0.87 (s, H_3-9′); ^{13}C NMR δ 186.9 (C-1), 149.0 (C-3), 136.5 (C-1″), 134.0 (C-2), 129.0 and 128.9 (C-2″-6″), 77.3 (C-2′), 55.2 (C-10′), 51.6 (C-1′), 48.5 (C-7′), 45.1 (C-4′), 38.6 (C-3′), 30.8 and 27.1 (C-5′,6′), 20.5 and 19.8 (C-8′,9′). Anal. Calcd for $C_{19}H_{24}O_3S$: C, 68.64; H, 7.28. Found: C, 68.32; H, 7.30.

(S_S,*E*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-phenyl-2-propen-1-one ($\mathbf{6_Sa}$): oil; 20% yield; ^{1}H NMR δ 8.10 (m, H-2″,6″), 7.84 and 7.82 (AB system, $J_{2,3}$ 14.6, H-2,3), 7.7−7.5 (m, H-3″-5″), 4.10 (dd, $J_{2',3'}$ 7.8 and 3.7, H-2′), 3.58 and 2.67 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 1.9−1.6 (m, H_2-3′,5′,6′, H-4′), 1.14 (s, H_3-8′), 0.86 (s, H_3-9′); ^{13}C NMR δ 186.7 (C-1), 149.9 (C-3), 136.5 (C-1″), 133.0 (C-2), 129.0 and 128.9 (C-2″-6″), 76.4 (C-2′), 53.1 (C-10′), 52.8 (C-1′), 49.3 (C-7′), 44.8 (C-4′), 39.9 (C-3′), 29.7 and 27.5 (C-5′,6′), 20.5 and 20.1 (C-8′,9′). Anal. Calcd for $C_{19}H_{24}O_3S$: C, 68.64; H, 7.28. Found: C, 68.74; H, 7.21.

Reaction of 5a with 3-[(1*S*-*exo*)-2-Bornylsulfinyl]propanenitriles 10.[3b] The following epimers were obtained by elution with petrol/ethyl acetate 95:5 and are reported in order of elution from the column.

(R_S,*E*)-3-[(1*S*-*exo*)-2-Bornylsulfinyl]-1-phenyl-2-propen-1-one ($\mathbf{7_Ra}$): oil; 20% yield; ^{1}H NMR δ 8.05 (m, H-2″,6″), 7.73 (AB d, $J_{2,3}$ 14.5, H-3), 7.69 (AB d, $J_{2,3}$ 14.5, H-2), 7.6−7.5 (m, H-3″-5″), 2.81 (dd, $J_{2',3'}$ 9.4 and 6.6, H-2′), 2.3−1.2 (m, H_2-3′,5′,6′, H-4′), 1.17 (s, H_3-10′), 1.05 (s, H_3-8′), 0.90 (s, H_3-9′); ^{13}C NMR δ 187.1 (C-1), 150.7 (C-3), 136.6 (C-1″), 133.7 (C-2), 128.9, 128.8, 127.9 (C-2″-6″), 70.7 (C-2′), 50.2 (C-1′), 47.4 (C-7′), 45.1 (C-4′), 39.0 and 27.2 (C-5′,6′), 28.1 (C-3′), 20.2 and 19.8 (C-8′,9′), 13.5 (C-10′). Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.11; H, 7.64. Found: C, 72.13; H, 7.60.

(S_S,*E*)-3-[(1*S*-*exo*)-2-Bornylsulfinyl]-1-phenyl-2-propen-1-one ($\mathbf{7_Sa}$): oil; 60% yield; ^{1}H NMR δ 8.06 (m, H-2″,6″), 7.83 (AB d, $J_{2,3}$ 14.5, H-3), 7.80 (AB d, $J_{2,3}$ 14.5, H-2), 7.6−7.5 (m, H-3″-5″), 2.81 (dd, $J_{2',3'}$ 9.2 and 6.8, H-2′), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.28 (s, H_3-10′), 1.05 (s, H_3-8′), 0.93 (s, H_3-9′); ^{13}C NMR δ 187.1 (C-1), 148.3 (C-3), 136.5 (C-1″), 133.8 (C-2), 129.3, 128.9, 128.8 (C-2″-6″), 73.1 (C-2′), 50.0 (C-1′), 47.7 (C-7′), 44.8 (C-4′), 38.7 and 26.7 (C-5′,6′), 31.5 (C-3′), 20.1 and 19.4 (C-8′,9′), 13.6 (C-10′). Anal. Calcd for $C_{19}H_{24}O_2S$: C, 72.11; H, 7.64. Found: C, 72.00; H, 7.34.

Reaction of 3-Butyn-2-one (5b) with 9. The following epimers were obtained by elution with petrol/$CHCl_3$ 50:50 and are reported in order of elution from the column.

(R_S,*E*)-4-[(1*S*)-Isoborneol-10-sulfinyl]-3-buten-2-one (6_Rb): oil; 45% yield; ^{1}H NMR δ 7.47 (AB d, $J_{3,4}$ 14.9, H-4), 6.97 (AB d, $J_{3,4}$ 14.9, H-3), 4.12 (dd, $J_{2',3'}$ 7.7 and 3.6, H-2′), 3.27 and 2.59 (AB system, $J_{10'A,10'B}$ 13.2, H_2-10′), 2.39 (s, H_3-1), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.09 (s, H_3-8′), 0.85 (s, H_3-9′); ^{13}C NMR δ 194.5 (C-2), 147.4 (C-4), 132.1 (C-3), 77.2 (C-2′), 55.0 (C-10′), 51.6 (C-1′), 48.5 (C-7′), 45.1 (C-4′), 38.5 (C-3′), 30.7 and 27.1 (C-5′,6′), 29.7 (C-1), 20.5 and 19.8 (C-8′,9′); MS *m*/*z* 271 (M + 1, 33), 149 (92), 135 (100), 55 (87). Anal. Calcd for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20. Found: C, 62.12; H, 8.30.

(S_S,*E*)-4-[(1*S*)-Isoborneol-10-sulfinyl]-3-buten-2-one (6_Sb): oil; 15% yield; ^{1}H NMR δ 7.56 (AB d, $J_{3,4}$ 15.0, H-4), 6.95 (AB d, $J_{3,4}$ 15.0, H-3), 4.06 (dd, $J_{2',3'}$ 7.4 and 3.6, H-2′), 3.51 and 2.60 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 2.39 (s, H_3-1), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.12 (s, H_3-8′), 0.85 (s, H_3-9′); ^{13}C NMR δ 194.5 (C-2), 148.4 (C-4), 132.1 (C-3), 76.4 (C-2′), 53.1 (C-10′), 52.6 (C-1′), 49.2 (C-7′), 44.7 (C-4′), 40.1 (C-3′), 31.8 and 27.5 (C-5′,6′), 29.6 (C-1), 20.4 and 20.1 (C-8′,9′); MS *m*/*z* 271 (M + 1, 29), 149 (55), 135 (56), 55 (100). Anal. Calcd for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20. Found: C, 61.81; H, 8.25.

Reaction of 5b with 10. The following epimers were obtained by elution with petrol/Et_2O 70:30 and are reported in order of elution from the column.

(R_S,*E*)-4-[(1*S*-*exo*)-2-Bornylsulfinyl]-3-buten-2-one (7_Rb): oil; 19% yield; ^{1}H NMR δ 7.43 (AB d, $J_{3,4}$ 14.8, H-4), 6.88 (AB d, $J_{3,4}$ 14.8, H-3), 2.74 (dd, $J_{2',3'}$ 9.4 and 6.6, H-2′), 2.36 (s, H_3-1), 2.3−1.2 (m, H_2-3′,5′,6′, H-4′), 1.13 (s, H_3-10′), 1.01 (s, H_3-8′), 0.89 (s, H_3-9′); ^{13}C NMR δ 194.8 (C-2), 149.0 (C-4), 131.5 (C-3), 70.7 (C-2′), 50.2 (C-1′), 47.3 (C-7′), 45.1 (C-4′), 39.0 and 28.0 (C-5′,6′), 29.7 (C-1), 27.1 (C-3′), 20.2 and 19.7 (C-8′,9′), 13.5 (C-10′); MS *m*/*z* 255 (M + 1, 4), 149 (5), 137 (100), 81 (66), 55 (40). Anal. Calcd for $C_{14}H_{22}O_2S$: C, 66.11; H, 8.72. Found: C, 66.07; H, 8.65.

(S_S,*E*)-4-[(1*S*-*exo*)-2-Bornylsulfinyl]-3-buten-2-one (7_Sb): oil; 76% yield; ^{1}H NMR δ 7.55 (AB d, $J_{3,4}$ 14.9, H-4), 6.94 (AB d, $J_{3,4}$ 14.9, H-3), 2.74 (dd, $J_{2',3'}$ 9.0 and 6.8, H-2′), 2.36 (s, H_3-1), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.25 (s, H_3-10′), 1.02 (s, H_3-8′), 0.92 (s, H_3-9′); ^{13}C NMR δ 194.9 (C-2), 147.5 (C-4), 132.5 (C-3), 73.1 (C-2′), 50.0 (C-1′), 47.7 (C-7′), 44.9 (C-4′), 38.8 and 26.8 (C-5′,6′), 31.5 (C-3′), 29.7 (C-1), 20.1 and 19.4 (C-8′,9′), 13.7 (C-10′); MS *m*/*z* 255 (M + 1, 4), 149 (4), 137 (100), 81 (78), 55 (52). Anal. Calcd for $C_{14}H_{22}O_2S$: C, 66.11; H, 8.72. Found: C, 66.32; H, 8.75.

Reaction of Methyl Propiolate (5c) with 9. The following products were obtained by elution with petrol containing ethyl acetate (10−20%) and are reported in order of elution from the column.

Methyl (R_S)-2-[(1*S*)-isoborneol-10-sulfinyl]-2-propenoate (8_Rc): oil; 6% yield; ^{1}H NMR δ 6.96 and 6.70 (AB system, $J_{3A,3B}$ 0.4, H_2-3), 4.14 (split dd, $J_{2',3'}$ 7.9 and 3.7, H-2′), 3.87 (s, OMe), 3.00 and 2.98 (AB system, $J_{10'A,10'B}$ 12.8, H_2-10′), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.06 (s, H_3-8′), 0.83 (s, H_3-9′). Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.72; H, 7.75. Found: C, 58.67; H, 7.80.

Methyl (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-2-propenoate (6_Rc): oil; 51% yield; $[\alpha]^{22}_D$ −107.6 (*c* 0.008); ^{1}H NMR δ 7.64 (AB d, $J_{2,3}$ 14.9, H-3), 6.71 (AB d, $J_{2,3}$ 14.9, H-2), 4.11 (dd, $J_{2',3'}$ 8.0 and 4.3, H-2′), 3.83 (s, OMe), 3.27 and 2.59 (AB system, $J_{10'A,10'B}$ 13.1, H_2-10′), 1.9−1.2 (m, H_2-3′,5′,6′, H-4′), 1.08 (s, H_3-8′), 0.85 (s, H_3-9′); ^{13}C NMR δ 164.2 (C-1), 149.7 (C-3), 125.9 (C-2), 77.0 (C-2′), 55.0 (C-10′), 52.5 (OMe), 51.6 (C-1′), 48.5 (C-7′), 45.1 (C-4′), 38.6 (C-3′), 30.8 and 27.2 (C-5′,6′), 20.5 and 19.9 (C-8′,9′); MS *m*/*z* 287 (M + 1, 59), 137 (68), 135 (100). Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.72; H, 7.75. Found: C, 58.62; H, 7.74.

Methyl (S_S)-2-[(1*S*)-isoborneol-10-sulfinyl]-2-propenoate (8_Sc), only picked out in the reaction mixture by typical ^{1}H NMR signals, i.e., δ 6.97 and 6.72 (two br s, H_2-3).

Methyl (S_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-2-propenoate (6_Sc): oil; 33% yield; $[\alpha]^{22}_D$ +75.2 (*c* 0.011); ^{1}H NMR δ 7.72 (AB d, $J_{2,3}$ 15.0, H-3), 6.68 (AB d, $J_{2,3}$ 15.0, H-2), 4.07 (dd, $J_{2',3'}$ 7.6 and 3.7, H-2′), 3.83 (s, OMe), 3.51 and 2.59 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 1.8−1.1 (m, H_2-3′,5′,6′, H-4′), 1.11 (s, H_3-8′), 0.84 (s, H_3-9′); ^{13}C NMR δ 164.2 (C-1), 150.5 (C-3), 125.6 (C-2), 76.3 (C-2′), 53.0 and 52.6 (C-1′,10′), 52.3 (OMe), 49.2 (C-7′), 44.7 (C-4′), 40.0 (C-3′), 31.7 and 27.5 (C-5′,6′), 20.4 and 20.1 (C-8′,9′). Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.72; H, 7.75. Found: C, 58.71; H, 7.63.

Reaction of 6_Ra with Phenyl Vinyl Sulfide (14). A solution of heterodiene **6_Ra** (100 mg, 0.3 mmol) and dienophile **14** (0.24 mL, 1.8 mmol) in 1,2-dichloroethane (2.5 mL) was maintained at reflux temperature. When the reaction appeared complete by TLC (after 43 h), the solvent was removed under reduced pressure and the reaction mixture was separated by column chromatography, eluting with petrol containing 15−20% ethyl acetate. The isolated products are reported in order of elution from the column.

1-[(1*S*)-Isoborneol-10-sulfinyl]ethyl phenyl sulfides (18) (about equal amounts of two diastereomers): oil; 15% yield; ^{1}H NMR δ 7.5−7.3 (m, ArH), 4.21 (q) and 3.96 (q) (J_{vic} 7.3, H-1), 4.04 (dd, $J_{2',3'}$ 8.1 and 3.9, H-2′), 3.07 and 2.68, and 2.96 and 2.89 (two AB systems, $J_{10'A,10'B}$ 12.7, H_2-10′), 1.8−1.4 (m, H_2-3′,5′,6′, H-4′), 1.70 (d) and 1.63 (d) (J_{vic} 7.3, H_3-2), 1.11 (s) and 1.01 (s) (H_3-8′), 0.85 (s) and 0.74 (s) (H_3-9′). Anal. Calcd for $C_{18}H_{26}O_2S_2$: C, 63.88; H, 7.75. Found: C, 63.95; H, 7.65.

(1*R*,3*R*,4*S*,7*S*)-2-Oxa-1-phenyl-3,7-diphenylthiobicyclo-[2.2.2]oct-5-ene (17): oil; 10% yield; ^{1}H NMR δ 7.9−7.3 (m, ArH), 6.02 (AB ddd, $J_{3,5}$ 2.6, $J_{4,5}$ 3.7, $J_{5,6}$ 10.0, H-5), 5.73 (AB ddd, $J_{4,6}$ 0.9, $J_{6,7}$ 3.2, H-6), 4.4−4.2 (m, H-3,4), 4.00 (ddd, $J_{7,8A(trans)}$ 6.0, $J_{7,8B(cis)}$ 9.2, H-7), 2.20 (AB ddd, $J_{4,8A}$ 3.5, $J_{8A,8B}$ 13.7, H_A-8), 2.08 (AB ddd $J_{4,8B}$ 4.6, H_B-8). Anal. Calcd for $C_{25}H_{22}OS_2$: C, 74.61; H, 5.51. Found: C, 74.32; H, 5.61.

(4*S*,6*R*,R_S)-4-[(1*S*)-Isoborneol-10-sulfinyl]-5,6-dihydro-2-phenyl-6-phenylthio-4*H*-pyran (16): oil; 20% yield; ^{1}H NMR δ 7.6−7.2 (m, ArH and H-3), 5.65 (dd, $J_{5,6}$ 7.1 and 3.2, H-6), 3.98 (dd, $J_{2',3'}$ 8.1 and 4.2, H-2′), 3.63 and 2.35 (AB system, $J_{10'A,10'B}$ 13.0, H_2-10′), 3.4−1.4 (m, H_2-3′,5,5′,6′, H-4,4′), 1.12 (s, H_3-8′), 0.83 (s, H_3-9′); MS *m*/*z* 469 (M + 1, 11), 189 (10), 161 (21), 159 (47), 154 (100), 123 (42), 77 (26), 55 (16). Anal. Calcd for $C_{27}H_{32}O_3S_2$: C, 69.20; H, 6.89. Found: C, 69.42; H, 6.50.

(1*S,3*R**,4*R**,7*R**)-3,7-Diethoxy-2-oxa-1-phenylbicyclo-[2.2.2]oct-5-ene (20).** A solution of heterodiene **6_Ra** (70 mg, 0.21 mmol) and ethyl vinyl ether (**15**) *(*0.12 mL, 1.26 mmol) in CH_2Cl_2 (2.5 mL) was maintained at reflux temperature. When the reaction appeared complete by TLC (after 12 days), the solvent was removed under reduced pressure and the reaction mixture purified by column chromatography. Elution with petrol/ethyl acetate 88:12 afforded compound **20** (15% yield) as an oil: ^{1}H NMR δ 8.1−7.5 (m, ArH), 5.98 (AB ddd, $J_{3,5}$ 2.7, $J_{4,5}$ 3.9, $J_{5,6}$ 9.9, H-5), 5.67 (AB ddd, $J_{4,6}$ 0.9, $J_{6,7}$ 3.9, H-6), 4.4−4.1 (m, H-3,4,7), 3.63 and 3.41 (m, OCH_2), 2.16 (AB ddd, $J_{4,8A}$ 3.3, $J_{7,8A(trans)}$ 4.4, $J_{8A,8B}$ 13.5, H_A-8), 1.97 (AB ddd $J_{4,8B}$ 4.6, $J_{7,8B(cis)}$ 9.3, H_B-8), 1.10 (t, J_{vic} 7.0, Me). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.41; H, 8.09. Found: C, 74.56; H, 8.00.

Reaction of 6_Ra with Methylmagnesium Iodide. MeMgI (4 mmol in 3.5 mL of anhydrous Et_2O), freshly prepared[22] and titrated with salicylaldehyde phenylhydrazone,[23] was added dropwise at − 78 °C to a solution of **6_Ra** (380 mg, 1.15 mmol) in anhydrous Et_2O (3.5 mL), maintained under stirring and argon atmosphere. The reaction mixture was slowly brought to room temperature (over ca. 1 h), and a saturated solution of NaH_2PO_4 (4 mL) was added. The crude product was extracted with Et_2O (3 × 3 mL) and the combined organic layers were dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave an oily residue which was purified by column chromatography eluting with petrol/ethyl acetate 80:20. The isolated (R_S,*E*)-4-[(1*S*)-isoborneol-10-sulfinyl]-2-phenyl-3-buten-2-ols (70% total yield, **22/23** 70:30) are reported in order of elution from the column.

(*S*,R_S,*E*)-4-[(1*S*)-Isoborneol-10-sulfinyl]-2-phenyl-3-buten-2-ol (22): oil; 49% yield; $[\alpha]^{22}_D$ - 100.8 (*c* 0.002); ^{1}H NMR δ 7.5−7.3 (m, ArH), 6.75 (AB d, $J_{3,4}$ 14.7, H-4), 6.58 (AB d, $J_{3,4}$

(22) Kruse, C. G.; Wijsman, A.; van der Gen, A. *J. Org. Chem.* **1979**, *44*, 1847−1851.

(23) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755−3756.

14.7, H-3), 4.08 (dd, $J_{2',3'}$ 8.0 and 4.3, H-2′), 3.19 and 2.44 (AB system, $J_{10'A,10'B}$ 13.2, H_2-10′), 1.8−1.1 (m, H_2-3′,5′,6′, H-4′), 1.74 (s, H_3-1), 1.08 (s, H_3-8′), 0.83 (s, H_3-9′); ^{13}C NMR δ 145.2 (C-4), 145.0 (C-1"), 130.7 (C-3), 128.9, 127.9, and 125.3 (C-2"-6"), 77.2 (C-2′), 74.8 (C-2), 55.6 (C-10′), 51.7 (C-1′), 48.4 (C-7′), 45.3 (C-4′), 38.7 (C-3′), 31.0 and 27.4 (C-5′,6′), 30.0 (C-1), 20.7 and 20.1 (C-8′,9′). Anal. Calcd for $C_{20}H_{28}O_3S$: C, 68.93; H, 8.10. Found: C, 68.62; H, 8.30.

(*R*,*R*$_S$,*E*)-4-[(1*S*)-Isoborneol-10-sulfinyl]-2-phenyl-3-buten-2-ol (23): oil; 21% yield; ^{1}H NMR δ 7.5−7.3 (m, ArH), 6.74 (AB d, $J_{3,4}$ 14.7, H-4), 6.62 (AB d, $J_{3,4}$ 14.7, H-3), 4.12 (dd, $J_{2',3'}$ 8.1 and 4.1, H-2′), 3.23 and 2.47 (AB system, $J_{10'A,10'B}$ 13.3, H_2-10′), 1.8−1.1 (m, H_2-3′,5′,6′, H-4′), 1.79 (s, H_3-1), 1.12 (s, H_3-8′), 0.85 (s, H_3-9′). Anal. Calcd for $C_{20}H_{28}O_3S$: C, 68.93; H, 8.10. Found: C, 69.00; H, 8.45.

(*S*,*R*$_S$,*E*)- and (*R*,*R*$_S$,*E*)-4-[(1*S*-*exo*)-2-Bornylsulfinyl]-2-phenyl-3-buten-2-ols (27) and (28). A solution of **7$_R$a** (200 mg, 0.63 mmol) in Et_2O (1.4 mL) was reacted with 0.76 mmol of MeMgI in Et_2O (0.63 mL) following the procedure reported above. Compounds **27** and **28** were isolated (75% total yield, **27/28** 50:50) by elution with petrol containing ethyl acetate (20 to 25%). More mobile epimer: oil; 37% yield; ^{1}H NMR δ 7.5−7.3 (m, ArH), 6.67 (AB d, $J_{3,4}$ 14.9, H-4), 6.49 (AB d, $J_{3,4}$ 14.9, H-3), 2.62 (dd, $J_{2',3'}$ 9.6 and 6.5, H-2′), 2.3−1.2 (m, H_2-3′,5′,6′, H-4′), 1.73 (s, H_3-1), 1.04 (s, H_3-10′), 1.00 (s, H_3-8′), 0.87 (s, H_3-9′); ^{13}C NMR δ 145.0 (C-1"), 144.0 (C-4), 131.8 (C-3), 128.5, 127.5, and 125.1 (C-2″-6″), 74.6 (C-2), 71.1 (C-2′), 49.9 (C-1′), 47.4 (C-7′), 39.2 and 27.3 (C-5′,6′), 29.6 (C-1), 28.5 (C-3′), 20.2 and 19.9 (C-8′,9′), 13.7 (C-10′). Anal. Calcd for $C_{20}H_{28}O_2S$: C, 72.25; H, 8.50. Found: C, 72.27; H, 8.88. Less mobile epimer: oil; 37% yield; ^{1}H NMR δ 7.5−7.3 (m, ArH), 6.66 (AB d, $J_{3,4}$ 14.8, H-4), 6.50 (AB d, $J_{3,4}$ 14.8, H-3), 2.65 (dd, $J_{2',3'}$ 9.3 and 6.7, H-2′), 2.4−1.2 (m, H_2-3′,5′,6′, H-4′), 1.73 (s, H_3-1), 1.01 (s, H_3-10′), 1.00 (s, H_3-8′), 0.87 (s, H_3-9′); ^{13}C NMR δ 145.0 (C-1"), 144.0 (C-4), 131.6 (C-3), 128.5, 127.5, and 125.0 (C-2″-6″), 74.7 (C-2), 71.0 (C-2′), 49.8 (C-1′), 47.4 (C-7′), 39.1 and 27.3 (C-5′,6′), 29.7 (C-1), 28.4 (C-3′), 20.2 and 19.9 (C-8′,9′), 13.7 (C-10′). Anal. Calcd for $C_{20}H_{28}O_2S$: C, 72.25; H, 8.50. Found: C, 71.98; H, 8.41.

***m*-CPBA Oxidation of 6$_R$a and Reaction of the Obtained (*E*)-3-[(1*S*)-Isoborneol-10-sulfonyl]-1-phenyl-2-propen-1-one (24) with Methylmagnesium Iodide.** The sulfone **24** was obtained in almost quantitative yield by *m*-CPBA oxidation of sulfoxide **6$_R$a**, following the previously reported procedure,[3a] and submitted, without isolation,[24] to nucleophile addition: thus, a solution of **24** (178 mg, 0.51 mmol) in Et_2O (1.5 mL) was reacted with 1.22 mmol of MeMgI in Et_2O (1 mL) following the procedure reported above. The elution of the chromatographic column with petrol/ethyl acetate 90:10 afforded (*E*)-4-[(1*S*)-isoborneol-10-sulfonyl]-2-phenyl-3-buten-2-ols (50% total yield, **25/26** 57:43) which are reported in order of elution from the column.

(*S*,*E*)-4-[(1*S*)-Isoborneol-10-sulfonyl]-2-phenyl-3-buten-2-ol (25): low melting solid; 28% yield; $[\alpha]^{24}_D$ - 65.8 (*c* 0.047); ^{1}H NMR δ 7.5−7.3 (m, ArH), 7.11 (AB d, $J_{3,4}$ 14.8, H-4), 6.75 (AB d, $J_{3,4}$ 14.8, H-3), 4.13 (m, H-2′), 3.41 and 2.86 (AB system, $J_{10'A,10'B}$ 13.6, H_2-10′), 1.8−1.3 (m, H_2-3′,5′,6′, H-4′), 1.79 (s, H_3-1), 1.07 (s, H_3-8′), 0.82 (s, H_3-9′): ^{13}C NMR δ 152.5 (C-4), 143.4 (C-1″), 128.8, 128.0, and 125.0 (C-2"-6"), 127.3 (C-3), 76.2 (C-2′), 74.1 (C-2), 54.2 (C-10′), 50.7 (C-1′), 49.1 (C-7′), 44.1 (C-4′), 39.0 (C-3′), 30.7 and 27.4 (C-5′,6′), 28.9 (C-1), 20.5 and 19.8 (C-8′,9′). Anal. Calcd for $C_{20}H_{28}O_4S$: C, 65.90; H, 7.75. Found: C, 66.22; H, 7.81. The same product was obtained by *m*-CPBA oxidation of sulfoxide **22**.[3a]

(*R*,*E*)-4-[(1*S*)-Isoborneol-10-sulfonyl]-2-phenyl-3-buten-2-ol (26): low melting solid; 21% yield; ^{1}H NMR δ 7.5−7.3 (m, ArH), 7.10 (AB d, $J_{3,4}$ 14.8, H-4), 6.74 (AB d, $J_{3,4}$ 14.8, H-3), 4.13 (m, H-2′), 3.43 and 2.85 (AB system, $J_{10'A,10'B}$ 14.1, H_2-10′), 1.8−1.3 (m, H_2-3′,5′,6′, H-4′), 1.79 (s, H_3-1), 1.07 (s, H_3-8′), 0.80 (s, H_3-9′). Anal. Calcd for $C_{20}H_{28}O_4S$: C, 65.90; H, 7.75. Found: C, 65.85; H, 7.81.

Acknowledgment. This work was carried out under the auspices of the National Project "Stereoselezione in Sintesi Organica, Metodologie ed Applicazioni" supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome. Financial support from the University of Messina is also acknowledged.

JO015595A

(24) ^{1}H NMR characterization of sulfone **24**: δ 8.02 (m, H-2″, 6″), 7.93 (AB d, $J_{2,3}$ 14.9, H-3), 7.44 (AB d, H-2), 7.7−7.5 (m, H-3″-5″), 4.19 (dd, $J_{2',3'}$ 7.9 and 4.2, H-2′), 3.56 and 2.98 (AB system, $J_{10'A,10'B}$ 13.6, H_2-10′), 1.9−1.2 (m, H_2-3′, 5′, 6′, H-4′), 1.09 (s, H_3-8′), 0.85 (s, H_3-9′).