Synthesis and Asymmetric Diels−Alder Reactions of Enantiopure 3-(Alkylsulfinyl)-1-methoxy-1,3-butadienes

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

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

David Neville Jones

Department of Chemistry, University of Sheffield, Dainton Building, Brook Hill, Sheffield S3 7HF, U.K.

Received December 9, 1996[⊗]

Simple syntheses of enantiopure (*E*)- and (*Z*)-3-(alkylsulfinyl)-1-methoxy-1,3-butadienes **2** and **3** were provided by the addition of (1*S*)-isoborneol-10-sulfenic and (*S*)-phenyl-2-hydroxyethanesulfenic acids **8** to (*E*)- and (*Z*)-1-methoxybut-1-en-3-ynes (**9**) and (**10**). These additions proceeded with asymmetric induction, the extent of which depended upon the nature of the chiral hydroxyalkyl group. Cycloadditions of methyl acrylate to the enantiopure dienes proceeded with complete regioselectivity and very high stereoselectivity when catalyzed by lithium perchlorate or zinc chloride in dichloromethane. The chirality at sulfur controlled the diastereofacial selectivity in these Diels−Alder cycloadditions.

Introduction

The combination of Diels−Alder (DA) reaction with asymmetric induction exerted by sulfoxides represents a very powerful method for C−C bond formation in a stereocontrolled manner. The notable optical activity, the ease of convertibility into different functional groups, the clean removal under mild conditions, and the existence of several efficient methods of obtaining enantiopure sulfoxides[1] make them versatile auxiliaries in one of the most effective reactions for the synthesis of six-membered rings.

Since the first pioneering work in 1983,[2] enantiopure vinyl sulfoxides have been commonly employed as dienophiles in DA reactions. Their use often results in high levels of regio- and stereoselectivity.[3] Enantiopure diene sulfoxides have received little attention, presumably owing to difficulties in their preparation. Since our preliminary accounts of the synthesis of enantiopure 2-sulfinyl dienes[4] and their use in asymmetric DA reactions,[4b,5] other methods for the construction of enantiopure sulfinyl dienes have been devised,[6] but information about their participation in cycloadditions remains scarce. García Ruano and co-workers have described asymmetric DA cycloadditions of enantiopure 1-(*p*-tolylsulfinyl)-1,3-butadienes,[7] in which the reactivity of the diene was diminished by the presence of the sulfoxide group.[1c] Maignan[8] reported one experiment only, which involved reaction of (E,R_S)-2-(*p*-tolylsulfinyl)-1,3-pentadiene with maleimide under very mild conditions to afford a single, enantiomerically pure adduct. Finally, Yang and co-workers[6g] reported good yields and high diastereomeric excesses in the DA reactions of *N*-phenylmaleimide with 2-sulfinylbutadienes, which, because of their instability, were generated *in situ* by thermolysis of 4-sulfinyl-3-sulfolenes.

We now provide details of our methods for the construction of enantiopure 3-(alkylsulfinyl)-1-methoxy-1,3-dienes from enantiopure hydroxythiols and the participation of these dienes in cycloadditions with methyl acrylate. Camphorsulfonic acid and mandelic acid, which are readily available members of the "chiral pool", provided the precursors for the hydroxythiols, which were chosen because we expected that the contiguity of the hydroxy and sulfur functions in their derivatives would facilitate the chromatographic separation of diastereoisomers and enhance diastereoface selection in pericyclic processes. Further, we expected the augmenting directing effects of the methoxy and sulfinyl groups to maximize the regioselectivity of the cycloadditions.

* To whom correspondence should be addressed. Phone: +39-90-6765165-6765190. Fax: +39-90-393895. E-mail: aversa@imeuniv.unime.it.

[⊗] Abstract published in *Advance ACS Abstracts,* May 15, 1997.

(1) Reviews: (a) Solladié, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, pp 148−157. (b) Walker, A. J. *Tetrahedron: Asymmetry* **1992**, *3*, 961−998. (c) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760.

(2) Maignan, C.; Raphael, R. A. *Tetrahedron* **1983**, *39*, 3245−3249.

(3) (a) De Lucchi, O.; Lucchini, V.; Marchioro, C.; Valle, G.; Modena, G. *J. Org. Chem.* **1986**, *51*, 1457−1466. (b) Arai, Y.; Matsui, M.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 1983−1985. (c) Ronan, B.; Kagan, H. B. *Tetrahedron Asymmetry* **1992**, *3*, 115−122. (d) Carreño, M. C.; García Ruano, J. L.; Urbano, A. *J. Org. Chem.* **1992**, *57*, 6870−6876. (e) Alonso, I.; Carretero, J. C.; García Ruano, J. L. *J. Org. Chem.* **1993**, *58*, 3231−3232. (f) Fuji, K.; Tanaka, K.; Abe, H.; Matsumoto, K.; Harayama, T.; Ikeda, A.; Taga, T.; Miwa, Y.; Node, M. *J. Org. Chem.* **1994**, *59*, 2211−2218. (g) Yang, T.; Chen, C.; Lee, D.; Jong, T.; Jiang, Y.; Mi, A. *Tetrahedron: Asymmetry* **1996**, *7*, 57−60.

(4) (a) Aversa, M. C.; Bonaccorsi, P.; Giannetto, P.; Jafari, S. M. A.; Jones, D. N. *Tetrahedron: Asymmetry* **1992**, *3*, 701−704. (b) Aversa, M. C.; Bonaccorsi, P.; Giannetto, P.; Jones, D. N. *Tetrahedron: Asymmetry* **1994**, *5*, 805−808.

(5) Adams, H.; Jones, D. N.; Aversa, M. C.; Bonaccorsi, P.; Giannetto, P. *Tetrahedron Lett.* **1993**, *34*, 6481−6484.

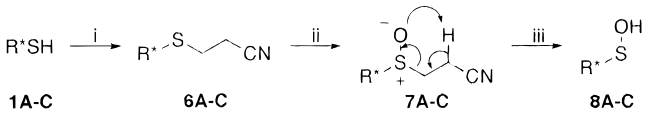
(6) (a) Bonfand, E.; Gosselin, P.; Maignan, C. *Tetrahedron Lett.* **1992**, *33*, 2347−2348. (b) Solladié, G.; Maugein, N.; Morreno, I.; Almario, A.; Carreño, M.C.; García Ruano, J. L. *Tetrahedron Lett.* **1992**, *33*, 4561−4562. (c) Girodier, L.; Maignan, C.; Rouessac, F. *Tetrahedron: Asymmetry* **1992**, *3*, 857−858. (d) Bonfand, E.; Gosselin, P.; Maignan, C. *Tetrahedron: Asymmetry* **1993**, *4*, 1667−1676. (e) Paley, R. S.; de Dios, A.; Fernández de la Pradilla, R. *Tetrahedron Lett.* **1993**, *34*, 2429−2432. (f) Paley, R. S.; Lafontaine, J. A.; Ventura, M. P. *Tetrahedron Lett.* **1993**, *34*, 3663−3666. (g) Yang, T.; Chu, H.; Lee, D.; Jiang, Y.; Chou, T. *Tetrahedron Lett.* **1996**, *37*, 4537−4540.

(7) (a) Arce, E.; Carreño, M. C.; Cid, M. B.; García Ruano, J. L. *J. Org. Chem.* **1994**, *59*, 3421−3426. (b) Carreño, M. C.; Cid, M. B.; Colobert, F.; García Ruano, J. L.; Solladié, G. *Tetrahedron: Asymmetry* **1994**, *5*, 1439−1442.

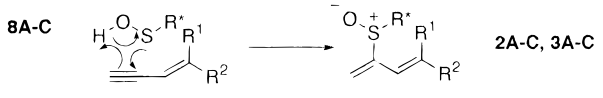
(8) Gosselin, P.; Bonfand, E.; Hayes, P.; Retoux, R.; Maignan, C. *Tetrahedron: Asymmetry* **1994**, *5*, 781−784.

S0022-3263(96)02286-4 CCC: $14.00

Scheme 1



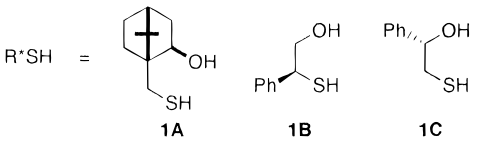
Reagents: i, CH_2=CHCN, THF, Triton B, - 78 up to 0°C; ii, *m*-CPBA, CH_2Cl_2, 0°C; iii, heat



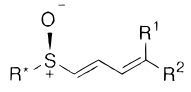
9 R^1 = H R^2 = OMe
10 R^1 = OMe R^2 = H

Results and Discussion

Synthesis of Chiral Dienes. The syntheses of 1-methoxy-3-(alkylsulfinyl)-1,3-butadienes **2A**−**C** and **3A**−**C**, based on the regioselective addition of sulfenic acids to enynes,[9] proceeded in four steps, commencing with the base-catalyzed addition of hydroxy thiols **1A**−**C** to acrylonitrile, followed by oxidation of the adducts **6A**−**C** with *m*-CPBA to give sulfoxides **7A**−**C** (Scheme 1). These



$2A_R$	R^1 = H	R^2 = OMe	$2A_S$
$3A_R$	R^1 = OMe	R^2 = H	$3A_S$
$2B_R$	R^1 = H	R^2 = OMe	$2B_S$
$3B_R$	R^1 = OMe	R^2 = H	$3B_S$
$2C_R$	R^1 = H	R^2 = OMe	$2C_S$
$3C_R$	R^1 = OMe	R^2 = H	$3C_S$

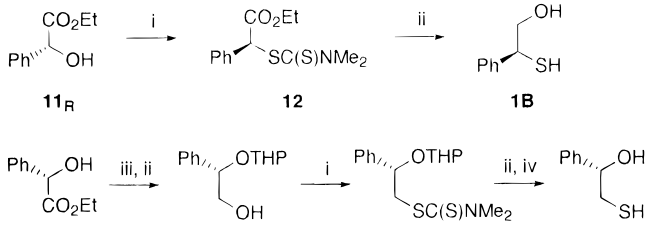


$4A_R$	R^1 = H	R^2 = OMe
$5A_R$	R^1 = OMe	R^2 = H

were thermolyzed in the presence of the appropriate enynes **9** or **10** to generate transiently the corresponding sulfenic acids **8A**−**C**, which were trapped by the enynes to provide the required 1-methoxy-3-(alkylsulfinyl)-1,3-butadienes. The final cycloadditions were almost completely regioselective, but small amounts (ca. 1%) of the dienes $\mathbf{4A_R}$ and $\mathbf{5A_R}$ were featured among the products of reaction of **8A** with the methoxyenynes **9** and **10**, respectively.

(9) Bell, R.; Cottam, P. D.; Davies, J.; Jones, D. N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2106−2115.

Scheme 2[a]



[a] Reagents: (i) $Zn[SC(S)NMe_2]_2$, DEAD, Ph_3P; (ii) DHP, PPTS; (iv) EtOH, PPTS.

10-Mercaptoisoborneol (**1A**) was chosen as a convenient chiral auxiliary because of its availability in both enantiomeric forms, its well-assessed preparation from commercially available 10-camphorsulfonic acid,[10] and the expected crystallinity of 10-camphorsulfonic derivatives.

2-Hydroxy-1-phenylethanethiol (**1B**) and 2-hydroxy-2-phenylethanethiol (**1C**) were exploited as chiral control elements since chiral auxiliaries derived from these vicinal hydroxy thiols potentially may be removed by phenyloxiran formation.[11] Moreover, we decided to compare the behavior of the structural isomers **1B** and **1C**, in order to evaluate whether the position of the asymmetric carbon with regard to sulfur atom had any effect on the asymmetric induction. Ethyl mandelate, commercially available in both enantiomeric forms, was employed as starting material for the preparation of thiols **1B** and **1C** (Scheme 2). Hydroxy thiol **1B** was obtained from ethyl (*R*)-mandelate ($\mathbf{11_R}$) using a modification of the Mitsunobu reaction, devised by Rollin, which occurs with complete inversion of configuration,[12] followed by $LiAlH_4$ reduction. Hydroxy thiol **1C** was obtained from ethyl (*S*)-mandelate ($\mathbf{11_S}$) in 70% overall yield, by protection of the hydroxy group, reduction of the ester function, followed by Mitsunobu−Rollin reaction on the phenylethanol **13**, reduction of dithiocarbamate **14**, and deprotection. (*S*)-2-Mercapto-1-phenylethanol (**1C**) was also prepared from commercially available (*S*)-phenyloxirane by the shorter but less efficient Lalancette and Frêche procedure (30% yield overall in our hands).[13] The longer procedure (Scheme 2) was also more convenient because the two optically pure phenyloxiranes are both more expensive than the optically pure ethyl mandelates.

None of the reactions in Scheme 2 was attended by detectable racemization despite the presence of potentially sensitive benzylic centers. The optical purity of hydroxy thiols **1B,C** was checked by ^{1}H NMR analysis using the chiral shift reagent $Eu(tfc)_3$ in CD_3CN, which was the solvent of choice,[14] because experiments in $CDCl_3$ failed owing to extensive broadening of signals.

Oxidation of the cyano hydroxy sulfide **6A** with *m*-CPBA (Scheme 1) proceeded diastereoselectively to give a 28:1 mixture of sulfoxides **7A** epimeric at sulfur. These were easily separated by chromatography on silica gel, but the mixture was used for the next step, since both epimers furnish the same sulfenic acid **8A** on thermolysis.

(10) Eliel, E. L.; Frazee, W. J. *J. Org. Chem.* **1979**, *44*, 3598−3599.
(11) Solladié-Cavallo, A.; Adib, A. *Tetrahedron* **1992**, *48*, 2453−2464.
(12) Rollin, P. *Tetrahedron Lett.* **1986**, *27*, 4169−4170.
(13) Lalancette, J. M.; Frêche, A. *Can. J. Chem.* **1971**, *49*, 4047−4053.
(14) Sweeting, L. M.; Crans, D. C.; Whitesides, G. M. *J. Org. Chem.* **1981**, *52*, 2273−2276.

Table 1. Chiral Sulfinyl dienes 2 and 3 from Addition of Sulfenic Acids 8 to Enynes 9 and 10

entry	sulfoxides	enynes	solvent[a]	time/min	products (yield %)
1	7A	9	xylenes	60	**2A$_R$** (60), **2A$_S$** (10)
2	7A	10	xylenes	30	**3A$_R$** (63), **3A$_S$** (14)
3	7B	9	toluene	45	**2B$_R$** (12), **2B$_S$** (33)
4	7B	10	toluene	45	**3B$_R$** (10), **3B$_S$** (30)
5	7C	9	toluene	45	**2C$_R$** and **2C$_S$** (25[b])
6	7C	10	toluene	45	**3C$_R$** and **3C$_S$** (25[b])

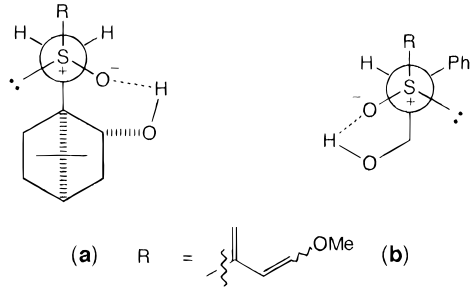
[a] At its bp. [b] Combined yield.

The isomeric cyano hydroxy sulfides **6B,C** behaved very differently on oxidation with *m*-CPBA, **6B** giving only one cyano hydroxy sulfoxide **7B**, whereas **6C** gave a 1:1 mixture of epimeric sulfoxides **7C** that were very difficult to separate by chromatography.[15]

Sulfenic acids are generally too instable to be isolated and consequently generated *in situ* by thermolysis of suitable sulfoxides. For this purpose, we chose cyano hydroxy sulfoxides **7** because they were stable up to 80 °C but decomposed cleanly on further warming. The cyano hydroxy sulfoxide **7A** thermolyzed at a convenient rate in boiling xylene (140 °C), whereas **7B,C** did so in boiling toluene (110 °C). Thermolysis of **7**, in the presence of enynes **9** or **10** in the appropriate boiling solvents, provided the sulfinyl dienes **2** and **3**. Reaction conditions and results are collected in Table 1.

Each of the sulfinyl dienes **2** and **3** were formed as mixtures epimeric at sulfur. For the sulfinyl dienes **2A,B** and **3A,B**, the epimers were readily separated by chromatography on silica gel, the major isomers **2A$_R$**, **3A$_R$**, **2B$_S$**, and **3B$_S$** being more mobile than their respective minor isomers **2A$_S$**, **3A$_S$**, **2B$_R$**, and **3B$_R$**. By contrast, the epimeric sulfinyl dienes **2C$_R$** and **2C$_S$** were formed in approximately equal amounts and were chromatographically almost identical, so separation was too difficult to be practicable on a preparatively useful scale. The sulfinyl dienes **3C$_R$** and **3C$_S$** shared these characteristics.

Assignments of configuration. The configuration of **2A$_R$** was assigned as (R_S) on the basis of X-ray crystallographic analysis of its cycloadduct **15A$_R$** with methyl acrylate (see later), a result that strengthened our confidence in assigning the configurations of hydroxy sulfoxides **2A,B** and **3A,B** on the basis of their chromatographic behavior. The more mobile epimers **2A$_R$** and **3A$_R$** were initially allocated the (R_S) configuration and the more mobile epimers **2B$_S$** and **3B$_S$** the (S_S) configuration.[4] This followed from the recognition that sulfoxides form strong intramolecular hydrogen bonds with suitably oriented contiguous hydroxy groups,[16] a phenomenon that is associated with enhanced chromatographic mobility by virtue of the consequent reduction in the effective polarity of the sulfoxide group. Models reveal that the (R_S) isomers **2A$_R$** and **3A$_R$** can readily adopt an unhindered conformation (**a**) that involves intramolecular hydrogen bonding, whereas for the (S_S) isomers **2A$_S$** and **3A$_S$** intramolecular hydrogen bonding requires the adoption of a less favorable conformation (as **a**, but with R and the sulfur lone electron pair interchanged). For the hydroxysulfinyl dienes **2B$_S$** and **3B$_S$** the preferred hydrogen-bonded conformation was considered to be **b**, which led to the assignment of the (S_S) configuration to sulfur, whereas for the corresponding (R_S) isomers **2B$_R$** and **3B$_R$** intramolecular hydrogen bonding requires the adoption of relatively unfavorable conformations with four bulky substituents gauche to each other in the Newman projections.



The major and chromatographically more mobile sulfoxide isomer obtained by peroxy acid oxidation of the hydroxy sulfide **6A** may be allocated the preferred conformation **a** (R = CH_2CH_2CN) and therefore the (S_S) configuration at sulfur by the same arguments, which is in complete accord with the configuration assigned on the basis of the well-established directing effect of a proximal hydroxy group on the stereoselectivity of peroxy acid oxidation at sulfur in the preferred conformation of the corresponding sulfide.[15] Similar considerations of hydroxy-directed oxidation at sulfur were employed by De Lucchi *et al.* to assign configuration at sulfur in the related (R_S,*Z*)-1-[(1*S*)-isoborneol-10-sulfinyl]-2-(phenylsulfonyl)ethylene, a conclusion that was anchored by X-ray analysis of a DA adduct of the aforesaid vinyl sulfoxide with cyclopentadiene.[3a] It is clear that the major sulfoxide formed by peroxy acid oxidation of a hydroxy sulfide should always be chromatographically more mobile than its epimer at sulfur, since similar hydrogen-bonding effects influence both stereoselectivity of oxidation and chromatographic characteristics.

Analogous hydrogen-bonding effects involving hydroxy and sulfenic acid groups may account for the predominance of one sulfoxide epimer from addition of the sulfenic acids **8A,B** to the methoxy enynes **9** and **10** (Scheme 1). These represent the first examples of asymmetric induction in sulfenic acid−alkyne additions, and the proposed influence of intramolecular hydroxy-sulfenic acid hydrogen bonding on the stereochemical consequences of this pericyclic process is supported by observations that intramolecular hydrogen bonding in other hydroxy sulfenic acids is strong[17] and contributes so significantly to their stability that in some cases they may be isolated.

Asymmetric DA Additions to Methyl Acrylate. Most of our investigations involved the readily accessible dienes **2A$_R$**, **2B$_S$**, and **2C$_S$**, but a few reactions were performed with **2A$_S$** and **3A$_R$**. We had too little of the other dienes for a meaningful study of their cycloadditions. Some relevant data are recorded in Table 2.

The (*E*)-dienes **2A$_R$**, **2A$_S$**, **2B$_S$**, and **2C$_S$** were reactive DA participants, undergoing cycloaddition with methyl acrylate at or below room temperature, whereas the diene **3A$_R$** reacted much more sluggishly, an expected consequence of its (*Z*)-configuration.[18] As expected,[19] the combined directing effects of the 1- and 3-substituents

(15) Glass, R. S.; Setzer, W. N., Prabhu, U. D. G.; Wilson, G. S. *Tetrahedron Lett.* **1982**, *23*, 2335−2338.

(16) Furukawa, N.; Fujihara, H. In *The Chemistry of Sulphones and Sulphoxides;* Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: Chichester, 1988; pp 541−581.

(17) Hogg, D. R. In *The Chemistry of Sulphenic Acids and their Derivatives*; Patai, S., Ed.; John Wiley & Sons: Chichester, 1990; pp 361−402.

(18) Zutterman, F.; Krief, A. *J. Org. Chem.* **1983**, *48*, 1135−1137.

Table 2. Cycloadditions of Sulfinyl dienes $2A_R$, $2A_S$, $2B_S$, $2C_S$, and $3A_R$ with Methyl Acrylate

							adducts		
entry	diene	catalyst	solvent	T/°C	time	yield/%	*endo*	*exo*	(ratio)
1	$2A_R$	none	none	25	16 h	55	**$15A_R$:$16A_R$** :	**$17A_R$:$18A_R$**	(54:31:8:7)
2	$2A_R$	$LiClO_4$	CH_2Cl_2	25	7 h	70	**$15A_R$:$16A_R$** :	**$17A_R$:$18A_R$**	(96:4:0:0)
3	$2A_S$	$ZnCl_2$	CH_2Cl_2	25	20 h	30	**$15A_S$:$16A_S$** :	**$17A_S$ + $18A_S$**	(0:89:11)
4	$3A_R$	none	none	reflux	6 d	68	**$17A_R$:$18A_R$** :	**$15A_R$:$16A_R$**	(27:47:11:15)
5	$3A_R$	$LiClO_4$	none	reflux	20 h	70	**$17A_R$:$18A_R$** :	**$15A_R$ + $16A_R$**	(17:80:3)
6	$2B_S$	none	CH_2Cl_2	25	42 h	20	**$15B_S$:$16B_S$** :	**$17B_S$:$18B_S$**	(22:56:6:16)
7	$2B_S$	$LiClO_4$	CH_2Cl_2	25	16 h	20	**$15B_S$:$16B_S$** :	**$17B_S$:$18B_S$**	(6:90:0:0)
8	$2C_S$	none	CH_2Cl_2	25	6 d	25	**$15C_S$:$16C_S$** :	**$17C_S$:$18C_S$**	(26:44:12:19)
9	$2C_S$	$LiClO_4$	CH_2Cl_2	25	3 d	40	**$15C_S$:$16C_S$** :	**$17C_S$:$18C_S$**	(2:93:0:0)

in the dienes ensured that cycloaddition occurred with complete regioselectivity, but the uncatalyzed cycloadditions were not particularly stereoselective, giving rise to four diastereoisomers with low *endo*/*exo* and diastereofacial selectivity.

The effect of Lewis acid catalysis was investigated in some detail with diene **$2A_R$**. All the catalysts investigated, except boron trifluoride etherate, served markedly to increase the *endo*:*exo* ratio, and the use of zinc chloride or lithium perchlorate in dichloromethane led also to high diastereofacial selectivity. The best catalyst was lithium perchlorate, the use of which as a suspension in dichloromethane gave only the *endo* isomers **$15A_R$** and **$16A_R$** in 70% yield in the ratio 96:4. This was the first illustration that lithium perchlorate suspended in dichloromethane-catalyzed DA reactions[20] and that it did so highly stereoselectively. Reetz and Fox[21] have shown that Mukaiyama aldol reactions and conjugate additions were more efficiently catalyzed in this way than by 5 M lithium perchlorate in diethyl ether, conditions that were previously advocated for the dramatic acceleration of DA reactions.[22]

The *endo* and *exo* pairs of adducts **15A**−**18A** could be separated by simple chromatography, but the composition of the mixture of four diastereoisomers was determined by proton NMR spectrometry. The *endo*/*exo* ratio was established from the relative intensities of the well-separated vinyl proton signals and the ratios **15A:16A** and **17A:18A** from the relative intensities of the lower field portion of the AB spectrum associated with the methylene group adjacent to sulfur. The relative proportions of adducts **15B**−**18B** were easily determined from the relative intensities of the vinyl proton signals in CD_3CN solution, while the ratio among adducts **15C**−**18C** was obtained by integration of the well-separated benzylic signals in C_6D_6 (Table 2).

Crystallization (ethyl acetate−light petroleum) of the mixture of *endo*-isomers (**$15A_R$ + $16A_R$**), obtained from **$2A_R$**, gave the optically pure diastereoisomer **$15A_R$**, the absolute configuration of which was established as (3*R*,4*R*,R_S) by X-ray crystallography.[23] This result also confirmed the configurations at sulfur in dienes **2A** and **3A** that were previously assigned on the basis of properties relating to intramolecular hydrogen bonding.[4a] Having firmly established the absolute configuration of adduct **$15A_R$**, the configurations of the *exo* products **$17A_R$** and **$18A_R$** were assigned on the basis of ^1H NMR data: $J_{3,4}$ and $J_{4,5}$ of **$15A_R$**−**$18A_R$** suggested the conformational preferences depicted in Figure 1; the subsequent comparison of H-3 and H-4 chemical shifts in the four adducts (see Figure 1) supported the attribution of configuration (3*R*,4*S*) to **$17A_R$** and (3*S*,4*R*) to **$18A_R$**.

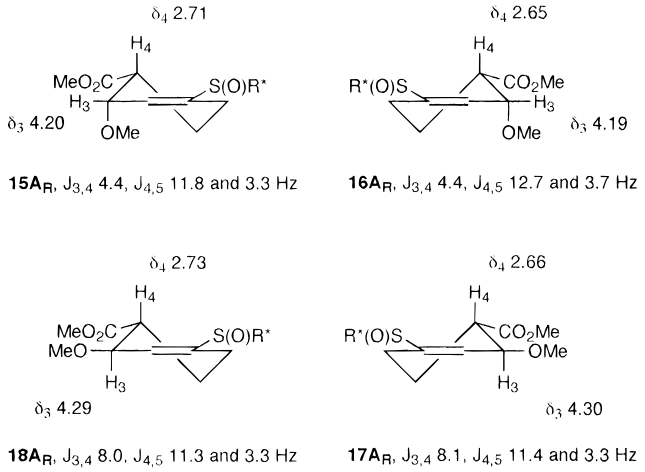


Figure 1. Conformational preferences of cycloadducts **$15A_R$**−**$18A_R$**.

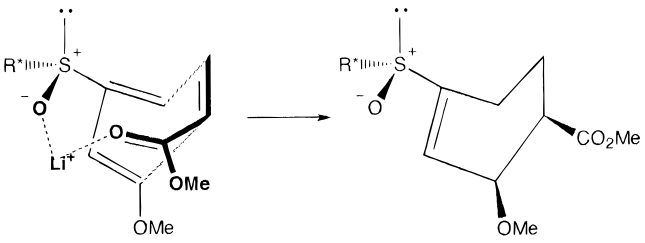


Figure 2. Favored approach of methyl acrylate in DA reaction of (R_S,*E*)-3-[(1*S*)-isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (**$2A_R$**) in the presence of $LiClO_4$.

Oxidation of **$15A_R$**, derived from the (R_S)-sulfinyl diene **$2A_R$**, with *m*-CPBA gave the sulfone **20A** in good yield, and oxidation of adduct **$16A_S$** [derived from the (S_S)-sulfinyldiene **$2A_S$**] gave the isomeric sulfone **21A** (Scheme 3). This established the absolute configurations of the adducts **$15A_S$** and **$16A_S$**. Zinc chloride-catalyzed cycloaddition of methyl acrylate with sulfonyl diene **19A**, readily obtained by oxidation of **$2A_R$** with *m*-CPBA, provided a 10:1 mixture of *endo* (**20A + 21A**) and *exo* (**22A + 23A**) adducts. The ratio **20A**:**21A** was 1:1, which showed that the isoborneol group did not significantly influence the stereoselectivity of cycloaddition, and so confirmed the fundamental role that sulfoxide chirality plays in determining diastereoselectivity of cycloadditions of 2-sulfinyl dienes. These considerations allowed, by analogy, the

(19) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976.

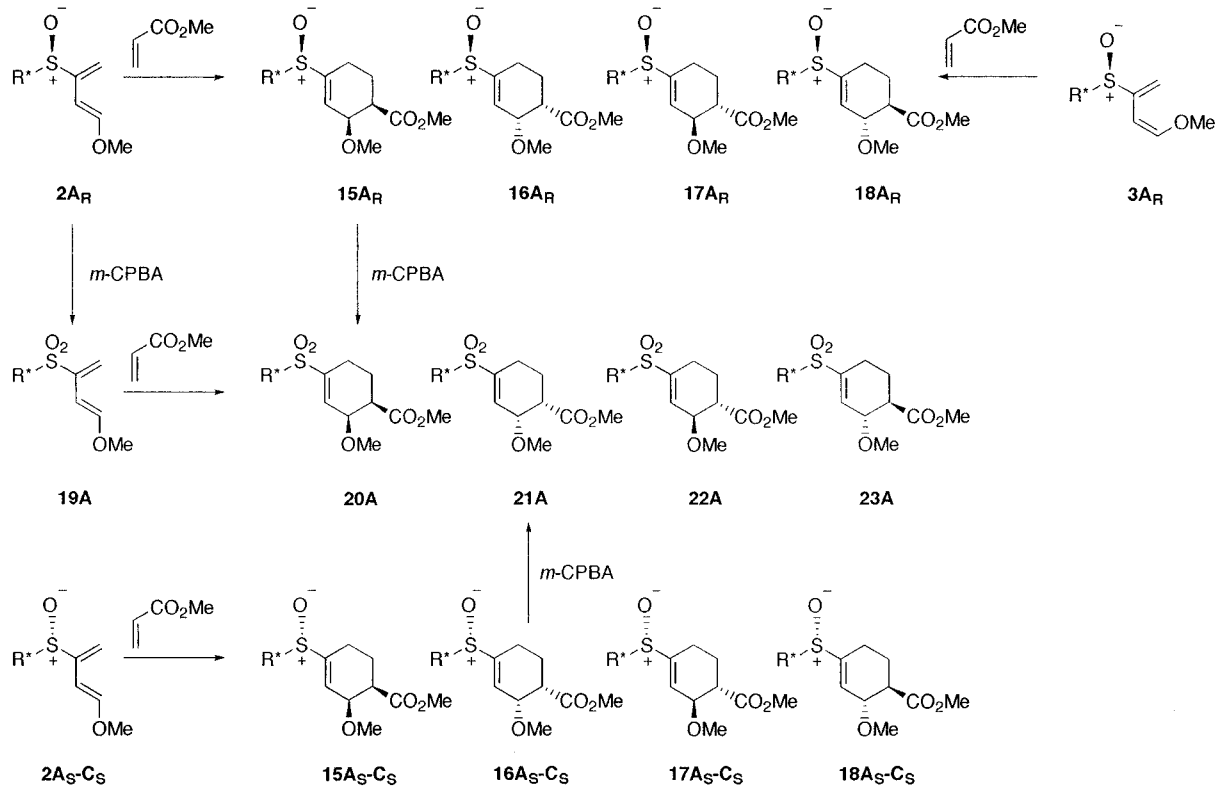
(20) $LiClO_4$ in Et_2O−CH_2Cl_2 (presumably in solution) has been used previously to catalyze cycloadditions of dienophilic sulfinyl maleates to cyclopentadiene, with moderate diastereofacial selectivity (Alonso, I.; Cid, M. B.; Carretero, J. C.; García Ruano, J. L.; Hoyos, M. A. *Tetrahedron: Asymmetry* **1991**, *2*, 1193−1207).

(21) Reetz, M. T.; Fox, D. N. A. *Tetrahedron Lett.* **1993**, *34*, 1119−1122.

(22) Grieco, P. A.; Nunes, J. J.; Gaul, M. D. *J. Am. Chem. Soc.* **1990**, *112*, 4595−4596.

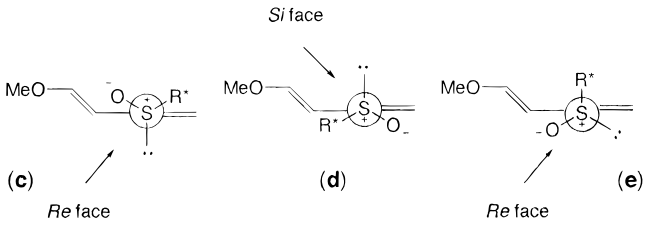
(23) Adams, A.; Bailey, N. A.; Jones, D. N.; Aversa, M. C.; Bonaccorsi, P.; Giannetto, P. *Acta Crystallogr.* **1995**, *C51*, 1357−1359.

Scheme 3



assignment of the absolute configurations to adducts **15B$_S$,C$_S$**−**18B$_S$,C$_S$**.

A tentative rationalization of stereochemical features, observed in the cycloadditions of 3-(alkylsulfinyl)-1-methoxy-1,3-butadienes **2** and **3** with methyl acrylate, may take into account the relative stabilities of the transition states originated from the *endo* approach of the dienophile to different conformations of the diene around the S--C-3 bond. The predominance of **15A$_R$** among the products of the uncatalyzed cycloaddition of **2A$_R$** may be interpreted on the basis of *Re* face approach of methyl acrylate to the diene in its **c** conformation; the isolation from the same reaction mixture of a certain percentage of the diastereomeric **16A$_R$** may be explained by considering the *Si* face approach of the dienophile to the diene in the less favored **d** conformation. The great improvement of diastereoselectivity and increased reaction rate observed in the $LiClO_4$-catalyzed DA reaction of **2A$_R$** (Table 2) suggest the approach of methyl acrylate to the *Re* face of the diene in its **e** conformation, the catalyst coordinating the sulfinyl oxygen of the diene and the carbonyl oxygen of the dienophile, as depicted in Figure 2.



Conclusions

The synthetic strategy based on the regioselective addition of sulfenic acids to enynes has been successfully applied to the preparation of enantiopure 2-sulfinyl dienes, which are not easily accessible by other synthetic routes.[6] The high degree of stereocontrol exhibited by $LiClO_4$-catalyzed cycloadditions of these alkylsulfinyl dienes with methyl acrylate indicates that chiral 2-sulfinyl dienes may fulfill a useful role in enantioselective synthesis. Asymmetric induction in these DA reactions of 2-sulfinyl dienes is overwhelmingly influenced by sulfur configuration, while other chiral elements present in the sulfoxide auxiliary have no significant effect. The high degree of stereochemical control observed in the preparation and cycloadditions of sulfinyl dienes derived from 10-mercaptoisoborneol **1A**, the good yield of cycloadducts, easy separation of diastereomeric mixtures, and crystallinity of the final adducts demonstrate the utility of camphor skeleton in the design of chiral auxiliaries based on sulfoxides.

Experimental Section

General Methods. Melting points were measured on a microscopic apparatus and are uncorrected. IR spectra were taken for neat oils, Nujol mulls, or $CHCl_3$ solutions with an FT spectrophotometer (see the Supporting Information). ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ solutions (unless otherwise stated) with $SiMe_4$ as internal standard; *J* values are given in Hz; the attributions are supported by attached proton test (APT), heteronuclear shift-correlated, and decoupling experiments. Mass spectra were measured by electron impact (EI, 70 eV) or fast atom bombardment (FAB, glycerol or *m*-nitrobenzyl alcohol). All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F 254), and the products were visualized with iodine. Silica gel 60 was used for column chromatography. Petrol refers to light petroleum, bp 60−80 °C. Elemental analyses were performed by REDOX, Milano, Italy. Substances for which C, H, N analyses are not reported were purified as specified and gave spectral data consistent with being >95% of the assigned structure.

***(S)*-(Ethoxycarbonyl)phenylmethyl *N,N*-Dimethyldithiocarbamate (12).** DEAD (9 mL, 56 mmol) was added

dropwise at 0 °C to a stirred dry toluene (180 mL) suspension containing ethyl (*R*)-mandelate (**11R**) (5 g, 28 mmol), Ph_3P (15 g, 57 mmol), and zinc dimethyldithiocarbamate (ZIRAM, 6.4 g, 21 mmol). After the mixture was stirred 24 h at room temperature, the workup of the reaction was effected by concentration of the mixture under reduced pressure and direct column chromatography: elution with petrol/EtOAc (90:10) afforded the dimethyldithiocarbamate **12** (5.7 g, 71%) as a crystalline compound: mp 103−105 °C; $[\alpha]^{25}_D$ +257 (c = 0.012, $CHCl_3$); ^{1}H NMR δ 7.5−7.3 (m, Ph), 5.74 (s, CHS), 4.29 and 4.16 (16 lines, J_{gem} 10.7, J_{vic} 7.1, CH_2), 3.52 and 3.36 (two s, NMe_2), 1.26 (t, CH_2CH_3); ^{13}C NMR δ 195.0 (CS), 170.0 (CO), 133.9 (C-1′), 128.9 and 128.8 (C-2′,3′,5′,6′), 128.5 (C-4′), 62.0 (CH_2), 59.5 (CHS), 45.2 and 41.5 (NMe_2), 14.0 (CH_2CH_3); FAB-MS m/z 284 (M + 1, 100), 238 (30), 163 (24). Anal. Calcd for $C_{13}H_{17}NO_2S_2$: C 55.10; H, 6.05; N, 4.94. Found: C, 55.07; H, 6.13; N, 4.93.

(*S*)-2-Mercapto-2-phenylethanol (1B).[24] Dimethyldithiocarbamate **12** (5.6 g, 19.8 mmol) was slowly added to 1.5 g (40 mmol) of $LiAlH_4$ suspended in dry Et_2O (60 mL) at 0 °C. Following the addition, the mixture was refluxed for 4 h. The reaction mixture was cooled at room temperature and $LiAlH_4$ carefully quenched by adding wet Et_2O, H_2O, finally HCl 3 N until pH 3 was measured. The organic phase was extracted with 10% NaOH (4 × 60 mL). HCl 12 N was added under stirring to the alkaline water solution until pH 3 was reached again. Then the acid water phase was extracted with Et_2O (4 × 70 mL) and the ethereal solution washed with H_2O (80 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give the mercaptoethanol **1B**, which did not need purification (2.7 g, 86%): mp 46−48 °C; $[\alpha]^{25}_D$ +90 (c = 0.022, $CHCl_3$); ^{1}H NMR δ 7.4−7.2 (m, Ph), 4.07 (ddd, $J_{1A,2}$ = 6.5, $J_{1B,2}$ = 7.6, $J_{2,SH}$ = 6.7, H-2), 3.90 (split ABd, $J_{1A,1B}$ = 11.1, H_A-1), 3.78 (split ABd, H_B-1), 2.23 (br s, OH), 1.97 (d, SH); ^{13}C NMR δ 140.4 (C-1′), 128.8 (C-3′,5′), 127.8 (C-4′), 127.4 (C-2′,6′), 68.3 (C-1), 46.3 (C-2); EI-MS m/z 154 (M^+, 18), 123 (100), 91 (77). Anal. Calcd for $C_8H_{10}OS$: C, 62.30; H, 6.54. Found: C, 62.29; H, 6.64.

Ethyl (2*S*)-2-Phenyl-2-(2-tetrahydropyranoxy)ethanoate. A solution of ethyl (*S*)-mandelate (**11S**) (5 g, 28 mmol) and 3,4-dihydro-2*H*-pyran (DHP, 3.5 g, 42 mmol) in dry CH_2Cl_2 (200 mL) containing PPTS[25] (0.7 g, 28 mmol) was stirred for 12 h at room temperature. The solution was then diluted with Et_2O and washed once with half-saturated brine to remove the catalyst. After evaporation of the solvent, ethyl (2*S*)-2-phenyl-2-(2-tetrahydropyranoxy)ethanoate was obtained in an essentially quantitative yield (7.4 g): the colorless oil, which did not need purification, was a mixture of diastereomers (epimeric at C-2" of the THP moiety) in a 1:1 ratio as determined by integration of the signals in the ^{1}H NMR spectrum: FAB-MS m/z 265 (M + 1, 14), 163 (23), 85 (100). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.10; H, 7.60. The two epimers can be separated by column chromatography eluting with petrol mixed with increasing amounts of EtOAc up to 5%. First eluted epimer: oil; ^{1}H NMR δ 7.5−7.3 (m, Ph), 5.31 (s, H-2), 4.89 (t, $J_{2",3"}$ = 2.7, H-2"), 4.19 and 4.15 (12 lines, J_{gem} = 10.9, J_{vic} = 7.2, CH_2CH_3), 3.7 and 3.5 (two m, H_2-6"), 1.9−1.5 (m, H_2-3",4",5"), 1.21 (t, Me); ^{13}C NMR δ 171.3 (C-1), 136.8 (C-1′), 128.4 (C-2′,6′), 128.2 (C-4′), 127.1 (C-3′,5′), 97.0 (C-2"), 75.6 (C-2), 61.8 (C-6"), 61.1 (CH_2-CH_3), 30.1, 25.3, and 18.6 (C-3",4",5"), 14.1 (Me). Second epimer: oil; ^{1}H NMR δ 7.5−7.3 (m, Ph), 5.21 (s, H-2), 4.59 (t, $J_{2",3"}$ = 3.3, H-2"), 4.20 and 4.13 (14 lines, J_{gem} = 10.8, J_{vic} = 7.0, CH_2CH_3), 4.0 and 3.5 (two m, H_2-6"), 2.0−1.5 (m, H_2-3",4",5"), 1.21 (t, Me); ^{13}C NMR δ 170.6 (C-1), 136.4 (C-1′), 128.4 (C-2′,4′,6′), 127.4 (C-3′,5′), 96.5 (C-2"), 76.8 (C-2), 62.2 (C-6"), 61.0 (CH_2CH_3), 30.2, 25.3, and 19.0 (C-3",4",5"), 14.0 (Me).

(2*S*)-2-Phenyl-2-(2-tetrahydropyranoxy)ethanol (13). The epimeric mixture of ethyl (2*S*)-2-phenyl-2-(2-tetrahydropyranoxy)ethanoates (7.4 g, 28 mmol) was slowly added to 0.6 g (15.8 mmol) of $LiAlH_4$ suspended in dry Et_2O (80 mL) at 0 °C. Following the addition, the mixture was refluxed for 2 h. The reaction mixture was cooled at room temperature and excess $LiAlH_4$ carefully quenched by adding wet Et_2O, H_2O, and finally HCl 3 N until the aqueous layer was neutral. The water phase was extracted with Et_2O (3 × 50 mL), and the combined organic extracts were washed with saturated $NaHCO_3$ solution (100 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford 6.2 g of alcohol **13** as a 1:1 mixture of diastereomers (epimeric at C-2"; clear, colorless oil, which did not need purification; almost quantitative yield): FAB-MS m/z 223 (M + 1, 16), 85 (82), 75 (100). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.29; H, 8.14. The two epimers **13** can be separated by column chromatography eluting with petrol/EtOAc (98:2). First eluted epimer: oil; ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.83 (dd, $J_{1A,2}$ = 8.1, $J_{1B,2}$ = 3.9, H-2), 4.53 (dd, $J_{2",3"}$ = 5.3, 2.5, H-2"), 4.02 (5 lines, $J_{5",6"A}$ = 5.2, $J_{6"A,6"B}$ = 11.8, H_A-6"), 3.72 (split ABd, $J_{1A,1B}$ = 11.8, H_A-1), 3.67 (split ABd, H_B-1), 3.56 (5 lines, $J_{5",6"B}$ = 5.6, H_B-6"), 1.9 (br s, OH), 1.9−1.4 (m, H_2-3",4",5"); ^{13}C NMR δ 138.7 (C-1′), 128.4 (C-2′,6′), 127.9 (C-4′), 126.7 (C-3′,5′), 97.9 (C-2"), 80.7 (C-2), 67.6 (C-1), 63.7 (C-6"), 31.0, 25.2, and 20.3 (C-3",4",5"). Second epimer: oil; ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.91 (t, $J_{2",3"}$ = 3.4, H-2"), 4.74 (dd, $J_{1A,2}$ = 6.6, $J_{1B,2}$ = 5.2, H-2), 3.74 (split ABd, $J_{1A,1B}$ = 10.9, H_A-1), 3.72 (split ABd, H_B-1), 3.59 (7 lines, $J_{5",6"A}$ = 8.2, 3.2, $J_{6"A,6"B}$ = 11.1, H_A-6"), 3.30 (5 lines, $J_{5",6"B}$ = 5.1, H_B-6"), 2.0 (br s, OH), 1.9−1.5 (m, H_2-3",4",5"); ^{13}C NMR δ 139.8 (C-1′), 128.3 (C-2′,6′), 127.6 (C-4′), 126.7 (C-3′,5′), 99.1 (C-2"), 79.8 (C-2), 66.6 (C-1), 62.6 (C-6"), 30.6, 25.2, and 19.4 (C-3",4",5").

(2*S*)-2-Phenyl-2-(2-tetrahydropyranoxy)ethyl *N*,*N*-Dimethyldithiocarbamate (14). The epimeric mixture **13** was reacted as reported for the preparation of **12**. After the mixture was stirred for 12 h at room temperature, concentration under reduced pressure and direct column chromatography [petrol/EtOAc (95:5)] afforded dimethyldithiocarbamate **14** (82%, 1:1 epimeric ratio): FAB-MS m/z 326 (M + 1, 96), 122 (92), 121 (100). Anal. Calcd for $C_{16}H_{23}NO_2S_2$: C, 59.04; H, 7.12; N, 4.30. Found: C, 59.11; H, 7.09; N, 4.30. Epimers can be separated by further column chromatography eluting with petrol/EtOAc (98:2). First eluted epimer: oil; ^{1}H NMR δ 7.5−7.3 (m, Ph), 4.98 (dd, $J_{2",3"}$ = 5.6, 3.3, H-2"), 4.93 (dd, J_{vic} 7.4, 5.1, PhC*H*), 3.9−3.2 (m, NMe_2, CH_2S, H_2-6"), 1.9−1.0 (m, H_2-3",4",5"); ^{13}C NMR δ 197.0 (CS), 141.9 (C-1′), 128.2 (C-2′,6′), 127.4 (C-4′), 126.6 (C-3′,5′), 98.8 (C-2"), 77.0 (Ph*C*H), 62.1 (C-6"), 45.4 and 41.4 (NMe_2), 44.6 (CH_2S), 30.5, 25.4, and 19.2 (C-3",4",5"). Second epimer: oil; ^{1}H NMR δ 7.5−7.3 (m, Ph), 4.48 (t, $J_{2",3"}$ = 2.5, H-2"), 4.07 (m, PhC*H*), 3.9−3.2 (m, NMe_2, CH_2S, H_2-6"), 1.9−1.0 (m, H_2-3",4",5"); ^{13}C NMR δ 197.2 (CS), 140.6 (C-1′), 128.4 (C-2′,6′), 127.9 (C-4′), 127.0 (C-3′,5′), 94.8 (C-2"), 75.5 (Ph*C*H), 61.7 (C-6"), 45.4 and 41.4 (NMe_2), 45.0 (CH_2S), 30.5, 25.5, and 18.9 (C-3",4",5").

(2*S*)-2-Phenyl-2-(2-tetrahydropyranoxy)ethyl Mercaptan. The epimeric mixture **14** was reacted as reported for the preparation of **13**: reflux time was 6 h. (2*S*)-2-Phenyl-2-(2-tetrahydropyranoxy)ethyl mercaptan was obtained as a 1:1 ratio of diastereomers (epimers at C-2"; clear, colorless oil, which did not need purification; almost quantitative yield): ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.96 (t, $J_{2",3"}$ = 2.9, H-2" of one epimer), 4.78 (dd, $J_{1,2}$ = 8.0, 5.1, H-2 of one epimer), 4.69 (dd, $J_{1,2}$ = 7.0, 5.6, H-2 of the other epimer), 4.47 (t, $J_{2",3"}$ = 3.3, H-2" of the other epimer), 4.1−3.3 (m, H_2-6"), 3.0−2.7 (m, H_2-1), 1.9−1.4 (m, H_2-3",4",5", SH); ^{13}C NMR δ 141.4 and 140.2 (C-1'), 128.5 and 128.2 (C-2',6'), 128.1 and 127.6 (C-4'), 127.1 and 126.6 (C-3',5'), 98.7 and 95.1 (C-2"), 80.1 and 78.2 (C-2), 62.3 and 61.9 (C-6"), 31.9 and 31.2 (C-1), 30.5, 30.4, 25.4, 25.3, 19.3, and 19.0 (C-3",4",5"). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.47; H, 7.60.

(*S*)-2-Mercapto-1-phenylethanol (1C).[13,24a] A solution of (2*S*)-2-phenyl-2-(2-tetrahydropyranoxy)ethyl mercaptan (1:1 epimeric ratio) (2 g, 8.4 mmol) and PPTS (0.21 g, 0.84 mmol) in EtOH (70 mL) was stirred at 55 °C (bath temperature) for 24 h. The solvent was evaporated *in vacuo*, and Et_2O (100 mL) was added. The organic phase was extracted with 10% NaOH (4 × 60 mL). HCl 12 N was added under stirring to the alkaline water solution until pH 3 was reached again. Then the acid water phase was extracted with Et_2O (4 × 70 mL)

(24) (a) Djerassi, C.; Gorman, M.; Markley, F. X.; Oldenburg, E. B. *J. Am. Chem. Soc.* **1955**, *77*, 568−571. (b) Alcudia, F.; Brunet, E.; García Ruano, J. L.; Rodriguez, J. H.; Sanchez, F. *J. Chem. Res., Synop.* **1982**, 284−285; *J. Chem. Res., Miniprint* **1982**, 2826−2850.

(25) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772−3774.

and the ethereal solution washed with H_2O (80 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give the mercaptoethanol **1C**, which did not need purification (1.11 g, 86%): oil; $[\alpha]^{25}_D$ +50 (c = 0.009, $CHCl_3$); ^{1}H NMR δ 7.4−7.2 (m, Ph), 4.71 (dd, $J_{1,2A}$ = 4.1, $J_{1,2B}$ = 8.2, H-1), 2.86 (8 lines, $J_{2A,2B}$ = 13.8, $J_{2A,SH}$ = 9.0, H_A-2), 2.79 (8 lines, $J_{2B,SH}$ = 8.2, H_B-2), 1.44 (t, SH); ^{13}C NMR δ 142.0 (C-1′), 128.4 (C-2′,6′), 127.9 (C-4′), 125.8 (C-3′,5′), 74.6 (C-1), 33.5 (C-2); EI-MS m/z 154 (M^+, 2), 107 (100), 85 (94). Anal. Calcd for $C_8H_{10}OS$: C, 62.30; H, 6.54. Found: C, 63.36; H, 6.52.

2-Cyanoethyl Sulfides 6A−C. General Procedure. Acrylonitrile (0.81 mL, 12.5 mmol) was added slowly to a solution (THF, 45 mL) of an equimolar amount of mercaptoalkanols **1A**,[10] **1B**, or **1C** and benzyltrimethylammonium hydroxide (Triton B, 0.4 mL, 40 wt % solution in MeOH) at −78 °C. The reaction mixture was slowly brought to room temperature, and water (80 mL) was added. The crude product was extracted with Et_2O (4 × 80 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (3 × 50 mL) and dried (Na_2SO_4). Evaporation of the solvent gave an oily residue that was purified by column chromatography eluting with petrol/Et_2O (85:15) to give [(cyanoethyl)thio]alkanols **6A−C** as pale yellow oils.

(1*S*)-10-[(2-Cyanoethyl)thio]isoborneol (6A): yield 91%; ^{1}H NMR δ 3.87 (dd, $J_{2,3}$ = 7.7, 3.9, H-2), 2.88 (ABd, $J_{10A,10B}$ = 10.9, H_A-10), 2.61 (ABd, H_B-10), 2.8−2.6 (m, H_2-1′,2′), 2.17 (br s, OH), 1.8−1.0 (m, H_2-3,5,6, H-4), 1.06 (s, H_3-8), 0.85 (s, H_3-9); ^{13}C NMR δ 118.4 (C-3′), 76.5 (C-2), 52.1 (C-1), 47.7 (C-7), 45.1 (C-4), 39.5 (C-3), 32.1 (C-10), 30.9 and 27.0 (C-5,6), 28.8 (C-1′), 20.6 and 19.9 (C-8,9), 18.8 (C-2′); EI-MS m/z 239 (M^+, 2), 221 ($M^+ - H_2O$, 16), 109 (79), 108 (100). Anal. Calcd for $C_{13}H_{21}NOS$: C, 65.23; H, 8.84; N, 5.85. Found: C, 65.20; H, 8.65; N, 5.90.

(*S*)-2-[2-Cyanoethyl)thio]-2-phenylethanol (6B): yield 84%; $[\alpha]^{25}_D$ +275 (c = 0.005, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.08 (dd, $J_{1,2}$ = 7.6, 6.2, H-2), 3.9 (m, H_2-1), 2.7 and 2.5 (two m, CH_2CH_2CN), 1.8 (br s, OH); ^{13}C NMR δ 139.7 (C-1′), 130.1 (C-3′,5′), 129.3 (C-4′), 129.1 (C-2′,6′), 119.1 (CN), 66.9 (C-1), 54.3 (C-2), 27.7 (SCH_2), 19.9 (CH_2CN); FAB-MS m/z 208 (M + 1, 14), 137 (100), 89 (71). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.75; H, 6.42; N, 6.66.

(*S*)-2-[(2-Cyanoethyl)thio]-1-phenylethanol (6C): yield 80%; $[\alpha]^{25}_D$ +58 (c = 0.050, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.84 (dd, $J_{1,2A}$ = 4.0, $J_{1,2B}$ = 8.4, H-1), 2.97 (split ABd, $J_{2A,2B}$ = 14.0, H_A-2), 2.88 (split ABd, H_B-2), 2.80 and 2.64 (two t, J_{vic} = 7.0, CH_2CH_2CN), 1.6 (br s, OH); ^{13}C NMR δ 142.3 (C-1′), 128.7 (C-2′,6′), 128.2 (C-4′), 125.7 (C-3′,5′), 118.0 (CN), 73.2 (C-1), 41.6 (C-2), 28.2 (SCH_2CH_2), 19.0 (CH_2CN); EI-MS m/z 207 (M^+, 2), 107 (100), 43 (83). Anal. Calcd. for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.70; H, 6.31; N, 6.68.

2-Cyanoethyl Sulfoxides 7A−C. General Procedure. *m*-CPBA carefully dried over P_2O_5 (2.2 g 80%, 10.2 mmol) was dissolved in CH_2Cl_2 (70 mL) and slowly added to a solution of an equimolar amount of 2-cyanoethyl sulfides **6** in CH_2Cl_2 (70 mL) at −15 °C. The reaction mixture was allowed to reach room temperature and stirred for 2 h. Anhydrous KF (2.5 g) was added and the mixture stirred overnight. After filtration, the evaporation of the solvent under reduced pressure gave 2-cyanoethyl sulfoxides **7**, usable for synthesizing sulfinyl dienes **2** and **3** without purification.

(1*S*)-10-[(2-Cyanoethyl)sulfinyl]isoborneol (7A): yield 92% of 28:1 mixture of sulfur epimers, which can be separated by column chromatography, eluting with petrol/EtOAc (80:20): FAB-MS m/z 256 (M + 1, 78), 238 (22), 135 (100). Anal. Calcd for $C_{13}H_{21}NO_2S$: C, 61.14; H, 8.29; N, 5.48. Found: C, 61.20; H, 8.32; N, 5.50.

(1*S*,*S*$_S$)-10-[(2-Cyanoethyl)sulfinyl]isoborneol (7A$_S$): first eluted oil; $[\alpha]^{25}_D$ −46 (c = 0.012, $CHCl_3$); ^{1}H NMR δ 4.05 (dd, $J_{2,3}$ = 8.2, 4.1, H-2), 3.37 (ABd, $J_{10A,10B}$ = 12.9, H_A-10), 3.1−2.9 (m, H_2-1′,2′), 2.42 (ABd, H_B-10), 2.8 (br s, OH), 1.9−1.1 (m, H_2-3,5,6, H-4), 1.11 (s, H_3-8), 0.85 (s, H_3-9); ^{13}C NMR δ 117.2 (C-3′), 76.8 (C-2), 53.2 (C-10), 51.3 (C-1), 48.2 (C-7), 47.7 (C-1′), 44.9 (C-4), 38.5 (C-3), 30.8 and 27.1 (C-5,6), 20.4 and 19.8 (C-8,9), 11.1 (C-2′).

(1*S*,*R*$_S$)-10-[(2-Cyanoethyl)sulfinyl]isoborneol (7A$_R$): oil; $[\alpha]^{25}_D$ −53 (c = 0.012, $CHCl_3$); ^{1}H NMR δ 4.03 (dd, $J_{2,3}$ = 8.2, 4.1, H-2), 3.15 (ABd, $J_{10A,10B}$ = 13.0, H_A-10), 3.1−2.9 (m, H_2-1′,2′), 2.60 (ABd, H_B-10), 2.8 (br s, OH), 1.9−1.1 (m, H_2-3,5,6, H-4), 1.10 (s, H_3-8), 0.90 (s, H_3-9).

(*S*,*R*$_S$)-2-[(2-Cyanoethyl)sulfinyl]-2-phenylethanol (7B$_R$): yield 89%; white crystals mp 137−138 °C; $[\alpha]^{25}_D$ +220 (c = 0.005, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 4.53 (split ABd, $J_{1A,2}$ = 7.4, $J_{1A,1B}$, 12.3, H_A-1), 4.21 (split ABd, $J_{1B,2}$ = 3.8, H_B-1), 4.08 (dd, H-2), 2.9−2.7 (m, CH_2CH_2CN), 2.5 (br s, OH); ^{13}C NMR δ 131.4 (C-1′), 129.7 (C-2′,6′), 129.4 (C-4′), 128.6 (C-3′,5′), 117.2 (CN), 69.0 (C-2), 64.0 (C-1), 44.6 (SCH_2), 10.6 (CH_2CN); FAB-MS m/z 224 (M + 1, 35), 121 (100), 45 (27). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 59.25; H, 5.79; N, 6.20. The formation of (*S*,*S*$_S$)-2-[(2-cyanoethyl)-sulfinyl]-2-phenylethanol (minor diastereomer) was not observed in a notable amount.

(*S*)-2-[(2-Cyanoethyl)sulfinyl]-1-phenylethanol (7C): almost quantitative yield of 1:1 oil mixture of sulfur epimers, hard to separate by column chromatography; ^{1}H NMR (epimeric mixture) δ 7.4−7.3 (m, Ph), 5.37 (dd, $J_{1,2}$ = 8.7, 3.5) and 5.27 (dd, $J_{1,2}$ = 10.2, 2.3) (H-1), 3.3−2.7 (m, 3 × CH_2, OH); ^{13}C NMR (epimeric mixture) δ 141.9 and 141.8 (C-1′), 128.8 (C-2′,6′), 128.3 (C-4′), 125.7 and 125.5 (C-3′,5′), 117.4 (CN), 68.6 and 67.6 (C-1), 60.8 and 58.3 (C-2), 46.7 and 46.5 (CH_2CH_2-CN), 11.1 (CH_2CN); FAB-MS m/z 224 (M + 1, 61), 206 (M − H_2O + 1, 100), 154 (89), 137 (62), 104 (81). Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 59.37; H, 5.89; N, 6.30.

1-Methoxy-3-sulfinylbuta-1,3-dienes 2 and 3. General Procedure. The sulfoxides **7** (1 g, 4.5 mmol) in toluene or mixed xylenes (12 mL) (see Table 1) containing (*E*)- or (*Z*)-1-methoxy-1-buten-3-yne (1.1 mL, 13.5 mmol) were maintained at reflux temperature [(*E*)-enyne **9** was prepared following the Brandsma procedure;[26] (Z)-isomer **10**, commercially available in MeOH/H_2O (4:1), was extracted with Et_2O and distilled under reduced pressure just before use]. When the reaction appeared complete by TLC, the solvent was removed under reduced pressure and the reaction mixture was separated by column chromatography.

Reaction of (1*S*)-10-[(2-Cyanoethyl)sulfinyl]isoborneols 7A with (*E*)-Enyne 9. The following products were obtained by elution with petrol containing increasing amounts of Et_2O up to 30% and are reported in order of raising retention times.

(*R*$_S$,*E*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (2A$_R$): oil; $[\alpha]^{25}_D$ +39 (c = 0.002, $CHCl_3$); ^{1}H NMR δ 6.86 (d, $J_{1,2}$ = 12.8, H-1), 5.71 and 5.59 (two s, H_2-4), 5.53 (d, H-2), 4.13 (dd, $J_{2',3'}$ = 8.1, 4.2, H-2′), 3.67 (s, OMe), 3.5 (br s, OH), 3.13 (ABd, $J_{10'A,10'B}$ = 13.5, H_A-10′), 2.60 (ABd, H_B-10′), 1.9−1.1 (m, H_2-3′,5′,6′, H-4′), 1.08 (s, H_3-8′), 0.82 (s, H_3-9′); ^{13}C NMR δ 150.9 (C-1), 148.2 (C-3), 112.3 (C-4), 98.1 (C-2), 76.9 (C-2′), 56.7 (OMe), 56.0 (C-10′), 51.6 (C-1′), 48.2 (C-7′), 45.1 (C-4′), 38.4 (C-3′), 30.9 and 27.1 (C-5′,6′), 20.5 and 19.8 (C-8′,9′); FAB-MS m/z 285 (M + 1, 66), 135 (100), 83 (45).

(*S*$_S$,*E*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (2A$_S$): oil; ^{1}H NMR δ 6.92 (d, $J_{1,2}$ = 13.0, H-1), 5.76 and 5.61 (two s, H_2-4), 5.53 (d, H-2), 4.15 (dd, $J_{2',3'}$ = 7.6, 4.0, H-2′), 3.65 (s, OMe), 2.7 (br s, OH), 3.38 (ABd, $J_{10'A,10'B}$ = 14.0, H_A-10′), 2.56 (ABd, H_B-10′), 1.9−1.1 (m, H_2-3′,5′,6′, H-4′), 1.12 (s, H_3-8′), 0.83 (s, H_3-9′); ^{13}C NMR δ 151.2 (C-1), 148.2 (C-3), 112.4 (C-4), 98.6 (C-2), 76.4 (C-2′), 56.8 (OMe), 54.0 (C-10′), 52.2 (C-1′), 48.9 (C-7′), 44.7 (C-4′), 40.5 (C-3′), 31.2 and 27.4 (C-5′,6′), 20.5 and 20.3 (C-8′,9′); FAB-MS m/z 285 (M + 1, 9), 135 (100), 55 (62).

Reaction of (1*S*)-10-[(2-Cyanoethyl)sulfinyl]isoborneol (7A) with (*Z*)-Enyne 10. The following products were obtained by elution with petrol containing increasing amounts of Et_2O up to 30% and are reported in sequence of raising retention times.

(*R*$_S$,*Z*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (3A$_R$): mp 95−97 °C; $[\alpha]^{25}_D$ +78 (c = 0.070, $CHCl_3$); ^{1}H NMR δ 6.17 (d, $J_{1,2}$ 6.9, H-1), 5.92 and 5.89 (two s, H_2-4), 5.07 (d, H-2), 4.14 (dd, $J_{2',3'}$ = 8.0, 4.2, H-2′), 3.75 (s, OMe), 3.4 (br s, OH), 2.99 (ABd, $J_{10'A,10'B}$ = 13.2, H_A-10′), 2.66 (ABd, H_B-10′), 1.9−1.1 (m, H_2-3′,5′,6′, H-4′), 1.07 (s, H_3-8′), 0.81 (s, H_3-

(26) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: New York, 1971.

9′); ^{13}C NMR δ 149.6 (C-1), 147.8 (C-3), 115.2 (C-4), 98.0 (C-2), 76.9 (C-2′), 60.7 (OMe), 56.1 (C-10′), 51.6 (C-1′), 48.1 (C-7′), 45.1 (C-4′), 38.4 (C-3′), 30.7 and 27.1 (C-5′,6′), 20.4 and 19.8 (C-8′,9′); FAB-MS *m*/*z* 285 (M + 1, 75), 135 (100), 83 (40).

(*S*$_S$,*Z*)-3-[(1*S*)-Isoborneol-10-sulfinyl]-1-methoxybuta-1,3-diene (3A$_S$): oil; $[\alpha]^{25}_D$ −34 (*c* = 0.004, $CHCl_3$); ^{1}H NMR δ 6.18 (d, $J_{1,2}$ = 6.8, H-1), 6.01 and 5.99 (two s, H_2-4), 5.04 (d, H-2), 4.12 (dd, $J_{2',3'}$ = 7.8, 3.8, H-2′), 3.77 (s, OMe), 3.32 (ABd, $J_{10'A,10'B}$ = 14.0, H_A-10′), 2.51 (ABd, H_B-10′), 2.4 (br s, OH), 1.9−1.1 (m, H_2-3′,5′,6′, H-4′), 1.10 (s, H_3-8′), 0.81 (s, H_3-9′); ^{13}C NMR δ 149.5 (C-1), 147.1 (C-3), 116.4 (C-4), 98.3 (C-2), 76.4 (C-2′), 61.0 (OMe), 53.8 (C-10′), 53.0 (C-1′), 50.2 (C-7′), 44.6 (C-4′), 39.7 (C-3′), 31.1 and 27.5 (C-5′,6′), 20.5 and 20.1 (C-8′,9′); FAB-MS *m*/*z* 285 (M + 1, 100), 135 (84), 75 (79).

Reaction of (*S*,*R*$_S$)-2-[(2-Cyanoethyl)sulfinyl]-2-phenylethanol (7B$_R$) with (*E*)-Enyne 9. The following products were obtained by eluting first with toluene only (to remove the excess enyne) then with toluene containing increasing amounts of CH_2Cl_2.

(*S*,*S*$_S$,*E*)-3-[(2-Hydroxy-1-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (2B$_S$): oil; $[\alpha]^{25}_D$ +127 (*c* = 0.004, $CHCl_3$); ^{1}H NMR δ 7.5−7.1 (m, Ph), 6.79 (d, $J_{1,2}$ = 12.9, H-1), 5.45 and 5.29 (two s, H_2-4), 5.36 (d, H-2), 4.7−4.1 (m, CH_2CH), 4.0 (br s, OH), 3.52 (s, OMe); ^{13}C NMR δ 151.9 (C-1), 146.9 (C-3), 133.1 (C-1′), 128.9, 128.7, and 128.6 (C-2′,3′,4′,5′,6′), 114.1 (C-4), 96.5 (C-2), 68.8 (CH_2*C*H), 64.6 (*C*H_2CH), 56.6 (OMe); FAB-MS *m*/*z* 253 (M + 1, 100), 121 (53), 83 (46). The minor epimer **(*S*,*R*$_S$,*E*)-3-[(2-hydroxy-1-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (2B$_R$)** was obtained in mixture with **2B$_S$** and identified by ^{1}H NMR: δ 7.5−7.1 (m, Ph), 6.72 (d, $J_{1,2}$ = 12.9, H-1), 5.32 and 5.07 (two s, H_2-4), 5.21 (d, H-2), 4.7−4.1 (m, CH_2CH), 4.0 (br s, OH), 3.57 (s, OMe).

Reaction of (*S*,*R*$_S$)-2-[(2-Cyanoethyl)sulfinyl]-2-phenylethanol (7B$_R$) with (*Z*)-Enyne 10. The following products were obtained by eluting first with toluene only (to remove the excess enyne) and then with toluene containing increasing amounts of CH_2Cl_2.

(*S*,*S*$_S$,*Z*)-3-[(2-Hydroxy-1-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (3B$_S$): oil; $[\alpha]^{25}_D$ +119 (c = 0.003, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 6.27 (d, $J_{1,2}$ = 6.8, H-1), 5.97 and 5.54 (two s, H_2-4), 5.03 (d, H-2), 4.54 (split ABd, J_{gem} = 12.4, J_{vic} = 8.0, C$H_A$$H_B$CH), 4.16 (split ABd, J_{vic} = 3.4, CH_AH_BCH), 4.01 (dd, CH_AH_BC*H*), 4.2 (br s, OH), 3.72 (s, OMe); ^{13}C NMR δ 151.7 (C-1), 146.0 (C-3), 132.0 (C-1′), 129.2, 129.1 and 128.4 (C-2′,3′,4′,5′,6′), 118.4 (C-4), 95.0 (C-2), 67.6 (CH_2*C*H), 64.0 (*C*H_2CH), 61.0 (OMe); FAB-MS *m*/*z* 253 (M + 1, 100), 121 (98), 83 (46). The minor epimer **(*S*,*R*$_S$,*Z*)-3-[(2-hydroxy-1-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (3B$_R$)** was obtained in mixture with **3B$_S$** and identified by ^{1}H NMR: δ 7.4−7.3 (m, Ph), 6.10 (d, $J_{1,2}$ = 6.7, H-1), 5.63 and 5.26 (two s, H_2-4), 4.81 (d, H-2), 4.6−3.9 (m, CH_2CH), 4.2 (br s, OH), 3.71 (s, OMe).

Reaction of (*S*)-2-[(2-Cyanoethyl)sulfinyl]-1-phenylethanol (7C) with (*E*)-Enyne 9. The mixture of dienes **2C** was obtained by eluting first with toluene to remove the excess enyne and then with petrol containing increasing amounts of EtOAc. Further column chromatography [benzene/2-propanol (98:2) as eluant] allowed the separation of the two diene epimers, with **2C$_S$** showing a slightly enhanced chromatographic mobility with respect to **2C$_R$**.

(*S*,*S*$_S$,*E*)-3-[(2-Hydroxy-2-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (2C$_S$): oil; $[\alpha]^{25}_D$ +83 (*c* = 0.001, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 6.84 (d, $J_{1,2}$ = 13.1, H-1), 5.80 and 5.72 (two s, H_2-4), 5.45 (d, H-2), 5.33 (dd, J_{vic} = 10.1, 2.1, C*H*CH_AH_B), 3.97 (br s, OH), 3.64 (s, OMe), 3.26 (split ABd, J_{gem} = 13.7, J_{vic} = 10.1, $CHCH_AH_B$), 2.79 (split ABd, $CHCH_AH_B$); ^{13}C NMR δ 151.3 (C-1), 146.3 (C-3), 142.0 (C-1′), 128.6 (C-2′,4′,6′), 125.7 (C-3′,5′), 113.4 (C-4), 97.6 (C-2), 68.9 (CHOH), 58.4 ($CHCH_2$), 56.8 (OMe).

(*S*,*R*$_S$,*E*)-3-[(2-Hydroxy-2-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (2C$_R$): oil; $[\alpha]^{25}_D$ −58 (*c* = 0.002, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 6.85 (d, $J_{1,2}$ = 13.1, H-1), 5.70 and 5.59 (two s, H_2-4), 5.43 (d, H-2), 5.39 (dd, J_{vic} = 8.8, 3.5, C*H*CH_2), 4.18 (br s, OH), 3.63 (s, OMe), 3.08 (split ABd, J_{gem} = 13.5, J_{vic} = 8.8, $CHCH_AH_B$), 3.03 (split ABd, $CHCH_AH_B$); ^{13}C NMR δ 151.5 (C-1), 148.0 (C-3), 142.0 (C-1′), 128.7 (C-2′,6′), 128.3 (C-4′), 125.8 (C-3′,5′), 112.6 (C-4), 96.9 (C-2), 71.3 (CHOH), 60.0 ($CHCH_2$), 56.7 (OMe).

Reaction of (*S*)-2-[(2-Cyanoethyl)sulfinyl]-1-phenylethanol (7C) with (*Z*)-Enyne 10. The mixture of dienes **3C** was obtained by eluting first with toluene to remove the excess enyne and then with petrol containing increasing amounts of EtOAc. Further column chromatography [benzene/2-propanol (98:2) as eluant] allowed the separation of the two diene epimers, with **3C$_S$** showing a slightly enhanced chromatographic mobility with respect to **3C$_R$**.

(*S*,*S*$_S$,*Z*)-3-[(2-Hydroxy-2-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (3C$_S$): oil; $[\alpha]^{25}_D$ +100 (*c* = 0.008, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 6.16 (d, $J_{1,2}$ = 6.8, H-1), 6.06 (s, H_2-4), 5.34 (dd, J_{vic} = 10.0, 1.7, C*H*CH_AH_B), 5.03 (d, H-2), 4.44 (br s, OH), 3.73 (s, OMe), 3.27 (split ABd, J_{gem} = 13.7, J_{vic} = 10.0, $CHCH_AH_B$), 2.74 (split ABd, $CHCH_AH_B$); ^{13}C NMR δ 149.8 (C-1), 145.5 (C-3), 142.3 (C-1′), 128.6 (C-2′,6′), 127.8 (C-4′), 125.7 (C-3′,5′), 116.9 (C-4), 97.8 (C-2), 69.1 (CHOH), 60.8 (OMe), 57.3 ($CHCH_2$); FAB-MS *m*/*z* 253 (M + 1, 16), 138 (54), 137 (100).

(*S*,*R*$_S$,*Z*)-3-[(2-Hydroxy-2-phenylethyl)sulfinyl]-1-methoxybuta-1,3-diene (3C$_R$): oil; $[\alpha]^{25}_D$ −71 (*c* = 0.002, $CHCl_3$); ^{1}H NMR δ 7.4−7.3 (m, Ph), 6.16 (d, $J_{1,2}$ = 6.7, H-1), 5.94 and 5.92 (two s, H_2-4), 5.41 (dd, J_{vic} = 9.6, 2.2, C*H*CH_AH_B), 5.04 (d, H-2), 4.27 (br s, OH), 3.72 (s, OMe), 3.06 (split ABd, J_{gem} = 13.2, J_{vic} = 2.2, $CHCH_AH_B$), 2.95 (split ABd, $CHCH_AH_B$); ^{13}C NMR δ 150.2 (C-1), 147.5 (C-3), 142.4 (C-1′), 128.6 (C-2′,6′), 128.0 (C-4′), 125.8 (C-3′,5′), 115.6 (C-4), 97.0 (C-2), 71.3 (CHOH), 60.9 (OMe), 60.5 ($CHCH_2$); FAB-MS *m*/*z* 253 (M + 1, 12), 138 (51), 137 (100).

General Procedure for DA Cycloadditions of Dienes 2A$_R$, 2A$_S$, 3A$_R$, 2B$_S$, and 2C$_S$ with Methyl Acrylate. Some experimental conditions are reported in Table 2. When the cycloaddition was performed without solvent the diene/dienophile ratio was 1:35, while for reactions performed in CH_2Cl_2 (2 mL for 0.53 mmol of diene) the ratio was 1:6. In catalyzed cycloadditions, the Lewis acid was always added to the solution of diene and methyl acrylate in a diene/catalyst ratio of 1:0.8 (for more details, see the Supporting Information). The reaction mixture was stirred until the diene totally disappeared, as verified by TLC monitoring. The crude mixture was column chromatographed, eluting with petrol/EtOAc (80:20), after evaporation under vacuum of the solvent, if present. The fractions containing cycloadducts were combined and analyzed by ^{1}H NMR (Table 2) using $CDCl_3$ for adducts **15A$_R$**−**18A$_R$**, CD_3CN for adducts **15B$_S$**−**18B$_S$**, and C_6D_6 for **15C$_S$**−**18C$_S$**. Further column chromatography was performed on the mixture of adducts **15A$_R$**−**18A$_R$** allowing the separation of the four diastereomeric cycloadducts.

(3*R*,4*R*,*R*$_S$)-1-[(1S)-Isoborneol-10-sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (15A$_R$): mp 112−114 °C; $[\alpha]^{25}_D$ +130 (*c* = 0.008, $CHCl_3$); ^{1}H NMR δ 6.71 (d, $J_{2,3}$ = 4.4, H-2), 4.20 (t, $J_{3,4}$ = 4.4, H-3), 4.12 (dd, $J_{2',3'}$ = 8.2, 4.1, H-2′), 3.97 (br s, OH), 3.76 (s, 3-OMe), 3.42 (s, 4-COOMe), 3.14 (ABd, $J_{10'A,10'B}$ = 12.9, H_A-10′), 2.71 (ddd, $J_{4,5}$ = 11.8, 3.3, H-4), 2.43 (ABq, H_B-10′), 2.4−0.9 (m, H_2-3′,5,5′,6,6′, H-4′), 1.08 (s, H_3-8′), 0.83 (s, H_3-9′); ^{13}C NMR δ 172.3 (CO), 146.4 (C-1), 126.3 (C-2), 77.0 (C-2′), 72.5 (C-3), 57.8 (3-OMe), 53.4 (C-10′), 51.8 (COO*Me*), 51.4 (C-1′), 48.3 (C-7′), 45.1 and 44.7 (C-4,4′), 38.4 (C-3′), 30.8 and 27.1 (C-5′,6′), 22.5 (C-6), 20.5 and 19.9 (C-8′,9′), 19.4 (C-5); FAB-MS *m*/*z* 371 (M + 1, 100), 217 (16), 135 (59). Anal. Calcd for $C_{19}H_{30}O_5S$: C, 61.59; H, 8.16. Found: C, 61.60; H, 8.13.

(3*S*,4*S*,*R*$_S$)-1-[(1*S*)-Isoborneol-10-sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (16A$_R$): mp 193−195 °C; $[\alpha]^{25}_D$ −138 (*c* = 0.004, $CHCl_3$); ^{1}H NMR δ 6.72 (d, $J_{2,3}$ = 4.4, H-2), 4.19 (t, $J_{3,4}$ = 4.4, H-3), 4.11 (ddd, $J_{2',3'}$ = 7.8, 3.8, $J_{2',OH}$ = 3.8, H-2′), 3.97 (d, OH), 3.76 (s, 3-OMe), 3.43 (s, 4-COOMe), 3.24 (ABd, $J_{10'A,10'B}$ = 13.1, H_A-10′), 2.65 (ddd, $J_{4,5}$ = 12.7, 3.7, H-4), 2.39 (ABq, H_B-10′), 2.5−1.2 (m, H_2-3′,5,5′,6,6′, H-4′), 1.09 (s, H_3-8′), 0.83 (s, H_3-9′). Anal. Calcd for $C_{19}H_{30}O_5S$: C, 61.59; H, 8.16. Found: C, 61.80; H, 8.10.

(3*R*,4*S*,*R*$_S$)-1-[(1*S*)-Isoborneol-10-sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (17A$_R$): mp 68−69 °C; $[\alpha]^{25}_D$ −223 (*c* = 0.013, $CHCl_3$); ^{1}H NMR δ 6.55 (br s, H-2),

4.30 (dd, $J_{2,3}$ = 1.9, $J_{3,4}$ = 8.1, H-3), 4.10 (m, H-2′), 3.76 (s, 3-OMe), 3.45 (s, 4-COOMe), 3.27 (ABd, $J_{10'A,10'B}$ = 13.0, H_A-10′), 2.66 (ddd, $J_{4,5}$ = 11.4, 3.3, H-4), 2.35 (ABq, H_B-10′), 2.3−1.2 (m, H_2-3′,5,5′,6,6′, H-4′), 1.09 (s, H_3-8′), 0.83 (s, H_3-9′). Anal. Calcd for $C_{19}H_{30}O_5S$: C, 61.59; H, 8.16. Found: C, 61.87; H, 8.06.

(3*S*,4*R*,R_S)-1-[(1*S*)-Isoborneol-10-sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (18A_R): mp 73−74 °C; $[\alpha]^{25}_D$ +35 (*c* = 0.013, $CHCl_3$); ^{1}H NMR δ 6.55 (br s, H-2), 4.29 (dd, $J_{2,3}$ = 1.9, $J_{3,4}$ = 8.0, H-3), 4.10 (m, H-2′), 3.75 (s, 3-OMe), 3.46 (s, 4-COOMe), 3.20 (ABd, $J_{10'A,10'B}$ = 13.0, H_A-10′), 2.73 (ddd, $J_{4,5}$ = 11.3, 3.3, H-4), 2.37 (ABq, H_B-10′), 2.3−1.2 (m, H_2-3′,5,5′,6,6′, H-4′), 1.09 (s, H_3-8′), 0.83 (s, H_3-9′); ^{13}C NMR δ 174.0 (CO), 144.3 (C-1), 127.7 (C-2), 77.0 (C-2′), 76.0 (C-3), 57.1 (3-OMe), 53.8 (C-10′), 52.1 (COO*Me*), 51.5 (C-1′), 48.8 (C-7′), 45.6 and 45.1 (C-4,4′), 38.4 (C-3′), 30.9 and 27.2 (C-5′,6′), 24.5 (C-6), 21.7 (C-5), 20.5 and 19.9 (C-8′,9′). Anal. Calcd for $C_{19}H_{30}O_5S$: C, 61.59; H, 8.16. Found: C, 61.49; H, 8.11.

(3*S*,4*S*,S_S)-1-[[(*S*)-2-Hydroxy-1-phenylethyl]sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (16B_S): oil; $[\alpha]^{25}_D$ +200 (*c* = 0.001, $CHCl_3$); ^{1}H NMR (CD_3CN) δ 7.4−7.3 (5H, Ph), 6.25 (dd, $J_{2,3}$ = 4.6, $J_{\text{long range}}$ 1.1, H-2),[27] 4.22 (split ABd, $J_{1',2'}$ = 5.6, $J_{2'A,2'B}$ = 11.7, H_A-2′), 4.11 (split ABd, H_B-2′), 4.01 (t, $J_{3,4}$ = 4.6, H-3), 3.96 (t, H-1′), 3.63 (s, 3-OMe), 3.04 (s, COOMe), 2.62 (ddd, $J_{4,5}$ = 13.5, 3.6, H-4), 2.8−1.9 (m, H_2-5,6); ^{13}C NMR δ 172.3 (CO), 145.6 (C-1), 132.4, 129.1, 129.0 and 128.8 (Ph), 128.5 (C-2), 72.0 (C-3), 68.4 (CHSO), 64.6 (CH_2-OH), 57.2 (3-OMe), 51.8 (COO*Me*), 44.4 (C-4), 21.9 (C-6), 19.1 (C-5); FAB-MS *m*/*z* 339 (M + 1, 7), 137 (100), 77 (54). Anal. Calcd for $C_{17}H_{22}O_5S$: C, 60.33; H, 6.56. Found: C, 60.39; H, 6.48.

(3*S*,4*S*,S_S)-1-[[(*S*)-2-Hydroxy-2-phenylethyl]sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (16C_S): oil; $[\alpha]^{25}_D$ +53 (c = 0.002, $CHCl_3$); ^{1}H NMR (C_6D_6) δ 7.4−7.1 (m, Ph), 6.81 (dd, $J_{2,3}$ = 4.5, $J_{\text{long range}}$ = 1.6, H-2), 5.29 (dd, $J_{1'A,2'}$ = 10.2, $J_{1'B,2'}$ = 1.8, H-2′),[28] 3.85 (t, $J_{3,4}$ = 4.3, H-3), 3.40 (s, 3-OMe), 3.03 (s, COOMe), 2.77 (split ABd, $J_{1'A,1'B}$ = 13.7, H_A-1′), 2.24 (split ABd, H_B-1′), 2.12 (ddd, $J_{4,5}$ = 12.8, 2.9, H-4), 2.0−1.2 (m, H_2-5,6); ^{13}C NMR δ 172.2 (CO), 144.8 (C-1), 141.8, 128.8, 128.2 and 125.6 (Ph), 127.4 (C-2), 72.3 (C-3), 69.0 (CHOH), 57.7 (3-OMe), 56.8 (CH_2SO), 51.8 (COO*Me*), 45.0 (C-4), 22.8 (C-6), 19.4 (C-5); FAB-MS *m*/*z* 339 (M + 1, 5), 137 (83), 77 (100). Anal. Calcd for $C_{17}H_{22}O_5S$: C, 60.33; H, 6.56. Found: C, 60.25; H, 6.48.

(3*S*,4*S*,S_S)-1-[(1*S*)-Isoborneol-10-sulfinyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (16A_S): mp 120−122 °C; $[\alpha]^{25}_D$ +80 (*c* = 0.005, $CHCl_3$); ^{1}H NMR δ 6.80 (d, $J_{2,3}$ = 4.0, H-2), 4.22 (t, $J_{3,4}$ = 4.0, H-3), 4.02 (m, H-2′), 3.74 (s, 3-OMe), 3.43 (s, 4-COOMe), 3.45 (ABd, $J_{10'A,10'B}$ = 13.5, H_A-10′), 2.81 (ddd, $J_{4,5}$ = 11.5, 4.0, H-4), 2.73 (ABq, H_B-10′), 2.5−1.1 (m, H_2-3′,5,5′,6,6′, H-4′), 1.07 (s, H_3-8′), 0.85 (s, H_3-9′); ^{13}C NMR δ 172.4 (CO), 144.3 (C-1), 129.0 (C-2), 75.8 (C-2′), 72.8 (C-3), 57.9 (3-OMe), 51.9 (COO*Me*), 51.5 (C-1′), 51.1 (C-10′), 49.2 (C-7′), 44.5 and 44.1 (C-4,4′), 40.8 (C-3′), 31.2 and 27.4 (C-5′,6′), 21.7 (C-6), 20.4 and 20.2 (C-8′,9′), 19.7 (C-5); FAB-MS *m*/*z* 372 (M + 2, 22), 371 (M + 1, 100), 353 (12). Anal. Calcd for $C_{19}H_{30}O_5S$: C, 61.59; H, 8.16. Found: C, 61.75; H, 8.16.

(3*R*,4*R*)-1-[(1*S*)-Isoborneol-10-sulfonyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (20A). *m*-CPBA carefully dried over P_2O_5 (99 mg 80%, 0.46 mmol) was dissolved in CH_2Cl_2 (4.25 mL) and slowly added to a solution of an equimolar amount of the adduct **15A$_R$** in CH_2Cl_2 (4.25 mL) at room temperature. When oxidation appeared complete by TLC (after 1 h about), anhydrous KF (140 mg) was added and the mixture stirred overnight. After filtration, the evaporation of the solvent under reduced pressure gave the sulfonylcyclohexene **20A** (140 mg, 78%), which did not need any purification: mp 91−93 °C; $[\alpha]^{25}_D$ +70 (c = 0.012, $CHCl_3$); ^{1}H NMR δ 7.08 (br d, $J_{2,3}$ = 4.4, H-2), 4.23 (t, $J_{3,4}$ = 4.4, H-3), 4.16 (dd, $J_{2',3'}$ = 8.0, 4.1, H-2′), 3.76 (s, 3-OMe), 3.45 (s, 4-COOMe), 3.40 (ABd, $J_{10'A,10'B}$ = 13.5, H_A-10′), 2.81 (ABd, H_B-10′), 2.7−1.1 (m, H_2-3′,5,5′,6,6′, H-4,4′), 1.07 (s, H_3-8′), 0.82 (s, H_3-9′); ^{13}C NMR δ 172.0 (CO), 143.6 (C-1), 134.4 (C-2), 76.3 (C-2′), 72.5 (C-3), 58.2 (3-OMe), 51.9 (COO*Me*), 51.4 (C-10′), 50.7 (C-1′), 49.2 (C-7′), 44.2 and 43.5 (C-4,4′), 39.0 (C-3′), 30.4 and 27.5 (C-5′,6′), 23.7 (C-6), 20.6 and 19.9 (C-8′,9′), 19.2 (C-5). Anal. Calcd for $C_{19}H_{30}O_6S$: C, 59.04; H, 7.82. Found: C, 58.96; H, 7.79.

(3*S*,4*S*)-1-[(1*S*)-Isoborneol-10-sulfonyl]-3-methoxy-4-(methoxycarbonyl)cyclohexene (21A). 21A was obtained (80%) by *m*-CPBA oxidation of the adduct **16A$_S$**, as reported above: oil; $[\alpha]^{25}_D$ −120 (*c* = 0.005, $CHCl_3$); ^{1}H NMR δ 7.06 (br d, $J_{2,3}$ = 4.1, H-2), 4.23 (t, $J_{3,4}$ = 4.1, H-3), 4.16 (dd, $J_{2',3'}$ = 7.9, 4.1, H-2′), 3.76 (s, 3-OMe), 3.45 (s, 4-COOMe), 3.34 (ABd, $J_{10'A,10'B}$ = 13.4, H_A-10′), 2.82 (ABd, H_B-10′), 2.7−1.1 (m, H_2-3′,5,5′,6,6′, H-4,4′), 1.07 (s, H_3-8′) 0.82 (s, H_3-9′); ^{13}C NMR δ 172.0 (CO), 143.8 (C-1), 134.2 (C-2), 76.2 (C-2′), 72.5 (C-3), 58.2 (3-OMe), 51.9 (COO*Me*), 51.5 (C-10′), 50.8 (C-1′), 49.3 (C-7′), 44.2 and 43.5 (C-4,4′), 39.1 (C-3′), 30.5 and 27.5 (C-5′,6′), 23.6 (C-6), 20.5 and 19.9 (C-8′,9′), 19.2 (C-5). Anal. Calcd for $C_{19}H_{30}O_6S$: C, 59.04; H, 7.82. Found: C, 59.01; H, 7.77.

***m*-CPBA Oxidation of Diene 2A$_R$ and DA Cycloaddition of the Obtained (*E*)-3-[(1*S*)-Isoborneol-10-sulfonyl]-1-methoxybuta-1,3-diene (19A) to Methyl Acrylate in CH_2Cl_2 and in the Presence of $ZnCl_2$.** The sulfonyl diene **19A** was obtained in almost quantitative yield by *m*-CPBA oxidation of diene **2A$_R$**, following the procedure reported above and submitted, without isolation,[29] to DA cycloaddition: thus, $ZnCl_2$ (57 mg, 0.42 mmol) was added to a solution of diene **19A** (159 mg, 0.53 mmol) and methyl acrylate (0.28 mL, 3.1 mmol) in CH_2Cl_2 (2 mL) under stirring at room temperature. The reaction mixture was stirred further on, until the diene totally disappeared, as verified by TLC monitoring. After evaporation of the solvent under vacuum, the crude mixture was column chromatographed, eluting with petrol/EtOAc (80:20), and the mixture of adducts analyzed by ^{1}H NMR: the *endo*/*exo* ratio, established from the relative intensities of the vinyl proton signals (multiplets at δ 7.1 for *endo* and 6.9 ppm for *exo* adducts), was 10:1, the two *endo* adducts **20A** and **21A** being present in equal amounts.

Acknowledgment. Financial support from the MURST of Italy is gratefully acknowledged. We also would like to thank Dr. S. M. A. Jafari for sharing preliminary results.

Supporting Information Available: Experimental procedure and spectral characterization for 1-sulfinyl-1,3-butadienes **4A$_R$** and **5A$_R$**, IR data of compounds **1B**, **1C**, **2A**, **2B$_S$**, **3A**, **3B$_S$**, **6**, **7**, **12**−**14**, **15A$_R$**, **16B$_S$**, **16C$_S$**, **20A**, and **21A**, detailed procedures for DA reactions of dienes **2A$_R$**, **2A$_S$**, **2B$_S$**, **2C$_S$,** and **3A$_R$** and related extended Table 2, and copies of ^{1}H and ^{13}C NMR spectra of dienes **2A$_R$**, **2A$_S$**, **2B$_S$**, **2C$_R$**, **2C$_S$**, **3A$_R$**, **3A$_S$**, **3B$_S$**, **3C$_R$**, **3C$_S$**, **4A$_R$**, and **5A$_R$** (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO962286P

(27) H-2 Multiplets of minor adducts appear at δ 6.16 (**15B$_S$**), 5.98 (**17B$_S$**), and 6.07 (**18B$_S$**).

(28) H-2′ Multiplets of minor adducts appear at δ 5.35 (**15C$_S$**), 5.53 (**17C$_S$**), and 5.43 (**18C$_S$**).

(29) NMR characterization of sulfonyl diene **19A**: δ 7.06 (d, $J_{1,2}$ = 12.7, H-1), 6.00 and 5.75 (two s, H_2-4), 5.58 (d, H-2), 4.19 (ddd, $J_{2',3'}$ = 8.1, 4.0 Hz, $J_{2',OH}$ = 4.0 Hz, H-2′), 3.70 (s, OMe), 3.36 (ABd, $J_{10'A,10'B}$ = 13.5 Hz, H_A-10′), 2.87 (ABd, H_B-10′), 3.31 (d, OH), 1.8−0.8 (m, H_2-3′,5′,6′, H-4′), 1.06 (s, H_3-8′), 0.81 (s, H_3-9′), 153.4 (C-1), 146.0 (C-3), 120.1 (C-4), 96.7 (C-2), 76.3 (C-2′), 57.0 (OMe), 52.1 (C-10′), 51.7 (C-1′), 50.0 (C-7′), 44.1 (C-4′), 39.0 (C-3′), 30.3 and 27.5 (C-5′,6′), 20.5 and 19.8 (C-8′,9′).