

## Control of Stereochemistry by Sulfoxide Chirality in Diels-Alder Reactions of 1-Methoxy-3-alkylsulfinylbutadienes

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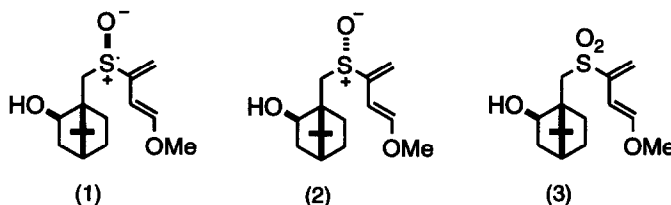
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**Abstract:** Cycloadditions of methyl acrylate to ( $R_S$ )- and ( $S_S$ )-(E)-3-[(1*S*)-isobornyl-10-sulfinyl]-1-methoxy-but-1,3-dienes in dichloromethane, catalysed by lithium perchlorate or zinc chloride, proceeded with complete regioselectivity and high stereoselectivity. Chirality at sulfur controlled diastereofacial selectivity.

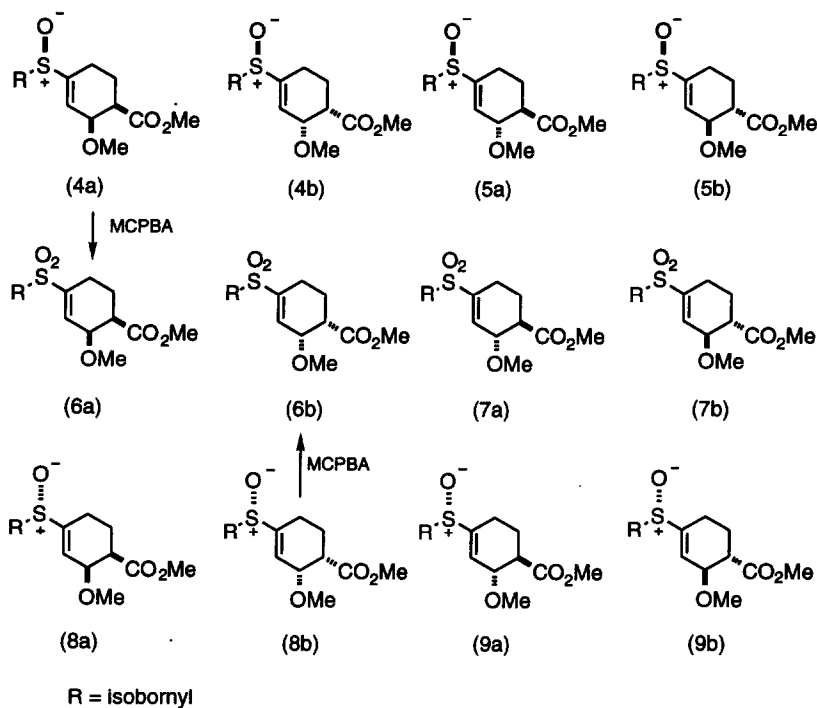
Control over asymmetric induction in Diels-Alder cycloadditions is a matter of continuing interest.<sup>1</sup> For this purpose the use of enantiopure dienophiles has found particular favour, but enantiopure dienes have received less attention.<sup>2</sup> Sulfoxides as chiral auxiliaries in enantiopure dienophiles have met with notable success in promoting asymmetric induction,<sup>3</sup> but their influence as chiral auxiliaries in sulfinyldienes has not been reported, although both 1- and 2-sulfinyldienes are available in non-racemic form.<sup>4</sup> We recently reported that ( $R_S$ )- and ( $S_S$ )-(E)-3-[(1*S*)-isobornyl-10-sulfinyl]-1-methoxy-but-1,3-dienes (1) and (2) may be readily constructed from 10-mercaptoisoborneol.<sup>5</sup> In this letter we reveal that they undergo Lewis acid-catalysed cycloaddition to methyl acrylate highly regioselectively and stereoselectively.



The results of uncatalysed and catalysed cycloaddition of the ( $R_S$ )-diene (1) with methyl acrylate are collected in the Table. As expected,<sup>6</sup> the combined directing effects of the 1- and 3-substituents in the diene (1) ensured that cycloaddition occurred with complete regioselectivity. The endo (4a+4b) and exo (5a+5b) isomers could be separated by simple chromatography, and all four isomers were separable by HPLC.<sup>7</sup> The composition of the mixture of four diastereoisomers was determined by proton NMR spectroscopy, the endo-exo ratio (4a+4b):(5a+5b) being established from the relative intensities of the vinyl proton signals, which were well separated, and the ratio of (4a):(4b) and of (5a):(5b) from the relative intensities of the lower field portion of the AB spectrum associated with the methylene group adjacent to sulfur.<sup>8</sup>

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. Cycloadditions in dichloromethane with all the catalysts, except one, proceeded in poor yield because of attendant decomposition of the diene. The best catalyst was lithium perchlorate, the use of which as a suspension in dichloromethane gave only the endo isomers (4a) and (4b) in 70% yield in the ratio 96:4. This is the first illustration that lithium perchlorate suspended in dichloromethane catalyses Diels-Alder reactions,<sup>9</sup> and that it can do so highly stereoselectively. Reetz and Fox<sup>10</sup> have shown that Mukaiyama aldol reactions and conjugate additions were more efficiently catalysed in this way than by 5M lithium perchlorate in diethyl ether, conditions which were previously advocated for the dramatic acceleration of Diels-Alder reactions.<sup>11</sup>



Crystallization of (4a+4b) from ethyl acetate-light petroleum gave the optically pure diastereoisomer (4a),<sup>7</sup> the absolute configuration of which was established by X-Ray crystallographic analysis (Figure 1). This result also confirmed the configurations at sulfur in the dienes (1) and (2), which were previously assigned on the basis of properties relating to intramolecular hydrogen bonding.<sup>5</sup>

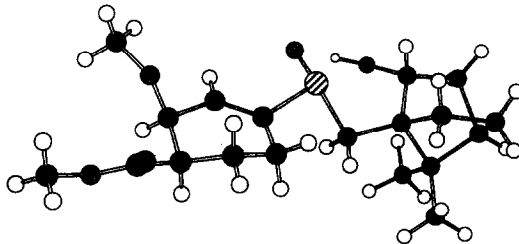


Figure 1

Zinc chloride catalysed reaction of the sulfonyldiene (3) with methyl acrylate in dichloromethane provided the endo-adducts (6a+6b) and exo-adducts (7a+7b) in the ratio 10:1. The ratio (6a):(6b) was 1:1, which indicated

that the chirality of the isobornyl moiety had no significant influence on diastereofacial selectivity. Under identical conditions, endo addition of methyl acrylate to the ( $S_S$ )-sulfinyldiene (2) proceeded with complete diastereofacial selectivity to give the adduct (8b), together with exo adducts (9a+9b). The endo-exo ratio was 89:11, but the ratio (9a):(9b) was not established. The adduct (8b), obtained pure by chromatography, gave on oxidation the sulfone (6b), whilst the sulfone (6a) was obtained by oxidation of the sulfoxide (4a), the configuration of which had been firmly established (Figure 1). These reactions confirmed that chirality at sulfur in both (1) and (2) controlled diastereofacial selectivity.

**Table**  
Cycloadditions of diene (1) with methyl acrylate

Catalyst	Solvent	Temp °C	Time	Yield%	Endo/exo ratio <sup>†</sup>	Diastereofacial selectivity.	
						Endo <sup>#</sup>	Exo <sup>§</sup>
None	None	25	16h	55	85:15	63:37	55:45
BF <sub>3</sub> ·Et <sub>2</sub> O	None	25	6h	47	83:17	65:35	69:31
Et <sub>2</sub> AlCl	CH <sub>2</sub> Cl <sub>2</sub>	-20	10d	28	93:7	70:30	63:37
EtAlCl <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	25	24h	10	93:7	73:27	
MgBr <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	25	20h	30	97:3	75:25	
ZnCl <sub>2</sub>	None	0	20h	71	95:5	83:17	58:42
ZnCl <sub>2</sub>	CH <sub>2</sub> Cl <sub>2</sub>	25	20h	30	99:1	94:6	
LiClO <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub>	25	7h	70	100:0	96:4	

<sup>†</sup> (4a+4b):(5a+5b); <sup>#</sup> (4a):(4b); <sup>§</sup> (5b):(5a)

The stereochemical control of cycloaddition exerted by configuration at sulfur in the dienes (1) and (2) may be rationalized in terms of mutual co-ordination of the metal with sulfinyl oxygen and carbonyl oxygen in transition state structures such as A and B respectively, in which the isobornyl group is subject to minimal steric compression (Figure 2).

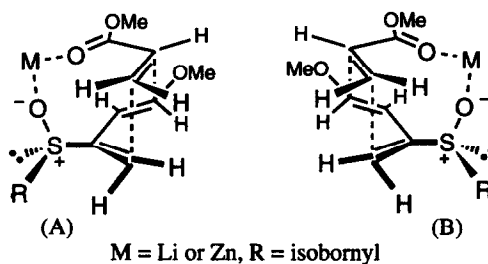


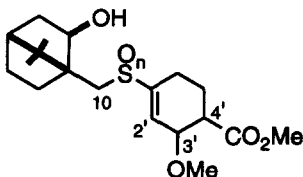
Figure 2

The manifold synthetic transformations of vinyl sulfoxides<sup>3a,12</sup> and vinyl sulfones,<sup>13</sup> coupled with the high degree of stereocontrol exhibited by these lithium perchlorate catalysed cycloadditions are encouraging indications that enantiopure 2-sulfinyldienes may fulfil a useful role in enantioselective synthesis.

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## References and Notes

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7. Pure samples of (4a) and (4b) were also obtained by crystallization of the mixture from ethyl acetate-light petroleum.
8. All new compounds were characterized by IR, <sup>1</sup>H NMR, and MS or elemental analysis. Selected data, (specific rotations in CHCl<sub>3</sub>; <sup>1</sup>H NMR at 300 MHz in CDCl<sub>3</sub>; R<sub>f</sub> refers to ethyl acetate-light petroleum 1:1): (4a) m.p. 112-114 °C, [α]<sub>D</sub>+130 (c, 0.008), [R<sub>f</sub> = 0.4]; δ 6.71 (1H, d, J = 4Hz, 2'-H), 4.20 (1H, t, J = 4Hz, 3'-H), 3.14 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.71 (1H, ddd, J = 3, 4, and 12Hz, 4'-H), 2.43 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (4b) m.p. 193-195 °C, [α]<sub>D</sub>-138 (c, 0.004), [R<sub>f</sub> = 0.4]; δ 6.72 (1H, d, J = 4Hz, 2'-H), 4.19 (1H, t, J = 4Hz, 3'-H), 3.24 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.65 (1H, ddd, J = 4, 4, and 12Hz, 4'-H), 2.38 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (5a) m.p. 73-74 °C, [α]<sub>D</sub>+35 (c, 0.013); [R<sub>f</sub> = 0.5]; δ 6.55 (1H, brs, 2'-H), 4.29 (1H, dd, J = 2 and 8Hz, 3'-H), 3.20 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.73 (1H, ddd, J = 3, 8, and 11Hz, 4'-H), 2.37 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (5b) m.p. 68-69 °C, [α]<sub>D</sub>-223 (c, 0.013); [R<sub>f</sub> = 0.5]; δ 6.55 (1H, brs, 2'-H), 4.30 (1H, dd, J = 2, 8Hz, 3'-H), 3.27 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.66 (1H, ddd, J = 3, 8, and 11Hz, 4'-H), 2.35 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (6a) m.p. 91-93 °C, [α]<sub>D</sub>+70 (c, 0.012); [R<sub>f</sub> = 0.5]; δ 7.08 (1H, d, J = 4Hz, 2'-H), 4.23 (1H, t, J = 4Hz, 3'-H), 3.40 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.81 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (6b) oil, [α]<sub>D</sub>-120 (c, 0.005); [R<sub>f</sub> = 0.5]; δ 7.06 (1H, d, J = 4Hz, 2'-H), 4.23 (1H, t, J = 4Hz, 3'-H), 3.34 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.82 (1H, AB, J = 13Hz, H<sub>B</sub>-10); (8b) m.p. 120-122 °C, [α]<sub>D</sub>+80 (c, 0.005); [R<sub>f</sub> = 0.4]; δ 6.80 (1H, d, J = 4Hz, 2'-H), 4.22 (1H, t, J = 4Hz, 3'-H), 3.45 (1H, AB, J = 13Hz, H<sub>A</sub>-10), 2.81 (1H, ddd, J = 4, 4, and 12Hz, 4'-H), 2.73, (1H, AB, J = 13Hz, H<sub>B</sub>-10).



9. Lithium perchlorate in diethyl ether-dichloromethane (presumably in solution) has been used previously to catalyse cycloadditions of dienophilic sulfinyl maleates to cyclopentadiene, with moderate diastereofacial selectivity (ref. 3b).
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