Diels−Alder Cycloadditions of Ethyl 2-Carbomethoxyethenesulfinates with Cyclopentadiene. Lewis Acid Enhancement and Adduct Identification with the Assistance of Competitive Stereodifferentiating Iodolactonization and Iodosultinization Reactions

Yvonne Lear and Adrian L. Schwan*,†

Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry, Department of Chemistry and Biochemistry, University of Guelph, Guelph, ON, Canada, N1G 2W1

Received July 6, 1999

Ethyl (*Z*)-2-carbomethoxyethenesulfinate (**1**) and ethyl (*E*)-2-carbomethoxyethenesulfinate (**2**) were each subjected to cyclopentadiene (ca. 3 equiv) in order to determine their reactivity in Diels−Alder reactions. Thermal reactions proceeded in less than 4 h, while Lewis Acid enhanced reactions were substantially faster and demonstrated greater selectivity. In particular, the $BF_3{\cdot}Et_2O$-mediated cycloaddition of **1** gave syn/endo cycloadduct **3a** as a major diastereomer in about 90% yield. The reactions of **2** were less synthetically useful. The structures of the cycloadducts were established through a combination of X-ray crystal structure determinations and through exposure of the compounds to an electrophilic iodine reagent. Each cycloadduct underwent an iodocyclization reaction with either the carboxylic ester or the sulfinate ester participating in the formation of a polycyclic lactone or sultine, respectively. The iodocyclization reactions allowed further elucidation of the cycloadduct structures.

Introduction

The development of a vast array of activating groups on dienophiles continues to sustain the synthetic value of the Diels−Alder reaction.[1,2] Sulfur-containing functionalities are important entries on the list of useful substituents, mostly due to the electron-withdrawing effects of sulfones and sulfoxides.[3] However, there is rapid growth regarding the Diels−Alder chemistry of addends bearing sulfur acid functionalities. For instance, the Metz group[4,5] and others[6−8] have demonstrated a number of examples of intramolecular Diels−Alder reactions of diene tethered 1-alkenesulfonic esters[4,7,8] and amides.[5,6] A thorough study in this area has led to useful synthetic chemistry, both in a general sense and with respect to specific targets.[4] A number of studies of the intermolecular Diels−Alder chemistry of sulfonic ester derivatives have been described.[9]

The accounts of Diels−Alder chemistry of unsaturated sulfinic acid derivatives are more limited. Lee and coworkers have shown that cyclohexyl 1-alkynesulfinate esters undergo Diels−Alder reaction with a variety of dienes,[10] while the Schwan group has recently disseminated the first examples of the intramolecular Diels−Alder chemistry of diene tethered 1-alkenesulfinic esters.[11] Intermolecular Diels−Alder reactions of 1-alkenesulfinic acid derivatives have not been reported although the concept can be seen as having extensive utility in organosulfur chemistry. As shown in a general sense in Scheme 1, simple manipulation of the product of such a cycloaddition can provide access to cyclohexenes bearing an array of sulfur functional groups. For instance, both sulfoxides and sulfones are accessible after functional group adaptation of the 1-alkenesulfinate ester. Similarly, if cyclization is followed by reduction,[12]

* To whom correspondence should be addressed. Tel: (519) 824-4120 ext 8781. Fax: (519) 766-1499. E-mail: SCHWAN@CHEMBIO.UOGUELPH.CA.

(1) Dell, C. P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3873−3905.

(2) (a) McClure, C. K.; Hansen, K. B. *Tetrahedron Lett.* **1996**, *37*, 2149−2152. (b) Crowley, P. J.; Percy, J. M.; Stansfield, K. *Tetrahedron Lett.* **1996**, *37*, 8237−8240. (c) Byeon, C.-H.; Chen, C.-Y.; Ellis, D. A.; Hart, D. J.; Li, J. *Synlett*, **1998**, 596−598. (d) Johnson, C. R.; Kadow, J. F. *J. Org. Chem.* **1987**, *52*, 1493−1500. (e) Garcia Ruano, J. L.; Estaban Gamboa, A.; Martin Castro, A. M.; Rodriguez, J. H. *J. Org. Chem.* **1998**, *63*, 3324−3332. (f) Sieburth, S. McN.; Lang, J. *J. Org. Chem.* **1999**, *64*, 1780−1781.

(3) (a) De Lucchi, O.; Pasquato, L. *Tetrahedron*, **1988**, *44*, 6755−6794. (b) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760. (c) Mikolajcyk, M.; Brabowicz, Kielbasinski, P. *Chiral Sulfur Reagents: Applications in Asymmetric and Stereoselective Synthesis*; CRC Press: Boca Raton, 1997; pp 158−169. (d) Westwell. A. D.; Rayner, C. M. In *Organosulfur Chemistry: Synthetic and Stereochemical Aspects*; Page, P., Ed.; Academic Press: New York, 1998; pp 192−211.

(4) (a) Bovenschulte, E.; Metz, P.; Henkel, G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 202−203. (b) Metz, P.; Fleischer, M. *Synlett* **1993**, 399−400. (c) Metz, P.; Fleischer, M.; Fröhlich, R. *Synlett* **1992**, 985−987. (d) Metz, P.; Fleischer, M.; Fröhlich, R. *Tetrahedron* **1995**, *51*, 711−732. (e) Metz, P.; Cramer, E. *Tetrahedron Lett.* **1993**, *34*, 6371−6374. (f) Metz, P.; Stölting, J.; Läge, M.; Krebs, B. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2195−2197. (g) Meiners, U.; Cramer, E.; Fröhlich, R.; Wibbeling, B.; Metz, P. *Eur. J. Org. Chem.* **1998**, 2073−2078.

(5) Metz, P.; Seng, D.; Fröhlich, R.; Wibbeling, B. *Synlett* **1996**, 741−742.

(6) Brosius, A. D.; Overman, L. E.; Schwink, L. *J. Am. Chem. Soc.* **1999**, *121*, 700−709.

(7) Galley, G.; Pätzel, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2297−2302.

(8) Doye, S.; Hotopp, T.; Winterfeldt, E. *Chem. Commun.* **1997**, 1491−1492.

(9) (a) Lee, A. W. M.; Chan, W. H. Jiang, L. S.; Poon, K. W. *Chem. Commun.* **1997**, 611−612. (b) Chan, W. H.; Lee, A. W. M.; Jiang, L. S.; Mak, T. C. W. *Tetrahedron: Asymmetry* **1997**, *8*, 2501−2504. (c) Jiang, L. S.; Chan, W. H.; Lee, A. W. M. *Tetrahedron* **1999**, *55*, 2245−2262. (d) Klein, L. L.; Deeb, T. M. *Tetrahedron Lett.* **1985**, *26*, 3935−3938.

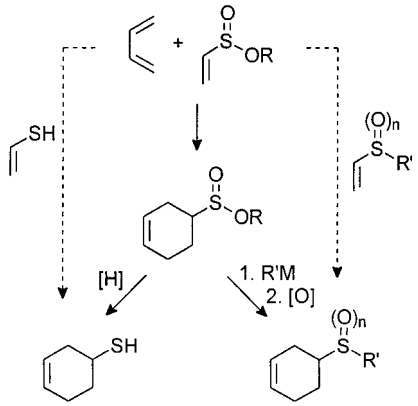
(10) Chan, W. H.; Lee, A. W. M. Lee, K. M *J. Chem. Res., Synop.* **1994**, 138−139.

(11) Schwan, A. L.; Snelgrove, J. L.; Kalin, M. L.; Froese, R. D. J.; Morokuma, K. *Org. Lett.* **1999**, *1*, 487−489.

(12) (a) Hanson, G.; Kemp, D. S. *J. Org. Chem.* **1981**, *46*, 5441−5443. (b) Dittmer, D. C.; Henion, R. S.; Takashina, N. *J. Org. Chem.* **1969**, *34*, 1310−1316.

10.1021/jo991082g CCC: $18.00
Published on Web 10/07/1999

Scheme 1



the 1-alkenesulfinate ester demonstrates its ability to act as an equivalent to an enethiol. This latter example is particularly intriguing, since the electron-deficient sulfinate is expected to accelerate cycloadditions with electron-rich dienophiles, while the thiol is known as an electron-releasing group. Furthermore, only a selected number of enethiols are known, and those are detectable only under special circumstances.[13]

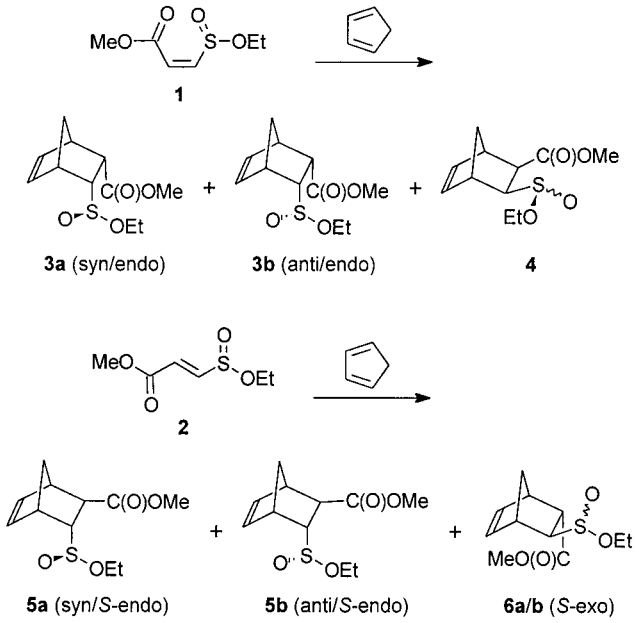
Finally, electronic evidence suggests[14,15] that the sulfinate group may be a better electron-withdrawing substituent than a sulfoxide, and if so, HOMO(diene)/LUMO(dienophile)-controlled cycloadditions involving sulfinates may be expected to be more rapid than the analogous chemistry of sulfoxides. This paper documents the initial results of our study pertaining to intermolecular cycloadditions of 1-alkenesulfinate esters with emphasis on product identification and on the responsiveness of our system toward Lewis acids.

Results and Discussion

Identification of Cycloadducts. General frontier MO theory and previous work in our laboratory suggest that 1-alkenesulfinate esters bearing a second electron-withdrawing functionality would be expected to react at a practically useful rate. Hence, the two compounds chosen for this study were 2-carbomethoxy-1-alkenesulfinate esters **1** and **2** (Scheme 2). Their general method of preparation has been previously outlined,[14] although improvements to the method have led to improved yields.[16]

Each of the compounds was reacted with excess cyclopentadiene in CH_2Cl_2 at 40 °C for a period of 1 h. The reactions were complete and relatively clean with cyclopentadiene dimer as the lone byproduct. *Z*-Dienophile **1** afforded three of a possible four diastereomers, with two of the products dominating the reaction mixture. Products **3a** and **3b** could be readily isolated and purified, but the minor constituent **4** was lost during the purification procedure.[17,18] The cycloaddition of dienophile **2** with cyclopentadiene produced four diastereomers, with little selectivity. Purification attempts led to the isolation of pure fractions **5a** and **5b**, while components **6a** and **6b** were exceedingly difficult to separate. On one occasion, a small fraction of pure **6a** was obtained (Table 1).

Scheme 2



Of the cycloadducts isolated, syn/endo isomer **3a**[19] exhibited highly crystalline character, and its structure could be secured by X-ray crystallographic analysis.[20] The identification of the other fractions could not be achieved through analysis of NMR spectra; the hydrogens α to the carboxylic ester and to the sulfinate functionality were very similar in the ^{1}H NMR spectra, allowing no means to initiate assignments of the observed resonances. To gain more information about the structure of the individual cycloadducts, we subjected them to halocyclization conditions typically employed to induce ester attack of the remote alkene.[21] The hope was that at the very least, the configuration of the carboxylic ester group in the various cycloadducts could be elucidated.

Cycloadducts **3a** and **3b** were individually treated with $CF_3CO_2^-Ag^+/I_2$/DME/rt[21a] to produce major products in each case (Scheme 3). The crude ^{1}H NMR reaction mixtures were inspected for the absence of a methoxy resonance near 3.7 ppm, characterizing the iodolacton-

(13) Le Nocher, A.-M.; Metzner, P. *Tetrahedron Lett.* **1992**, *33*, 6151−6154.

(14) Schwan, A. L.; Strickler, R. R.; Lear, Y.; Kalin, M. L.; Rietveld, T. E.; Xiang, T.-J.; Brillon, D. *J. Org. Chem.* **1998**, *63*, 7825−7832.

(15) Oxner, O. In *Correlation Analysis in Chemistry: Recent Advances*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; Chapter 10.

(16) See the Supporting Information for the improved experimental procedures.

(17) The minor product in the cycloaddition mixture of dienophile **1** was assigned the structure of a cycloadduct on the basis of its GC retention time in relation to adducts **3** and on the basis of a GC−mass spectrum of the material. Its MS fragments were comparable to its isomeric cycloadducts. The sulfinyl configuration of **4** could not be finalized.

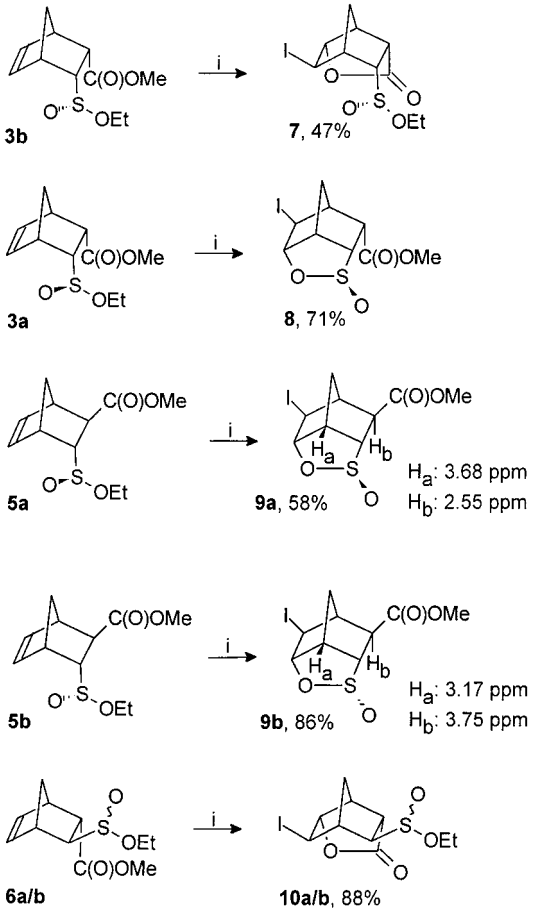
(18) In Scheme 2, we have labeled the products of the cycloadditions with their proper stereochemistry. It should be noted that at the time of the reactions, the structures of the products was not known and they were only ascertained with the aid of X-ray analysis and iodocyclization experiments. We feel release of all of our information in this mode gives the smoothest presentation, although the data is not presented in the sequence consistent with discovery.

(19) We adopt the nomenclature system based on configurational assignments as has been employed for sulfoxides; see ref 2a. When the S−OEt bond is positioned parallel to the bridgehead C−H bond on the same side of the molecule, the sulfinyl oxygen is either under the bicycle (syn) or is extended away from the molecule (anti).

(20) ORTEP diagrams of compounds **3a** and **8** and other pertinent X-ray data are part of the Supporting Information.

(21) (a) Cha, C.-K.; Lee, S.-J.; Tseng, W.-H. *Tetrahedron Lett.* **1997**, *38*, 2725−2728. (b) Alonso, I.; Cid, M. B.; Carretero, J. C.; García Ruano, J. L.; Hoyos, M. A. *Tetrahedron: Asymmetry* **1991**, *2*, 1193−1207.

Scheme 3



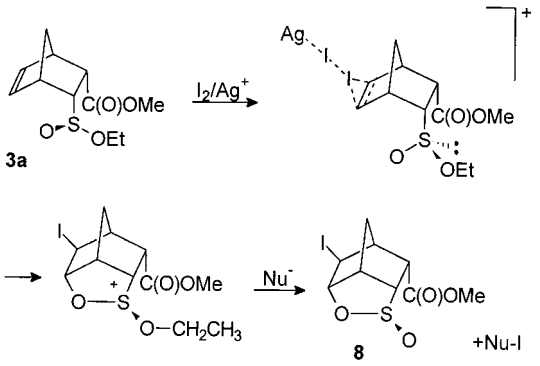
Reagents: i) $AgOC(O)CF_3$, I_2, DME, rt.

ization reaction and the probable formation of a lactone. Indeed, this was observed for the reaction of **3b** where lactone **7** was the product, but the methoxy resonance was still present in the reaction mixture of **3a**. Rather, to our surprise, the ethyl group of sulfinate **3a** was lost, suggesting that the *sulfinate ester had participated in an iodocyclization reaction*. The product of that mixture was crystalline and X-ray analysis confirmed that sultine **8** was obtained.[20,22]

The iodocyclization experiments of **3a**/**b** confirm that cycloadducts **3** both possess the endo configuration and in combination with the X-ray structural assignment of **3a**, **3b** must be the sulfur epimer of **3a**. Scheme 4 suggests a mechanism for the iodocyclization of sulfinate **3a**, a reaction that should be named an *iodosultinization*. The confident assignment of structures **3a** and **8** allow us to suggest that in the cyclization of the sulfinate, it is the sulfinyl oxygen that attacks the activated carbon atom on the opposite side of the ring and not the ethoxy oxygen. Hence, after the ethyl group is lost from the sulfonium salt, the result is a sultine possessing a sulfinyl group with the opposite configuration of the starting sulfinate.

The stereodivergent character of these iodocyclization reactions can be rationalized through analysis of molec-

Scheme 4



ular models of epimers **3**. In **3a**, as shown in Scheme 4, alignment of the sulfinyl oxygen for participation in cyclization leads to the positioning of the ethoxy group anti to the existing bicycle thereby minimizing steric barriers to cyclization. However, if one arranges sulfinate **3b** to a conformation suitable for iodosultinization, a severe steric interaction between the ethoxy group and the existing endo carboxylic ester moiety makes that conformation highly unfavorable and iodosultinization impossible. The steric barrier to lactonization is substantially less when the sulfinate group reverts to a less hindered conformation and the cyclization of **3b** proceeds by participation of the carboxylic ester. Steric barriers are well recognized for the different configurations of sulfoxides,[23] but this appears to be the first example of bifurcating chemical reactions created by the different steric needs of two epimers of a sulfinate ester.

Similar iodocyclizations were performed on cycloadducts **5a** and **5b** and on a mixture of products **6**. In these instances, the loss of either an ethyl or a methyl group would again indicate which of the esters occupied the endo position. In the reactions, **5a** and **5b** each lost their ethyl group to afford sultines **9a** and **9b**, while both products **6** lost their methyl groups on conversion to lactones **10**. Thus, compounds **6** possessed the endo carboxylic ester and the exo sulfinate esters. Neither cycloadducts **6** nor their corresponding lactones **10** were differentiated any further.

Isomers **9** were clearly products of iodosultinization, and were certainly epimers at sulfur but the experiments performed to this point did not allow any more precise assignments. As the only difference in these compounds was their configuration at sulfur, it was decided that a thorough NMR analysis of the isomers may prove valuable. With the assistance of COSY and HSQC NMR experiments, all of the ^{13}C and ^{1}H NMR resonances of **9a** and **9b** could be assigned. It was previously shown that hydrogens occupying a 1,3 syn-diaxial relationship with S−O bonds in five- and six-membered cyclic sultines exhibit a chemical shift considerably downfield from hydrogens that engage similar structural connectivity but do not possess the 1,3 diaxial arrangement.[24,25]

On the basis of this knowledge, Ha and Hb of sultines **9** were chosen for particular comparisons (Scheme 3). Ha in **9a** clearly rests in a 1,3-diaxial relationship with the

(22) All of the iodocyclization reactions proceeded cleanly to afford a lone product except for the **3b** to **7** conversion. In that reaction, a byproduct was noted by TLC and by ^{1}H NMR analysis of the crude mixture, but it could not be isolated. Analysis of that NMR suggested that the substrate had incorporated a methoxyethyl unit presumably by solvent (DME) intervention in the usual mode of cyclization.

(23) (a) Kosugi, H.; Ku, J. Kato; M. *J. Org. Chem*. **1998**, *63*, 6939−6946. (b) Alayrac, C.; Fromont, C.; Metzner, P.; Trong Anh, N. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 371−374.

(24) (a) Harpp, D. N.; Gleason, J. G. *J. Org. Chem*. **1971**, *36*, 1314−1316. (b) Sharma, N. K.; de Reinach-Hirtzbach, F.; Durst, T.; *Can. J. Chem*. **1976**, *54*, 3012−3025. (c) Durst, T.; Huang, J. C.; Sharma, N. K.; Smith, D. J. H. *Can. J. Chem*. **1978**, *56*, 512−516.

Table 1. Diels-Alder Reactions of Cyclopentadiene and 1 (Scheme 2)

no.	Lewis acid[a]	time	endo (**3a**:**3b**)/exo[b]	total yield[c] (%)
1	none	1 h, 40 °C	14 (1.1:1):1	98 (98)
2	none	4 h	18 (1.3:1):1	(87)
3	$BF_3{\cdot}Et_2O$	5 min	45 (11:1):1	100
4	$ZnBr_2$	30 min	38 (0.90:1):1	100 (93)
5	Et_2AlCl	30 min	23 (1.9:1):1	90
6	$Yb(OTf)_3$	30 min	23 (1.9:1):1	86
7	$MgBr_2$	30 min	27 (1.5:1):1	94
8	$TiCl_4$	100 min	25 (0.67:1):1	49[d]
9	ZnI_2	40 min	23 (1.6:1):1	94
10	$SnCl_4$	5 min	34 (1.0:1):1	100
11	$ZnCl_2$	15 min	34 (1.4:1):1	100

[a] Experiments were carried out with 1.2 equiv of Lewis Acid at room temperature except where noted. [b] Ratios were determined by GC analysis. [c] GC yields, isolated yields are in parentheses. [d] Decomposition occurred.

Table 2. Diels-Alder Reactions of Cyclopentadiene and 2 (Scheme 2)

no.	Lewis acid[a]	time	S-endo (**5**)/(syn:anti) (**5a**:**5b**)	S-exo (**6**)[b] (ratio)	total yield[c] (%)
1	none	1 h, 40 °C	**1.6** (1:1.4)	**1** (1.6:1)	97
2	none	24 h	**1.7** (1:1.3)	**1** (1.5:1)	82
3	$BF_3{\cdot}Et_2O$	18 h	**1.6** (1:1.4)	**1** (1.6:1)	(85)
4	$ZnBr_2$	5 min	**2.8** (1:1.1)	**1** (1.2:1)	95 (83)
5	Et_2AlCl	15 min	**2.5** (1:1.0)	**1** (1.3:1)	100
6	$Yb(OTf)_3$	80 min	**1.4** (1:1.1)	**1** (1.3:1)	100
7	$MgBr_2$	50 min	**1.1** (1:1.2)	**1** (1.6:1)	100
8	$TiCl_4$	5.5 h	**0.75** (1:1.1)	**1** (2.0:1)	69[d]
9	ZnI_2	2 h	**2.4** (1:1.2)	**1** (1.2:1)	100
10	$SnCl_4$	24 h	**1.6** (1.3:1)	**1** (1.3:1)	34[d]
11	$ZnCl_2$	2 h	**2.4** (1:1.1)	**1** (1.3:1)	98

[a] Experiments were carried out with 1.2 equiv of Lewis Acid at room temperature except where noted. [b] Ratios were determined by ^1H NMR analysis. [c] GC yields, isolated yields are in parentheses. [d] Decomposition occurred.

S−O bond in the five-membered sultine, while Ha in **9b** does not. On the other hand, Hb in **9b** exists in a similar 1,3-relationship, as part of a seven-membered ring, and Hb of **9a** does not. Hence, the observed ^1H NMR chemical shifts of Ha = 3.68 ppm for **9a** and Ha = 3.17 ppm for **9b** are consistent with the sulfinyl configurations as shown. The chemical shifts of Hb provide equally supportive data since Hb of **9b** resonates at 3.75 ppm while Hb = 2.55 ppm in **9a**.

Given the mode of involvement of the sulfinyl unit in the iodosultinization reactions of Scheme 4, one can now infer the structures of cycloadducts **5a** and **5b**, based on their respective products of iodosultinization. The sulfur inversion during cyclization demands that **5a** has the syn arrangement of its sulfinyl unit while **5b** possesses the opposite sulfur stereochemistry.[26]

Lewis Acid Enhancements and Modes of Cycloaddition. The thermal reaction of **1** with cyclopentadiene afforded endo cycloadducts **3a** and **3b** (93% total) as a mixture of configurations at the sulfur center. The thermal reaction at room temperature increased selectivity somewhat, but the extended duration of the reaction led to reduced overall yield (Table 1). The structure of diester **1** and the observed reaction behavior to this point prompted investigation with Lewis acids. Several reactions were performed employing an array of Lewis acids.[27] The chosen additives increased the endo/exo (i.e., **3**:**4**) product ratio to >23:1 while in most cases the sulfur epimer ratio remained close to 1. However, the use of $BF_3{\cdot}Et_2O$ was particularly noteworthy as it provided the largest **3**:**4** ratio of 45:1 and moreover, it induced a ratio of 11:1 for the pair of endo adducts. Indeed the overall yield of the single isomer **3a** was found to be 90%.

The cycloaddition chemistry of **2** was somewhat less satisfying, as both the thermal reactions and those in the presence of Lewis Acids did not provide synthetically useful ratios of products (Table 2). In all trials, four diastereomers were obtained and among the pairs of endo and exo isomers, there was little preference of either configuration of sulfur. The best endo:exo (e.g., **5**:**6**) ratio that could be attained was using $ZnBr_2$. There was substantial decomposition in the $TiCl_4$-influenced reactions of **1** and **2**.

Clearly sulfinate **1** is a more accommodating dienophile in that it affords cleaner reaction mixtures which favor primarily one or two isomers and **1** is more responsive to rate-accelerating and stereoselectivity-enhancing capabilities of several Lewis acids. The endo:exo selectivity exhibited by **1** in its reaction with cyclopentadiene is only slightly less than that reported for the same reaction of bifunctional dienophiles menthyl (*Z*)-(S)$_S$-3-(2-pyridylsulfinyl)propenoate[28] and methyl (*Z*)-3-phenylsulfinylpropenoate,[29] and it compares favorably to that of methyl (*Z*)-(R)$_S$-3-phenylsulfinyl propenoate.[30] On the other hand, although the cycloadducts resulting from **2** form in less synthetically useful ratios, the endo/exo selectivity of **2** is nevertheless superior to that of methyl (*E*)-3-phenylsulfinylpropenoate.[29]

The highly stereoselective formation of **3a** is consistent with sulfinate **1** assuming an s-trans conformation for cycloaddition (Figure 1a). This conformation has been invoked previously to account for observed selectivity in the cycloaddition of related vinylic sulfoxides bearing *E*-carboxylic esters. The s-trans arrangement is preferred as it minimizes unfavorable steric and dipole−dipole interactions of the two polar functionalities.[31] As a monodentate Lewis acid,[32] $BF_3{\cdot}Et_2O$ would be expected to coordinate to one of the two ester groups of **1** and enhance both dipolar and steric repulsions, thereby ensuring that **1** assumes the s-trans orientation. The

(25) The broad applicability of the syn-diaxial rule has been called into question in one instance. Ottenheijm and co-workers (Liskamp, R. M. J.; Zeegers, H. J. M.; Ottenheijm, H. C. J. *J. Org. Chem*. **1981**, *46*, 5408−5413) suggest that the rule is not applicable for five-membered sultines bearing pseudoaxial or pseudoequatorial substituents since those researchers did not observe any chemical shift differences of the appropriate hydrogens. We believe the rigid character of our polycycles satisfactorily allows the intended application of the syn-diaxial effect.

(26) Additional, though less compelling, evidence in support of the relative assignments of **9a** and **9b** comes from the behavior of cyclic, epimeric sulfoxides. The sulfoxide isomer possessing the less hindered sulfinyl unit has been shown to elute slower on TLC, due to increased accessibility for association with the absorbent (Siegl, W. O.; Johnson, C. R. *J. Org. Chem*. **1970**, *35*, 3657−3663). We observe the same tendency with sultines **9a**/**b**.

(27) Experiments were run with 3 equiv of freshly distilled cyclopentadiene. Reaction temperature was room temperature unless otherwise noted; lower temperatures did not improve the selectivity of the Lewis acid mediated reactions. 1.2 equiv of Lewis acid were employed as lesser amounts were less effective.

(28) Arai, Y.; Hayashi, Y, Yamamoto, M.; Takayama, H.; Koizumi, T. *Chem Lett.*, **1987**, 185−186.

(29) Proust, S. M.; Ridley, D. D. *Aust. J. Chem*. **1984**, *37*, 1677−1688.

(30) Maignan, C.; Guessous, A.; Rouessac F. *Tetrahedron Lett.* **1984**, *25*, 1727−1728.

(31) Koizumi, T.; Arai, Y.; Takayama, H.; Kuriyama, K.; Shiro, M. *Tetrahedron Lett.* **1987**, *28*, 3689−3692.

(32) Tou, J. S.; Reusch, W. *J. Org. Chem*. **1980**, *45*, 5012−5014.

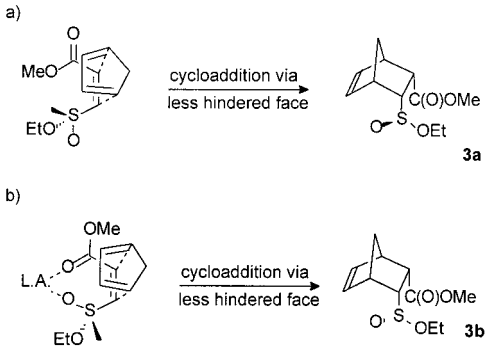
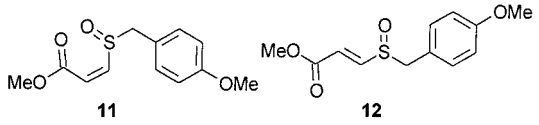


Figure 1. Cycloaddition modes of dienophile **1** and cyclopentadiene. (a) From s-trans configuration to give major product **3a**. (b) From s-cis configuration to give minor product **3b.**

double simultaneous coordination of both sulfinyl and carbonyl oxygens that is expected with bidentate Lewis acids, such as those based on Zn or Ti[33] does not lead to much preference during the cycloaddition. Such a conformation would afford **3b** (as depicted in Figure 1b), rather than the major product, **3a.**

Final Experiments and Conclusions. As a means to directly compare the reactivity of sulfinates **1** and **2** with sulfoxides, competition experiments were performed employing the sulfoxides from which **1** and **2** were generated. Thus in the same mixture, sulfinate **1** and sulfoxide **11** were allowed to react competitively with cyclopentadiene. Similarly, sulfinate **2** and its synthetic precursor, sulfoxide **12** were reacted. In each case it was found that 2.3−2.5 times more adducts containing the sulfinate group were isolated. These simple experiments clearly indicate that the α,β-unsaturated sulfinate moiety is more prone to Diels−Alder cycloaddition than an α,β-unsaturated sulfoxide by a factor of >2.5.[34,35]



The experiments described herein indicate that the sulfinate group, like the sulfoxide, demonstrates a stronger preference for the endo position than does the carboxylic ester moiety. It is not known whether this preference is caused by stronger 2[re] orbital effects in the transition state for cycloaddition or whether it is induced by some other, as yet unidentified force.[36]

A search of the chemical literature indicates that there is only one previous report of a halogen-induced attack of a double bond by an intramolecularly disposed sulfinate ester. That work involves the bromination of a series of allenyl sulfinate esters.[37] It is hoped that the iodosultinization reaction introduced herein holds more general character, and represents a lead to an array of useful halosultinization reactions. Indeed the cyclization demonstrates how a sulfur functionality can assist in the regiospecific oxidation of a remote double bond. Furthermore, use of the iodosultinization in a context similar to that presented here represents a new reaction for the construction of oxa- (and thia-) cage compounds.[38]

Experimental Section

The general experimental methods and procedures have been described previously.[14] The preparation of dienophiles **1** and **2** is part of the Supporting Information. The preparation of sulfoxides **11** and **12** have been published elsewhere.[14]

Reactions of 1 with Cyclopentadiene under Lewis Acid Conditions. A solution of the sulfinate ester **1** (60.0 mg, 0.337 mmol), cyclopentadiene (85.0 μL, 1.01 mmol), and a Lewis acid (0.404 mmol) in dry CH_2Cl_2 was stirred until TLC showed the disappearance of the sulfinate ester. The mixture was then washed with $NaHCO_3$(aq), water, and brine and was dried ($MgSO_4$). After solvent evaporation, the reaction mixture was analyzed by GC to determine isomer ratios; yield was obtained by calibration against an added internal standard of naphthalene (yields and ratios are given in Tables 1 and 2). When Lewis acids were employed, 1.2 equiv of the Lewis acid was introduced to the mixture at the beginning. Products were isolated by flash chromatography on silica gel (20% EtOAc in hexane) in some instances. Spectral data are presented in products' order of elution. The third isomer present was detected only by GC/MS.

Cycloadduct 3a: mp 63−64 °C; ^{1}H NMR($CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 3H), 1.42 (d, J = 8.9 Hz, 1H), 1.60 (dt, J = 8.9, 1.8 Hz, 1H), 3.28 (br s, 1H), 3.38 (dd, J = 9.1, 3.2 Hz, 1H), 3.38 (m, 1H), 3.47 (dd, J = 9.1, 3.4 Hz, 1H), 3.66 (s, 3H), 3.90−4.10 (m, 2H), 6.25 (dd, J = 5.6, 2.9 Hz, 1H), 6.48 (dd, J = 5.6, 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.7, 45.7, 47.1, 47.9, 49.2, 51.8, 65.4, 72.4, 134.7, 136.3, 172.2. Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.60. Found: C, 54.30; H, 6.46.

Cycloadduct 3b: ^{1}H NMR($CDCl_3$) δ 1.38 (t, J = 7.1 Hz, 3H), 1.42 (d, J = 8.9 Hz, 1H), 1.56 (dt, J = 8.9, 1.8 Hz, 1H), 3.28 (br s, 2H), 3.42 (dd, J = 9.2, 3.1 Hz, 1H), 3.47 (dd, J = 9.2, 3.1 Hz, 1H), 3.69 (s, 3H), 4.06−4.16 (m, 2H), 6.28 (dd, J = 7.3, 2.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.9, 46.5, 46.6, 47.7, 49.2, 52.0, 64.3, 73.4, 134.1, 136.0, 172.5; Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.60. Found: C, 54.24; H, 6.49.

Reaction of 2 with Cyclopentadiene under Lewis Acid Conditions. A solution of the sulfinate ester **2** was treated as described above of **1**. The reaction mixture was analyzed by GC with an internal standard of naphthalene to determine yield and by ^{1}H NMR to determine the isomer ratios (yields and ratios are given in Tables 1 and 2). Products were isolated by flash chromatography on silica gel and/or by centrifugal chromatography (Chromatotron, 20% EtOAc in hexane).

Cycloadduct 5a: ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.54 (d, J = 9.0 Hz, 1H), 1.75 (d, J = 9.0 Hz, 1H), 2.30 (dd, J = 3.1, 1.3 Hz, 1H), 3.14 (m, 1H), 3.31 (m, 1H), 3.75 (s, 3H), 3.75 (dd, J = 3.9, 4.2 Hz, 1H), 3.98−4.06 (m, 2H), 6.32, (s, 2H); ^{13}C NMR ($CDCl_3$) δ 15.7, 43.9, 44.9, 46.8, 47.9, 52.3, 64.5, 70.9, 135.3, 138.1, 173.4. Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H 6.60. Found: C, 53.50; H, 6.44.

Cycloadduct 5b: ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3H), 1.53 (dd, J = 9.0, 1.7 Hz, 1H), 1.72 (d, J = 9.0 Hz, 1H),

(33) Arai, Y.; Kuwayama, S.-I.; Takeuchi, Y.; Koizumi, T. *Tetrahedron Lett.* **1987**, *28*, 6205−6206.

(34) By its design, the experiment requires that the addend reacting faster also gets consumed sooner. Thus even though equal concentrations of reactants are present at the outset, the course of the competition gives an advantage to the more sluggish reactant, as it will slowly gain a concentration advantage over the faster reactant. Therefore, the measured ratio of adducts represents the *minimum* rate difference between the two competitors.

(35) In the competition experiments, the peaks attributable to sulfinate and sulfoxide cycloadducts could be identified and quantified by ^{1}H NMR. Diels−Alder reactions of **11** and **12** with cyclopentadiene had been performed independently and the major products from those reactions were obtained. Hence we were able to confidently identify and quantify all the peaks in the competition experiments. See the Supporting Information for data concerning the sulfoxide cycloadditions.

(36) We have performed preliminary studies of the thermal and Lewis acid enhanced cycloadditions of ethyl ethenesulfinate with cyclopentadiene. Reactions are substantially longer (e.g., refluxing CH_2Cl_2, 20 days), and the mixtures seem to be prone to decomposition. Our investigations with less substituted 1-alkenesulfinates are continuing.

(37) Braverman, S.; Reisman, D. *Tetrahedron Lett.* **1977**, 1753−1756.

(38) Wu, H.-J.; Chao, C.-S.; Lin, C.-C. *J. Org. Chem.* **1998**, *63*, 7687−7693.

2.67 (dd, J = 4.4, 1.7 Hz, 1H), 3.18−3.20 (m, 2H), 3.73 (s, 3H), 3.82 (dd, J = 4.4, 3.5 Hz, 1H), 4.08−4.11 (m, 2H), 6.10 (dd, J = 5.6, 2.7 Hz, 1H), 6.33 (dd, J = 5.6, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.9, 44.1, 44.8, 47.1, 47.8, 52.3, 64.2, 71.2, 135.0, 137.8, 173.6. Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.60. Found: C, 54.11; H, 6.73.

Cycloadduct 6a: ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 3H), 1.46 (dd, J = 9.0, 1.4 Hz, 1H), 1.82 (d, J = 9.0 Hz, 1H), 3.08 (dd, J = 4.5, 1.9 Hz, 1H), 3.15 (m, 1H), 3.29 (m, 1H), 3.44 (dd, J = 4.1, 4.1 Hz, 1H), 3.67 (s, 3H), 4.06−4.16 (m, 2H), 6.13 (dd, J = 5.4, 2.6 Hz, 1H), 6.30 (dd, J = 5.4, 3.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 43.1, 44.3, 45.4, 46.6, 52.0, 64.8, 66.7, 136.4, 137.0, 172.9. Anal. Calcd for $C_{11}H_{16}O_4S$: C, 54.08; H, 6.60. Found: C, 54.24; H, 6.75.

Cycloadduct 6b: (data based on analysis of isomer mixtures) ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.53 (d, J = 9.0 Hz, 1H), 1.73 (d, J = 9.0 Hz, 1H), 3.01−3.04 (m, 2H), 3.30 (m, 1H), 3.35 (m, 1H), 3.66 (s, 3H), 4.03−4.13 (m, 2H), 6.11 (dd, J = 5.6, 2.6 Hz, 1H), 6.28 (dd, J = 5.6, 3.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 43.1, 43.9, 46.0, 47.2, 52.0, 64.2, 67.4, 136.3, 137.3, 172.8.

Typical Procedure for Iodocyclization Reactions. Iodine (57.4 mg, 0.226 mmol) was added to a solution of cycloadduct **3a** (50.0 mg, 0.205 mmol) in DME (5 mL). CF_3COOAg (49.9 mg, 0.226 mmol) was added and the mixture stirred for 20 h. The mixture was diluted with EtOAc (5 mL), and the resulting precipitate was filtered and washed with additional EtOAc (5 mL). The organic extracts were washed with $Na_2S_2O_3$(aq), water, and brine and dried over $MgSO_4$. After solvent evaporation, flash chromatography on silica gel (EtOAc) afforded **8** (50.0 mg, 71%) as a white crystalline solid.

Iodocyclization of cycloadduct 3a to sultine 8: mp 155.0−155.5 °C (darkens 130−133 °C); ^{1}H NMR ($CDCl_3$) δ 1.97 (dt, J = 11.6, 1.3 Hz, 1H), 2.55 (dt, J = 11.6, 1.5 Hz, 1H), 2.88 (m, 1H), 3.25 (dd, J = 11.0, 3.9 Hz, 1H), 3.61 (dd, J = 11.0, 4.3 Hz, 1H), 3.70 (m, 1H), 3.75 (s, 3H), 4.24 (d, J = 2.8 Hz, 1H), 5.51 (d, J = 5.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.6, 36.4, 46.3, 47.6, 48.0, 52.4, 70.2, 97.7, 169.5. Anal. Calcd for $C_9H_{11}IO_4S$: C, 31.59; H, 3.24. Found: C, 31.73; H, 3.40.

Iodocyclization of cycloadduct 3b to lactone 7: mp 142−144 °C (darkens 130−135 °C); 47% yield; ^{1}H NMR($CDCl_3$) δ 1.40 (t, J = 7.1 Hz, 3H), 1.90 (d, J = 11.8 Hz, 1H), 2.51 (d, J = 11.8 Hz, 1H), 2.98 (dd, J = 10.5, 3.3 Hz, 1H), 3.17 (m, 1H), 3.24 (dd, J = 10.5, 3.3 Hz, 1H), 3.41 (m, 1H), 4.12−4.24 (m, 2H), 4.45 (d, J = 2.7 Hz, 1H), 5.23 (d, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 23.7, 37.1, 38.4, 48.3, 49.0, 66.4, 69.3, 88.6, 174.7; HRMS(CI) calcd for $C_{10}H_{14}IO_4S$ 356.96576, found 356.96670.

Iodocyclization of cycloadduct 5a to sultine 9a: oil; 58% yield; ^{1}H NMR ($CDCl_3$) δ 2.10 (d, J = 11.8 Hz, 1H), 2.47 (dd, J = 11.8, 1.4 Hz,1H), 2.55 (dd, J = 3.5,1.4 Hz, 1H), 2.94 (br s, 1H), 3.65−3.73 (m, 1H), 3.77 (s, 3H), 3.78 (d, J = 2.8 Hz, 1H), 3.88 (dd, J = 3.8, 3.9 Hz, 1H), 5.44 (d, J = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 30.0, 34.9, 45.0, 46.5, 49.2, 53.0, 71.5, 96.3, 170.5; HRMS(EI) calcd for $C_9H_{11}IO_4S$ 341.94228, found 341.94120.

Iodocyclization of cycloadduct 5b to sultine 9b: oil; 86% yield; ^{1}H NMR ($CDCl_3$) δ 1.97 (d, J = 11.7 Hz, 1H), 2.31 (dd, J = 11.7, 1.5 Hz, 1H), 3.01 (br, 1H), 3.17 (m, 1H), 3.75 (s, 4H), 3.99 (d, J = 2.6 Hz, 1H), 4.22 (dd, J = 4.8, 2.3 Hz, 1H), 5.16 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.5, 36.3, 41.0, 48.1, 51.5, 52.8, 67.2, 98.3, 171.6; HRMS(EI) calcd for $C_9H_{11}IO_4S$ 341.94228, found 341.94120.

Iodocyclization of cycloadducts 6a/b to lactones 10a/b: oil; 88% yield of a mixture of isomers. *Major isomer*: ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 1H), 1.38 (t, J = 7.1 Hz, 3H), 2.29 (s, 1H), 3.03 (s, 2H), 3.24−3.26 (m, 2H), 3.88 (d, J = 1.7 Hz, 1H), 4.12−4.18 (m, 2H), 5.15 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 27.5, 34.4, 37.4, 45.8, 48.0, 65.0, 68.8, 88.4, 176.2; HRMS(EI) calcd for $C_{10}H_{13}IO_4S$ 355.95793, found 355.95739. Minor isomer: ^{1}H NMR ($CDCl_3$) δ 1.40 (t, J = 7.1 Hz, 3H), 2.17 (d, J = 12.2 Hz, 1H), 2.42 (d, J = 12.2 Hz, 1H), 3.03 (s, 2H), 3.18 (s, 1H), 3.26−3.30 (m, 1H), 3.89 (s, 1H), 4.15−4.19 (m, 2H), 5.18 (d, J = 4.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.8, 27.0, 35.2, 39.5, 46.2, 47.6, 64.8, 69.6, 88.5, 175.5.

Acknowledgment. The authors gratefully acknowledge the Petroleum Research Fund, administered by the American Chemical Society, and NSERC of Canada for generously funding this research. The authors thank Prof. George Ferguson for acquisition of the X-ray crystal structures.

Supporting Information Available: Selected experimental procedures and spectral data for certain compounds, ORTEP diagrams, X-ray data, and copies of NMR spectra of compounds **2**, **5a**, **7**, **9a**,**b**, and **10a/b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991082G