Face Selectivity in Diels-Alder Reactions of Chiral Dienes Containing Allylic Substituents

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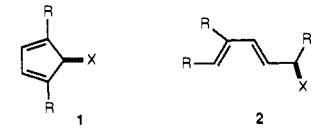
Abstract: Face selectivity in Diels-Alder reactions of six dienes of general structure **3** and **4** was examined. These dienes were chosen as models for conformationally locked 1(*E*)-substituted 1,3-dienes containing a center of chirality at the allylic position. In all cases but one, cycloaddition occurred preferentially from the diene face anti to the allylic substituent (see Table I). Cycloaddition of the hydroxy-substituted diene **8a** with *N*-phenylmaleimide (NPM) occurred with a weak syn preference in toluene, but with an anti preference in other solvents. Thus, no evidence for a syn directing effect of an allylic heteroatom substituent whose origin is other than hydrogen bonding was found. These results demonstrates that the syn cycloaddition preferences observed with many 5-heterosubstituted 1,3-cyclopentadienes will *not* extrapolate to 1,3-dienes containing 1(*E*)-allylic substituents. This difference is easily rationalized by the fact that the substituent of a 1(*E*)-substituted 1,3-diene is spatially close to the dienophile in the syn-endo transition state (see Figure 3), while the endo transition state for cycloaddition of a 5-substituted 1,3-cyclopentadiene (see Figure 6) has these groups far apart. The high anti face selectivity ($\Delta\Delta G^{\ddagger} > 2$ kcal/mol) observed in cycloadditions of dienes with vinyl sulfinyl or allylic ether substitution is attributed to nonbonded electrostatic interactions and will be useful in the design of facially selective Diels-Alder reactions.

The importance of the Diels-Alder reaction in organic synthesis derives in large part from its ability to generate two carbon-carbon σ bonds and up to four contiguous stereogenic centers in one synthetic operation.[2] The stereochemistry elaborated at the termini of the new σ bonds evolves from the stereochemistry of the diene and dienophile and the topography (endo or exo) of the cycloaddition. A third stereochemical feature arises when either of the cycloaddends possesses two different reactive faces, often by virtue of containing at least one center of chirality. This issue of facial stereoselectivity has attracted significant recent attention, primarily within the context of asymmetric organic synthesis.[2b]

A number of reports demonstrate that a single allylic heteroatom substituent on either a dienophile[2,3] or diene[3a,4-12] can control diastereofacial selectivity in intermolecular Diels-Alder reactions. A majority of the dienes studied to date fall into two classes: 5-substituted 1,3-cyclopentadienes **1**[8-12] and chiral acyclic 1,3-dienes **2** containing allylic oxygen or nitrogen substitution.[4-7] With



X = OH, OMe, OAc, Cl, Br, I, $SiMe_3$, NH_2, NHAc, SMe, SOMe, SO_2Me X = OR, NHCOOR

the former diene class, cycloaddition often[8-10,12] though not exclusively[10-12] occurs from the more sterically hindered face syn to the 5-substituent when this group is an electronegative heteroatom. A variety of models have been advanced for rationalizing diastereofacial selectivity in Diels-Alder cycloadditions; these include simple steric effects,[2,6,13] van der Waals-London attractions,[10] various orbital interactions,[7,12,14,15] torsional effects,[16] and most recently electrostatic interactions.[17]

The rational use of allylic substituents in the design of facially selective Diels-Alder reactions for organic synthesis requires both better calibration on the magnitude of allylic substituent effects as well as further insight into the origin of these effects. It is risky to extrapolate the results from 5-substituted 1,3-cyclopentadienes to other diene types because of the cyclic nature of these dienes and the special electronic interactions[14,18] that are possible. In this paper, we report the results of a study of facial selectivity in Diels-Alder cycloadditions of dienes of general structures **3** and **4**. These dienes were chosen for two reasons: (1) they have

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(2) (a) See, for example, Desimoni, G.; Tacconi, G.; Bario, A.; Pollini, G. P. *Natural Product Syntheses Through Pericyclic Reactions*; ACS Monograph 180; American Chemical Society: Washington, DC, 1984; Chapter 5. (b) For recent reviews, see: Paquette, L. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Chapter 7. Wurziger, H. *Kontakte (Darmstadt)* **1984**, 3. Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, 876.

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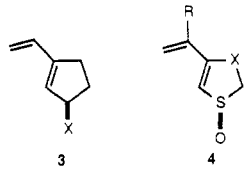
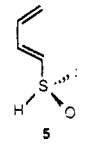


3 4

allylic substituents that are external to the diene π system (i.e. they are models for 1(*E*)-substituted 1,3-dienes) and (2) the 5-membered ring removes the conformational ambiguity that arises in interpreting results obtained with acyclic dienes such as **2**. The sulfinyl dienes were included in this investigation, since a recent computational study[19] had suggested that electrostatic effects[17] would favor reaction of a sulfinyl diene held in the conformation illustrated by structure **5** from the face syn to the sulfoxide oxygen.



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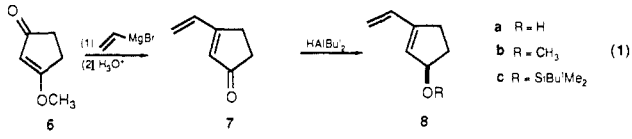
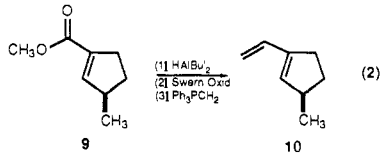
Results

Preparation of Dienes. The oxygenated dienes **8** and 3-methyl-1-vinylcyclopentene (**10**) were obtained from 3-methoxy-2-cyclopentenone (**6**) and the known ester **9**[20] by conventional sequences (see eq 1 and 2). The sulfinyl diene **16** was prepared



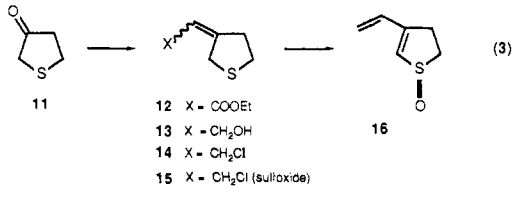
a R = H
b R = CH_3
c R = $SiBu^tMe_2$

(1)



(2)

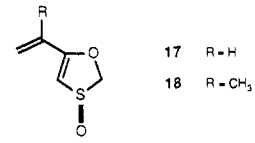
from tetrahydrothiophen-3-one (**11**) by the five-step sequence outlined in eq 3. Condensation of **11** with sodium triethyl



12 X = COOEt
13 X = CH_2OH
14 X = CH_2Cl
15 X = CH_2Cl (sulfoxide)

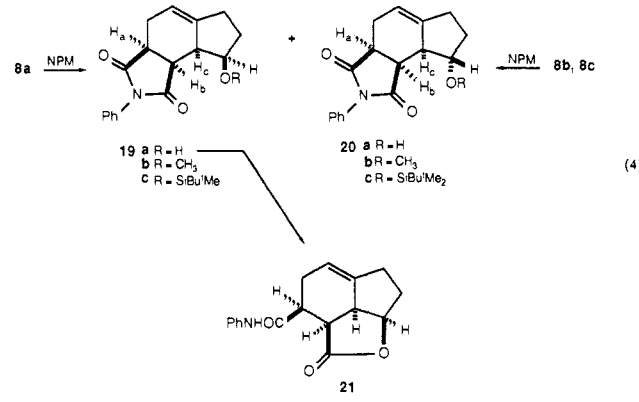
(3)

phosphonoacetate followed by reduction with diisobutylaluminum hydride at −78 °C provided a mixture of stereoisomeric allylic alcohols **13** in >90% overall yield. Conversion to the corresponding allylic chlorides[21] followed by oxidation at sulfur with sodium periodate provided sulfoxides **15** in 75% yield from **13**. Elimination to the desired diene **16** was then accomplished in 64% yield by treatment of **15** with 0.95 equiv of lithium hexamethyldisilazane at −78 °C. That **16** contained the desired 4,5-dihydrothiophene *S*-oxide ring followed from the absence of an ^1H NMR signal at ca. δ 3.6, which is characteristic[22] of the methylene hydrogens of a 2,5-dihydrothiophene *S*-oxide. The preparation of the 5-vinyl-1,3-oxathiol 3-oxides **17** and **18** has been described elsewhere.[23]



17 R = H
18 R = CH_3

Cycloadditions of 5-Substituted 2-Ethenylcyclopentenes. Diene alcohol **8a** reacted with *N*-phenylmaleimide (NPM) at room temperature in toluene to give a 1.8:1 mixture of two initial adducts **19a** and **20a**, respectively (see eq 4). Careful monitoring of this



19 a R = H
b R = CH_3
c R = $SiBu^tMe$

20 a R = H
b R = CH_3
c R = $SiBu^tMe_2$

(4)

21

cycloaddition by HPLC indicated that the ratio of those adducts remained constant from 1 to 5 h, although at long reaction times **19a** was partially converted to the tricyclic lactone **21**. Purification of the crude product mixture on silica gel resulted in the complete conversion of **19a** → **21** and provided pure samples of **20a** and **21** in 28% and 53% yields, respectively.

The facile conversion of **19a** to the tricyclic lactone **21** provides strong chemical evidence that **19a** is the endo adduct formed from addition syn to the hydroxyl group. Tricyclic lactone **21** showed diagnostic absorptions in the infrared spectrum at 3326, 1740, and 1694 cm^{-1} for the NH, the 5-membered ring lactone, and the amide groups, respectively. The minor adduct **20a** is assigned as the endo adduct resulting from anti addition on the basis of the 9-Hz coupling constants observed for J_{ab} and J_{bc}, which are nearly identical with those observed for these hydrogens of **19a** (J_{ab} = 8.6, J_{bc} = 7.8 Hz) as deduced from ^1H NMR analysis of the crude cycloadduct mixture. Molecular models indicate that, according to the Karplus relationship, J_{bc} would be considerably smaller (H_b–H_c dihedral angle ~130°) in an adduct resulting from exo addition.

The face selectivity of the cycloaddition of **8a** with NPM was markedly solvent dependent. Most strikingly, cycloaddition of these components in methanol at room temperature occurred preferentially from the anti face to give **19a** and **20a** in a 1:4 ratio, respectively. A smaller anti preference (1:1.8) was also observed in tetrahydrofuran (THF).

In contrast to **8a**, the diene ethers **8b** and **8c** reacted with NPM at room temperature in toluene to give, in each case, a single isolated adduct: **20b** (73%, 86% based on consumed **8b**) and **20c** (84%). In the former case, 3% of another product could be detected by capillary GC analysis but, because of its similar chromatographic properties to **20b**, could not be isolated. In marked contrast to **8a**, the reaction of diene ether **8b** with NPM proceeded identically in methanol, toluene, or THF. That **20c** resulted from addition anti to the OSi-*t*-$BuMe_2$ group was readily confirmed by cleavage of the silyl ether with aqueous acetic acid to give **20a**. Similarly, **20b** could be correlated with **20a** by methylation of the latter with CH_3I and Ag_2O.

Qualitatively similar results were obtained in the cycloadditions of dienes **8** with tetracyanoethylene (TCNE). Reaction of diene alcohol **8a** with TCNE at room temperature in THF for 2 h, followed by chromatography on silica gel, gave crystalline **22a** in 42% yield along with a mixture of **23a**, tricyclic imidate **24**, and traces of what are believed to be products of an ene reaction

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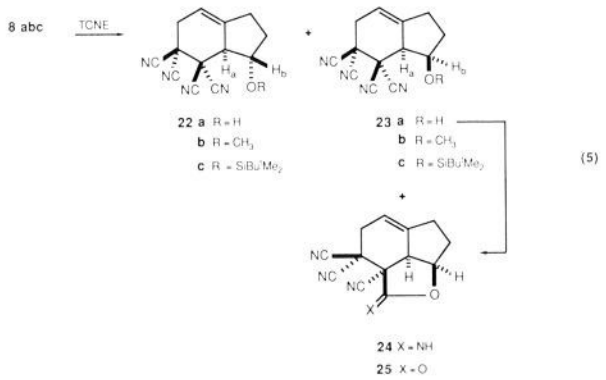
(see eq 5). Further purification of this mixture on silica gel

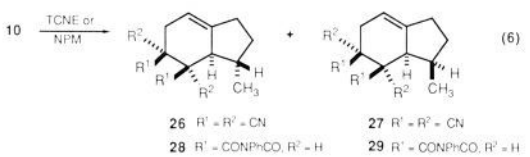


(5)

provided a pure sample of imidate **24**. Imidate **24** showed a broad singlet at δ 7.6 in its ^{1}H NMR spectrum for the NH hydrogen and an apparent triplet (J = 5.1 Hz) at δ 5.18 for the methine hydrogen α to oxygen. Detailed analysis of the 500-MHz ^{1}H NMR spectrum of the crude product mixture (85% mass recovery) revealed the presence of **22a**, **24**, and unstable **23a** in a ratio of 12.5:1.9:1, respectively. Nearly identical ratios of products were produced in cycloadditions carried out in toluene or CH_2Cl_2. Adduct **23a** displayed a characteristic multiplet at δ 4.13 (H_b) in the ^{1}H NMR spectrum and was slowly converted to **24** upon standing at room temperature or upon attempted isolation.

The dienyl silyl ether **8c** reacted with TCNE at room temperature in THF to give a crystalline product mixture in 86% yield, which GLC analysis showed to be a 3:1 mixture of **22c** (mp 121–122 °C) and **23c** (mp 128–129.5 °C), respectively. The stereoselectivity was slightly less in toluene (**22c**:**23c** = 2.2:1). The strong (8–15%) DNOE observed between hydrogens H_a and H_b of the minor isomer **23c** and the corresponding weak (0–2%) DNOE observed between these hydrogens of the major isomer **22c** unambiguously defined the stereochemistry of these adducts. Cleavage of the *tert*-butyldimethylsilyl group of **22c** with aqueous HF in acetonitrile gave **22a** in 86% yield, while treatment of **23c** under similar conditions yielded the tricyclic lactone **25** (C=O 1764 cm^{-1}). In a similar fashion, dienyl ether **8b** underwent cycloaddition with TCNE at room temperature primarily from the anti face to give a 5.6:1 (in THF) or 4.9:1 (in toluene) mixture of adducts **22b** and **23b**, respectively. ^{1}H NMR DNOE experiments similar to those described for the corresponding silyl ether unambiguously defined the stereochemistry of cycloadducts **22b** and **23b**.

Vinylcyclopentene **10** underwent cycloaddition with NPM at room temperature in toluene to give, in 75% yield, a 4.9:1 mixture (by capillary GC analysis) of stereoisomeric adducts **28** and **29**, which could be separated by careful preparative HPLC (see eq 6). Essentially identical stereoselectivity was observed in THF



(6)

(4.6:1) or methanol (5.2:1). The stereochemical assignments for **28** and **29** followed from observation of the methyl doublet of the minor isomer at δ 1.45 in the ^{1}H NMR spectrum, nearly 0.23 ppm downfield of the corresponding signal of **23**. This result is consistent with the methyl group being on the concave face of cycloadduct **29** and thus in the deshielding cone of the proximal carbonyl group. In a similar fashion, cycloaddition of **10** with TCNE at room temperature in THF gave, in 91% yield, a 6.2:1 (4.6:1 in toluene) mixture of adducts **26** and **27**, respectively. Fractional crystallization from hexane provided a pure sample of the major isomer **26**, while a highly enriched sample of **27** could be obtained by preparative GLC. ^{1}H NMR DNOE experiments readily established the stereostructures of **26** and **27**.

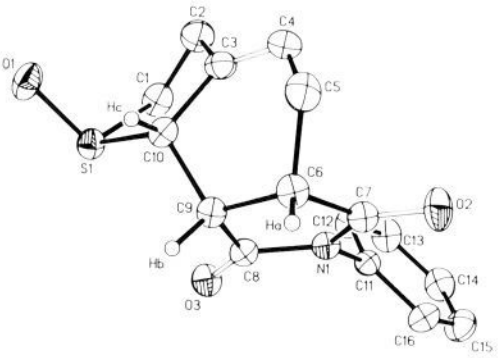


Figure 1.

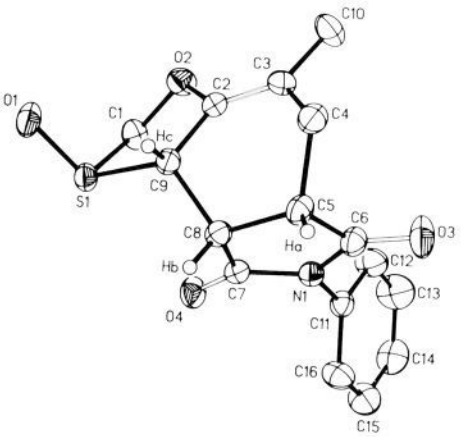
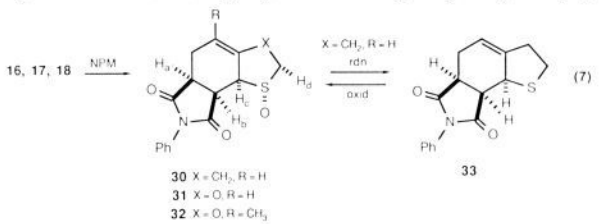


Figure 2.

Cycloadditions of Diene Sulfoxides 16–18. Diene sulfoxides **16–18** underwent cycloaddition with NPM at 70–80 °C in toluene to give in each case a single cycloadduct in good yield (see eq 7).



(7)

Chemical evidence that **30** was the endo adduct resulting from addition anti to the sulfoxide oxygen was obtained by reduction of **30** with P_2I_4[24] to obtain the tetrahydrothiophene derivative **33**. Reoxidation with $NaIO_4$ or *m*-chloroperoxybenzoic acid, reagents known to oxidize sulfides from the sterically less hindered face,[25] afforded **30** as the sole product. This stereochemical result is consistent with the puckered nature of the endo adduct, which is approached by the oxidants only from the convex face. The stereostructure of **30** was ultimately established unambiguously by single-crystal X-ray diffraction and an ORTEP drawing of the molecular model is shown in Figure 1. The boat conformation observed for the central ring in the crystal nicely rationalizes the large coupling constants observed in the ^{1}H NMR spectrum between the bridgehead hydrogens (J_{bc} = 6.4, J_{ab} = 8.9 Hz).

The stereostructure for **31** was initially assigned on the basis of the long-range coupling observed between the bridgehead hydrogen H_c and the cis hydrogen of the methylene group of the oxathiole ring. The signal at lower field (δ 5.14 vs 4.62), which one can confidently assign[26] to the hydrogen cis to the sulfoxide oxygen (H_d), showed a coupling of 1.2 Hz to H_c, consistent with

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Table I. Cycloaddition Selectivity

entry	diene	allyl subst	dienophile	cycloaddition conditions: solvent	temp, °C	stereoselectivity: syn, %	anti, %	$\Delta\Delta G^{\ddagger}$ [a]
1	**10**	CH_3	NPM	toluene	23	17	83[b]	0.93
2	**10**	CH_3	NPM	THF	23	18	82[b]	0.89
3	**10**	CH_3	NPM	CH_3OH	23	16	84[b]	0.98
4	**10**	CH_3	TCNE	toluene	23	18	82[b]	0.89
5	**10**	CH_3	TCNE	THF	23	12	88[b]	1.17
6	**8a**	OH	NPM	toluene	23	64	36[d]	-0.34
7	**8a**	OH	NPM	THF	23	36	64[d]	0.34
8	**8a**	OH	NPM	CH_3OH	23	20	80[d]	0.82
9	**8a**	OH	TCNE	toluene	23	25	75[c]	0.65
10	**8a**	OH	TCNE	THF	23	19	81[c]	0.85
11	**8a**	OH	TCNE	CH_2Cl_2	23	26	74[c]	0.62
12	**8b**	OCH_3	NPM	toluene	23		97[b,e]	>2
13	**8b**	OCH_3	NPM	THF	23		97[b,e]	>2
14	**8b**	OCH_3	NPM	CH_3OH	23		96[b,e]	>1.8
15	**8b**	OCH_3	TCNE	toluene	23	17	83[b]	0.93
16	**8b**	OCH_3	TCNE	THF	23	15	85[b]	1.02
17	**8c**	OSi-*t*-$BuMe_2$	NPM	toluene	23		100[c]	>2
18	**8c**	OSi-*t*-$BuMe_2$	TCNE	toluene	23	31	69[b]	0.47
19	**8c**	OSI-*t*-$BuMe_2$	TCNE	THF	23	25	75[b]	0.65
20	**11**	SO	NPM	toluene	80		100[c]	>2
21	**16**	SO	NPM	CH_3OH	23		100[c,f]	>2
22	**17**	SO	NPM	toluene	70		100[c]	>2
23	**18**	SO	NPM	toluene	70		100[c]	>2

[a] $\Delta G^{\ddagger}_{syn} - \Delta G^{\ddagger}_{anti}$ in kilocalories/mole. [b] Determined by capillary GLC. [c] Determined by 500-MHz ^1H NMR spectroscopy. [d] Determined by HPLC. [e] A minor component (3–4%) was observed by capillary GLC analysis. This value, therefore, represents a lower limit for the anti selectivity. The ratio of **20b** to this uncharacterized minor adduct was constant from 1 to 5 h. [f] Reaction stopped at 80% conversion.

long-range *W* coupling.[27] This result suggests a cis relationship between hydrogens H_d and H_c. The stereochemistry for adduct **32**, which showed the same characteristic long-range couplings in the ^1H NMR spectrum, was confirmed by single-crystal X-ray diffraction. As with adduct **30**, the central ring of **32** adopts a half-boat conformation (see Figure 2).

The face selectivity of the reaction of diene sulfoxides **16–18** with TCNE could not be determined, since neither of these dienes reacted over the temperature range of 23–67 °C with this powerful electron-deficient dienophile.[28]

A number of experiments were conducted to pursue whether or not the cycloaddition product ratios obtained from preparative-scale experiments represented true kinetic cycloaddition stereoselectivities. In cases where both cycloadducts were formed, control experiments using the purified adducts (or enriched samples) confirmed that there was no equilibration at room temperature of the syn and anti adducts in any of the solvents studied (see the Experimental Section for details). Similar control experiments could not be carried out for the reaction of NPM with dienes **8b**, **16**, **17**, and **18** since only the anti adduct was obtained in these cases. Attempts to prepare the sulfinyl epimer of **30** by oxidation of sulfide **33** with *tert*-butyl hypochlorite, a reagent reported[30] to oxidize sulfides from the more hindered face, were unfortunately unsuccessful. Careful monitoring of the cycloaddition of NPM with these four dienes failed to reveal any intermediate products, and we assume that these cycloadditions also occur in a kinetically controlled fashion.

Discussion

Table I summarizes the stereoselectivities observed in the cycloaddition reactions examined in this study. In most cases the product ratios were demonstrated to reflect kinetic control in the cycloaddition step. In cycloadditions with NPM, the only adduct(s) detected were the result of endo cycloaddition. Thus, the product ratios observed with this dienophile reflect solely facial stereoselectivities, as they do with TCNE. We will focus initially on the dienes **8** and **10**, which differ only in the allylic substituents at the diene terminus. The preference ($\Delta\Delta G^{\ddagger}$ = 0.9–1.2 kcal/mol) observed for diene **10** to react with both NPM and TCNE from the fact anti to the allylic methyl substituent is most easily rationalized by simple destabilizing steric interactions between the dienophile and the allylic methyl group in the endo-syn transition state (see Figure 3, X = C, $R_{syn} = CH_3$).

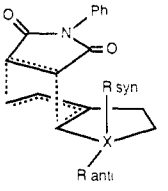

Figure 3.

The allylic ether substituents (OCH_3 and OSi-*t*-$BuMe_2$) are also anti directors. In cycloadditions with NPM, these groups exert a stronger effect on face selectivity ($\Delta\Delta G$ = >1.8 kcal/mol) than a methyl substituent and lead to the formation of a *single* endo-anti product. As with diene **10**, the stereoselectivity of the cycloaddition of dienes **8b** and **8c** with NPM or TCNE showed little solvent dependence.[31,32] Thus, in marked contrast to what has been reported for cycloadditions of 5-oxygenated 1,3-cyclopentadienes,[8-10,12] we find *no evidence* for a syn directing effect of ether substituents in cycloadditions of allylically oxygenated dienes of general structure **3**. In particular, the anti preference observed in the cycloaddition of diene **8b**, which contains the sterically small[33] (vide infra) allylic OCH_3 substituent, with the

(27) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: New York, 1978; pp 334–341.

(28) Diene sulfoxides **16–18** are apparently more electron-deficient than dienes **8** and **10** (compare their reactivities with NPM) and apparently too electron-deficient to react with TCNE. This result is not without precedent. For example, 2,3-dicyanobutadiene is reported[29] to react with NPM but not TCNE.

(29) Cobb, R. L. *J. Org. Chem.* **1978**, *43*, 931.

(30) Durst, T. In *Comprehensive Organic Chemistry*; Barton, D., Ollis, D., Jones, D. N., Eds.; Pergamon: Oxford, 1979; Vol. 3, Chapter 11.6, pp 124–126.

(31) With dienes **8** and **10** the highest anti preference was obtained in cycloadditions with TCNE in THF. The solvent effects observed are extremely small (0.1–0.2 kcal/mol), however.

(32) For a definitive study of solvent polarity effects on endo–exo ratios of Diels–Alder reactions of cyclopentadiene, see Berson, J. A.; Hamlet, Z.; Mueller, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 297.

(33) For reviews of steric effects and parameters that have been used to describe the steric size of substituents, see: (a) Gallo, R. J. *Prog. Phys. Org. Chem.* **1983**, *14*, 115. (b) Charton, M. In *Steric Effects in Drug Design*; Charton, M., Motoc, I., Ed.; Springer-Verlag: Berlin, 1983; pp 57–118. (c) Many cyclohexane A values, which are often used as one measure of the steric size of substituents, are summarized in: Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199.

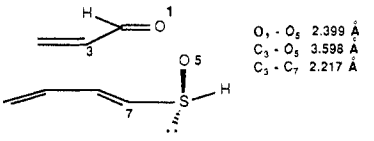

Figure 4.

sterically undemanding dienophile TCNE, was nearly identical with that observed with the methyl-substituted diene **10**.

In marked contrast to dienes **10**, **8b**, and **8c**, cycloaddition of the hydroxy-substituted diene **8a** with NPM was markedly solvent dependent; the OH substituent varied from a weak syn director in toluene to a modest anti director in methanol (see Table I, entries 6–8). The permanent dipole moment of the syn transition state is expected to be larger than that of the anti transition state (see Figure 3); thus, this trend is opposite to what would be expected on the basis of simple solvent dielectric effects.[32] Since the OCH_3 group, which is similar to OH in both size[34] and electronic character, showed no syn directing effect in the cycloaddition of **8b** with NPM in toluene, the preference for forming the syn adduct from the reaction of **8a** with NPM in toluene is not reasonably ascribed to "orbital" or electrostatic effects. We would suggest that the preference for forming the syn adduct **19a** in this latter cycloaddition is the result of a stabilizing hydrogen bond between the syn OH substituent and the proximal carbonyl oxygen of the imide dienophile (see Figure 3, X = C, R_{syn} = OH). This intramolecular stabilization would be expected to be of little importance in CH_3OH where external solvation of the carbonyl and hydroxy substituents should dominate.[35]

The sulfinyl group is a powerful anti director as evidenced by the complete anti face selectivity seen in the cycloaddition of sulfinyl dienes **16–18** with NPM. This result, in the case of sulfinyl diene **16**, was not altered if the cycloaddition was carried out in CH_3OH instead of toluene (see Table I, entries 20 and 21). The observed anti preference in the cycloaddition of **16–18** is *opposite* to the prediction of a recently advanced model,[17,19] which focuses on the effect of an allylic substituent in perturbing the electrostatic interactions at the two faces of the diene termini.

The inability of a simple electrostatic model[17] to predict facial stereoselectivities in the cycloaddition of sulfoxide dienes **16–18** with NPM is not surprising since the dominant electrostatic interactions in the endo transition state occur between the oxygen of the sulfinyl group and the carbonyl oxygen of the imide dienophile (Figure 3, X = S, R_{syn} = O). An assessment of the potential severity of this interaction followed from construction of a model for the endo-syn transition state for the reaction of (*E*)-1-sulfinyl-1,3-butadiene with acrolein (see Figure 4), which used as a template the ab initio transition state for ethylene plus butadiene.[36,37] This model reveals a distance between the sulfinyl oxygen and the proximal oxygen of the dienophile of 2.40 Å for this symmetrical transition state,[38] thus suggesting a highly destabilizing interaction[39] between the related groups in the reaction of sulfinyl dienes **16–18** with NPM.

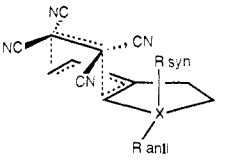

Figure 5.

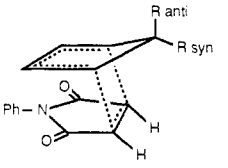

Figure 6.

The high anti preference observed also in the reaction of methoxy diene **8b** with NPM is suggested to derive from both simple destabilizing steric interactions in the syn transition state and repulsive electrostatic interactions[39] between the proximal oxygen of the imide dienophile and the allylic oxygen of the diene (Figure 3, X = C, R_{syn} = OCH_3). The considerably stronger anti directing ability of OCH_3 than CH_3 in cycloadditions with NPM is not consistent with conventional measures of the steric size of these groups (e.g. *A* values,[33c] 0.6 for OCH_3 and 1.7 for CH_3 or upsilon parameters,[33b] 0.36 for OCH_3 and 0.52 for CH_3) but could be rationalized by the importance of electrostatic repulsion in destabilizing the endo-syn transition state for reaction of diene **8b** with NPM. On the other hand, electrostatic interactions are less important in cycloadditions with TCNE. This is seen in the fact that with respect to this dienophile allylic CH_3 and OCH_3 substituents have comparable effects on facial selectivity (compare Table I entries 4 and 5 with 15 and 16). As illustrated in Figure 5, the nitrile substituents are not directed toward the allylic substituent in the syn Diels–Alder transition state, and, thus, destabilizing electronic interactions with the OCH_3 substituent should be less important in cycloadditions with TCNE.

Conclusion

We find no evidence for a syn directing effect of an allylic oxygen substituent (with the exception of a group capable of hydrogen bonding) in cycloaddition reactions of dienes of general structure **3** and **4**. This result indicates that the syn facial selectivity often observed[8–10,12] in Diels–Alder reactions of 5-heterosubstituted 1,3-cyclopentadienes will not extrapolate to other dienes containing 1(*E*)-allylic substituents. We suggest that the "special" nature of 5-substituted 1,3-cyclopentadienes derives from the fact that the endo transition state for cycloaddition of these dienes with many common dienophiles will be free of destabilizing steric and electrostatic interactions between the dienophile and the syn 5-substituent (see, e.g., Figure 6).[40–42] Since this will not be the case for endo cycloadditions of dienes containing *E*-oriented allylic substituents at the diene terminus (see, e.g., the destabilizing interaction of R_{syn} and O in Figure 3), syn direction by allylic heteroatom substituents in this more generally employed class of dienes is *not* to be expected. The high anti face selectivity ($\Delta\Delta G^{\ddagger}$ > 2 kcal/mol) observed in cycloadditions of dienes containing allylic sulfoxide or ether substitution with NPM is attributed to destabilizing electronic interactions between the allylic heteroatom

(34) The steric effect of the OH group is well-established to be extremely solvent dependent,[33] so direct comparisons here are not possible. A values[33c] and upsilon parameters[33b] are typically somewhat larger for OH than for OCH_3.

(35) The increase in the anti adduct **20a** in going from toluene to THF to CH_3OH could alternatively be ascribed to better solvation of the OH group by external solvent in the anti transition state. (This group is shielded from external solvent by the dienophile in the syn transition state, see Figure 3.) However, this explanation for the solvent effect provides no rationalization for why cycloaddition in toluene occurs preferentially from the hydroxyl face.

(36) (a) Burke, L. A.; Leroy, G.; Sana, M. *Theor. Chim. Acta* **1975**, *40*, 313. (b) Burke, L. A.; Leroy, G. *Ibid.* **1977**, *44*, 219. (c) Townsend, R. F.; Ramunni, G.; Segal, G.; Hehre, W. J.; Salem, L. *J. Am. Chem. Soc.* **1976**, *98*, 2190. (d) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1984**, *25*, 4609. (e) Bernardi, F.; Bottoni, A.; Robb, M. A.; Field, M. J.; Hiller, I. H.; Guest, M. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1051.

(37) The sulfinyl and formyl moieties employed were culled from the ab initio structures for (*E*)-1-sulfinyl-1,3-butadiene and acrolein, respectively (cf. ref 19). These moieties were substituted for the appropriate hydrogens in the butadiene–ethylene transition structure and were used without any additional optimization of geometry.

(38) A recent ab initio study suggests that diene or dienophile substitution can lead to significant distortion of the transition structure, while maintaining reaction "concertedness". See: Burke, L. A. *Int. J. Quantum Chem.* **1986**, *29*, 511.

(39) Electrostatic interactions, which fall off as the inverse first power of distance, should dominate[19] at long distances over filled orbital interactions (steric effects), which decrease with a much higher inverse power.

(40) MNDO[13] and STO-3G[41] transition structures for ethylenecyclopentadiene have been reported.

(41) Burke, L. A., in press.

(42) Professor Fallis (Memorial University of Newfoundland) has kindly informed us that 2,5-dimethylthiophene oxide cycloadds to benzophenone from the face syn to oxygen. This result is consistent with the lack of destabilizing electrostatic interactions in the appropriate syn transition state, which would be similar in structure to that illustrated in Figure 6.

and the dienophile in the syn transition state. Secondary electrostatic interactions of this type should be useful in the design of facially selective Diels–Alder reactions.

Rationalizations[17] of the facial outcome of cycloadditions of acyclic dienes **2**, which are based on syn addition of the dienophile to a preferred conformation of the acyclic diene, are not supported by the investigations reported here, since these 1(*E*)-substituted 1,3-dienes should experience destabilizing electronic interactions between a syn electronegative substituent and the dienophile similar to those depicted in Figure 3. With respect to electrostatic models for predicting face selectivity in cycloaddition reactions,[17] our results illustrate that it will be necessary to consider *all* electrostatic interactions between the reacting partners, not just those between the carbons involved in bonding.

Experimental Section[43]

3-Vinylcyclopentenone (7), Vinylmagnesium bromide (5.90 mL of a 1.47 M solution in THF, 8.60 mmol) was added dropwise at −78 °C to a solution of 3-methoxycyclopentenone (0.80 g, 7.2 mmol) and dry THF (15 mL). This solution was maintained at −78 °C for 1 h, allowed to warm to room temperature, and slowly poured into a mixture of crushed ice (100 g) and concentrated HCl (3 mL). This mixture was stirred for 2 h and then extracted with CH_2Cl_2 (3 × 50 mL). The organic extracts were dried ($MgSO_4$) and concentrated to give 0.762 g (98%) of **7** as a golden-colored oil whose purity was sufficient for the next reaction: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.85 (dd, J = 10.6, 17.5 Hz, =CCH=), 6.06 (s, OCCH=), 5.80 (d, J = 17.5 Hz, =CH*H*), 5.55 (d, J = 10.6 Hz, =C*H*H), 3.78 (m, $OCCH_2$), 3.45 (m, CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 209.6, 172.0, 132.8, 131.2, 122.4, 34.8, 26.6 ppm; IR (film) 2924, 1705, 1673, 1629, 1573, 1440, 1409, 1347 cm^{-1}; MS (CI), *m/e* 109 (MH^+); MS (EI), *m/e* 108.0564 (100%, 108.0575 calcd for C_7H_8O), 79 (67%), 52 (30%).

3-Vinyl-2-cyclopenten-1-ol (8a). Diisobutylaluminum hydride (1.5 mL, 8.3 mmol) was added to a solution of **7** (0.75 g, 6.9 mmol) and ether (14 mL) at −78 °C. The resulting creamy yellow mixture was stirred for 2 h at −78 °C and allowed to warm to room temperature where it became homogeneous. NaF (1.39 g, 33.2 mmol) was added, followed by the dropwise addition of H_2O (0.50 mL, 25 mmol). The resulting mixture was stirred at 0 °C for 0.5 h and then allowed to warm to room temperature. This mixture was filtered through a bed of Celite, and the collected aluminum salts were washed with ether (60 mL). The combined filtrates were concentrated to give 0.635 g (84%) of **8a** as a golden colored oil whose purity was sufficient for the next reaction: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.57 (dd, J = 10.6, 17.4 Hz, =CCH=), 5.70 (s, OCCH=), 5.21 (d, J = 17.3 Hz, =C*H*H), 5.18 (d, J = 10.4 Hz, =CH*H*), 4.9 (br s, HOC*H*), 3.8–3.2 (m, OH and $HOCHCH_2$), 2.9–2.7 (m, CH_2CH_2C=); ^{13}C NMR (75 MHz, $CDCl_3$) 145.9, 133.2, 132.0, 116.8, 77.4, 33.5, 29.0 ppm; IR (film) 3371, 3341, 2959, 1640, 1592, 1041, 845 cm^{-1}; MS (CI), *m/e* 93 ($MH^+ - H_2O$); MS (EI), *m/e* 110.0721 (100%, 110.0732 calcd for $C_7H_{10}O$), 95 (37%), 91 (44%).

3-[(*tert*-Butyldimethylsilyl)oxy]-1-vinylcyclopentene (8c). *tert*-Butyldimethylsilyl chloride (0.516 g, 3.42 mmol) and imidazole (0.272 g, 3.99 mmol) were added to a solution of **8a** (0.314 g, 2.86 mmol) and dry DMF (6 mL). The resulting solution was maintained at room temperature for 16 h, diluted with ether (25 mL), and washed with H_2O (4 × 15 mL). The organic extract was dried ($MgSO_4$) and concentrated to give 0.520 g (89%) of **8c**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.57 (dd, J = 10.6, 17.4 Hz, C=CH=), 5.67 (s, C=CH), 5.17 (d, J = 17.4 Hz, =CH*H*), 5.14 (d, J = 10.6 Hz, =C*H*H), 4.95 (m, $CHOSiR_3$), 2.62 (m, 1 H), 2.3 (m, 2 H), 1.75 (m, 1 H), 0.9 (s, 9 H), 0.1 (s, 6 H); IR (film) 2956, 2930, 2857, 1075, 1068, 907, 836 cm^{-1}; MS (EI), *m/e* 224.1602 (23%, 224.1596 calcd for $C_{13}H_{24}OSi$), 167 (14%), 75 (100%).

3-Methoxy-1-vinylcyclopentene (8b), A solution of **8a** (1.0 g, 9.1, mmol) and dry ether (5 mL) was added to a rapidly stirred suspension of KH (0.68 g, 0.17 mol) and dry ether (20 mL). This mixture was stirred at room temperature for 0.5 h. Methyl iodide (3.0 mL, 45 mmol) was added, and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with methanol (2 mL) and poured into a separatory funnel containing pentane (30 mL). This mixture was washed with H_2O (3 × 20 mL) and brine (1 × 20 mL). The organic layer was dried (K_2CO_3), and the solvent was removed by distillation (concentric tube column). The crude material was purified by distillation (short path), giving 0.476 g (42%) of **8b** as a clear liquid (bp 87–89 °C, 66 mm): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.58 (dd, J = 10.6, 17.5 Hz, =CHC=), 5.83 (br s, C=CH), 5.2 (d, J = 17.6 Hz, C=C*H*H), 5.18 (d, J = 10.6 Hz, C=CH*H*), 4.5 (m, C*H*OMe), 4.33 (s, OCH_3), 3.75–2.8 (m, 4 H); IR (film) 2928, 2905, 2592, 1336, 1094, 907 cm^{-1}; MS (EI), *m/e* 124.0889 (100%, 124.0888 calcd for $C_8H_{12}O$), 93 (21%), 77 (22%).

3-Methyl-1-cyclopentenylmethanol (34), Diisobutylaluminum hydride (11.2 mL, 62.9 mmol) was added dropwise to a solution of methyl 3-methyl-1-cyclopentenecarboxylate[20] (4.40 g, 28.6 mmol) and dry ether (60 mL) at −78 °C. The resulting solution was maintained at −78 °C for 2 h, warmed to 0 °C, and diluted with ether (120 mL). NaF (10.6 g, 252 mmol) was added followed by the dropwise addition of water (3.4 mL, 0.18 mol). The resulting mixture was stirred at 0 °C for 0.5 h and then allowed to warm to room temperature. The solution was filtered through a bed of Celite, and the aluminum salts were washed with CH_2Cl_2 (150 mL). The combined filtrates were concentrated, and the crude liquid was distilled (short path) to give 2.31 g (78%) of **34** as a colorless liquid (bp 85–87 °C, 13mm): ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.52 (br s, C=C*H*), 4.18 (br s, CH_2OH), 2.8 (m, $CHCH_3$), 2.5–2.0 (m, 3 H), 1.7–1.3 (m, 2 H), 1.02 (d, J = 6.9 Hz, CH_3); IR (film) 3332, 2926, 2885, 2885, 1016 cm^{-1}; MS (EI), *m/e* 112.0884 (20%, 112.0888 calcd for $C_7H_{12}O$), 97 (34%), 81 (100%).

3-Methyl-1-cyclopentene-1-carboxaldehyde (35), Alcohol **34** (0.692 g, 6.18 mmol) was oxidized in CH_2Cl_2 (15 mL) at −78 °C with oxalyl chloride (1.10 mL, 12.4 mmol), DMSO (1.10 mL, 15.5 mmol), and TEA (3.40 mL, 24.7 mmol) via the procedure described be Swern.[44] The reaction mixture was allowed to warm to room temperature, diluted with ether–pentane (1:1) (30 mL), and washed with 1/2 saturated brine (2 × 5 mL). The remaining organic material was dried ($MgSO_4$) and concentrated, giving the crude aldehyde as a dark orange oil. This crude product was purified by chromatography (silica gel, 200–400 mesh, pentane–ether 3:1) giving 0.492 g of **35** as a light yellow liquid (72%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.79 (s, COH), 6.74 (m, C=CH), 3.0 (m, $CHCH_3$), 2.7–2.1 (m, 3 H), 1.6–1.4 (m, 1 H), 1.14 (d, J = 7.07 Hz, CH_3); IR (film) 2960, 1690, 1683, 1621, 1614, 1360, 1260 cm^{-1}; MS (CI), *m/e* 111 (MH^+); MS (EI), *m/e* 110.0736 (48%, 110.0732 calcd for $C_7H_{10}O$), 81 (100%).

3-Methyl-1-vinylcyclopentene (10), *n*-Butyllithium (11.0 mL of a 2.40 M solution in hexanes, 26.4 mmol) was added to a −78 °C suspension of methyltriphenylphosphonium bromide (9.44 g, 26.4 mmol) and dry ether (50 mL). This mixture was allowed to warm to room temperature and stirred for 1 h. The light yellow solution was recooled to −78 °C, and **35** (1.45 g, 13.2 mmol) was added. This solution was allowed to warm to room temperature, and the resulting mixture was stirred for 24 h. The solution was diluted with ether (50 mL) and then washed with 0.1 M HCl (2 × 35 mL), water (2 × 35 mL), and brine (1 × 35 mL). The organic solution was dried (K_2CO_3) and passed through a short plug of silica. Concentration (distillation with a concentric tube column) gave 30 mL of liquid that deposited triphenylphosphene oxide upon cooling. Filtration followed by further concentration of the filtrate gave 5 mL of material, which was distilled through a 10-cm Vigreaux column to give a fraction (bp 50–65 °C, 100 mm) that was enriched in **10** (1 g, ca. 50% pure by GLC with the remainder being hydrocarbons). A pure sample was isolated from this mixture by preparative GLC ($^1/_4$ in. × 6 ft column containing 3% SP 2100, oven temperature 28 °C): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.5 (dd, J = 10.6, 17.1 Hz, =CHC=) 5.63 (br s, C=C*H*$CHCH_3$), 5.1 (m, C=CH_2), 2.84 (m, $CHCH_3$), 2.6–2.0 (m, 3 H), 1.53–1.30 (m, 1 H), 1.03 (d, J = 6.93 Hz, CH_3); IR (solution, $CDCl_3$) 2962, 2968, 1638, 1603, 1456, 1216, 993 cm^{-1}; MS (EI), *m/e* 108.0955 (41%, 108.0939 calcd for C_8H_{12}), 93 (100%), 83 (41%).

(*E*)- and (*Z*)-3-(Carbethoxymethylidene)tetrahydrothiophene (12), Triethyl phosphonoacetate (34.8 mL, 0.176 mol) was added dropwise at room temperature to a suspension of NaH (4.2 g, 0.18 mol) and dry THF (250 mL). The resulting clear brown solution was stirred for 0.5 h and cooled to −78 °C, and tetrahydrothiophen-3-one (10.0 mL, 0.117 mol) was then added. This solution was maintained at −78 °C for 0.5 h, allowed to warm to room temperature, diluted with ethyl ether (1000 mL), washed with water (3 × 400 mL) and brine (2 × 400 mL), dried ($MgSO_4$), and concentrated. The crude liquid was distilled through a 10-cm Vigreux column to give 20.5 g (~100%) of **12** (bp 109–110 °C, 4.1 mm) that contained traces of phosphorus residues: ^{1}H NMR showed that the product consisted of a 60:40 mixture of *E* and *Z* isomers. Flash chromatography (silica gel, 240–400 mesh, 3:1 hexane–ether) gave a sample (>99.5% pure by GLC analysis) free from phosphorus residues. Characteristic data for the product mixture: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.9–5.8 (m, C=CH), 4.18 (t, J = 7 Hz, OCH_2), 3.98–3.59 (m), 3.19 (m), 2.96 (t, J = 6.6 Hz) 1.29 (t, J = 7 Hz, CH_3); IR (film) 2995, 2950, 2910, 1720, 1660, 1220, 1040 cm^{-1}; MS (CI), *m/e* 173 (MH^+); MS (EI), *m/e* 172.0571 (60%, 172.0558 calcd for $C_8H_{12}O_2S$), 143 (73%), 97 (100%).

(43) General experimental details were recently described.[23]

(44) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(*E*)- and (*Z*)-3-(2-Hydroxyethylidene)tetrahydrothiophene (13), Diisobutylaluminum hydride (25.2 mL, 0.142 mol) was added dropwise to a solution of **12** (11.1 g, 64.4 mmol) and dry ether (100 mL) at −78 °C. The resulting solution was maintained at −78 °C for 1 h, allowed to warm to 0 °C, and diluted with ether (400 mL). NaF (23.8 g, 0.566 mol) was added in three portions followed by the dropwise addition of H_2O (7.7 mL, 0.42 mol). The resulting mixture was stirred at 0 °C for 0.5 h and then warmed to room temperature. The solution was filtered through a bed of Celite, and the aluminum salts were washed with ether (500 mL). The combined filtrates were concentrated, and the crude liquid was distilled (short path) to give 8.23 g (98%) of pure **13** as a 60:40 mixture of *E* and *Z* isomers (bp 89–92 °C, 0.15 mm). Characteristic data for the product mixture: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.6 (m, C=CH), 4.12 (m, CH_2O), 3.45 (m, SCH_2), 2.88–2.80 (m, 2 H), 2.67 (m, 2 H), 1.7 (s, OH); IR (film) 3340, 1675, 1435, 1220, 1080, 1010 cm^{-1}; MS (CI), *m/e* 131 (MH^+); MS (EI), *m/e* 130.0450 (19%, 130.0452 calcd for $C_6H_{10}OS$), 112 (100%), 99 (50%).

(*E*)- and (*Z*)-3-(2-Chloroethylidene)tetrahydrothiophene (14), Methanesulfonyl chloride (1.3 mL, 17 mmol) was added dropwise at 0 °C to a stirred suspension of **13** (2.0 g, 15 mmol), collidine (2.24 mL, 16.9 mmol), LiCl (0.652 g, 15.4 mmol), and dry DMF (8 mL). The resulting mixture was stirred at 0 °C for 2 h, allowed to warm to room temperature, and then poured into 50 mL of H_2O and extracted with ice-cold ether–pentane (1:1) (3 × 50 mL). The organic extracts were washed with saturated aqueous $CuNO_3$ (3 × 25 mL) and brine (1 × 25 mL), dried ($MgSO_4$), and concentrated to afford 2.19 g (96%) of **14** (60:40 mixture of *E* and *Z* isomers by ^{1}H NMR analysis) as a gold oil whose purity was sufficient for the next reaction. A small sample was purified by flash chromatography (silica gel, 3:1 hexane–ether) to give **14** as a pure colorless oil. Characteristic data for the product mixture: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.71–5.61 (m, C=CH), 4.09 (d, *J* = 6.5 Hz, CH*H*Cl), 4.07 (d, *J* = 7.15 Hz, C*H*HCl), 3.51 (m, SCH_2), 2.92–2.84 (m, 2 H), 2.72 (m, 2 H); IR (film) 2950, 1675, 1500, 1470, 1380, 1260, 1215, 1180, 760 cm^{-1}; MS (CI), *m/e* 149 (MH^+); MS (EI), *m/e* 148.0102 (55%, 148.0113 calcd for C_6H_9ClS), 113 (100%), 99 (75%).

(*E*)- and (*Z*)-3-(2-Chloroethylidene)tetrahydrothiophene *S*-Oxide (15), Sodium periodate (28.5 mL of a 0.50 M solution in H_2O, 14.3 mmol) was added dropwise to a solution of **14** (2.0 g, 14 mmol) and methanol (30 mL). This mixture was stirred at 0 °C for 2 h, allowed to warm to room temperature, filtered to remove inorganic material, and concentrated to half the initial volume. The resulting aqueous solution was extracted with $CHCl_3$ (4 × 25 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to give 1.85 g (80%) of **15** as a golden-colored oil whose purity was sufficient for the next reaction (a 60:40 mixture of *E* and *Z* isomers by ^{1}H NMR analysis). Characteristic data for the product mixture: ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.97–5.85 (m, C=CH), 4.12–4.09 (m, 2 H), 3.9–2.6 (m, 6 H); IR (film) 2980, 2940, 1675, 1270, 1220, 1140, 760 cm^{-1}; MS (EI), *m/e* 164.0060 (17%, 164.0062 calcd for C_6H_9ClOS), 129 (100%), 79 (76%).

4,5-Dihydro-3-ethenylthiophene *S*-Oxide (16), Lithium hexamethyldisilizane (5.0 mL of a 0.69 M solution in THF, generated from *n*-BuLi and hexamethyldisilizane following standard protocols, 3.4 mmol) was added dropwise at −78 °C via cannula to a solution of **15** (0.595 g, 3.62 mmol) in dry THF (10 mL). The solution was maintained at −78 °C for 10 min, allowed to warm to 0 °C, and then quenched with 2 mL of saturated aqueous NH_4Cl. The resulting solution was diluted with $CHCl_3$ (60 mL) and washed with H_2O (2 × 20 mL), and the aqueous layers were extracted with $CHCl_3$ (2 × 30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash chromatography (silica gel 240–400 mesh, 18:9:2 hexane–CH_2Cl_2–*i*-PrOH) to give 296 mg (64%) of **16** as a chromatographically pure golden-colored oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 10.7, 17.5 Hz, =CH=), 6.58 (s, =CHSO), 5.57 (d, *J* = 17.5 Hz, =C*H*H), 5.55 (d, *J* = 10.7 Hz, =CH*H*), 3.50–3.32 (m, 2 H), 3.06–2.82 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 152.83, 131.37, 131.31, 122.88, 51.03, 30.88 ppm; IR (film) 3100, 3060, 2980, 2940, 1640, 1580, 1440, 1420, 1300, 1260, 1190, 1140, 1130, 940, 820, 780 cm^{-1}; MS (CI), *m/e* 129 (MH^+); MS (EI), *m/e* 128.0303 (100%, 128.026 calcd for C_6H_8OS), 99 (92%), 53 (58%).

Reaction of 8a and *N*-Phenylmaleimide, A solution of NPM (0.157 g, 0.909 mmol), **8a** (0.100 g, 0.909 mmol), and toluene (1 mL) was maintained at room temperature for 36 h and then concentrated. HPLC analysis of the crude material revealed two products in a ratio of 1.8:1. Radial chromatography (silica gel, $CHCl_3$) gave two fractions. ^{1}H NMR analysis indicated that the first fraction (0.136 g, 53%) was the tricyclic lactone **21** (mp 224.5–225 °C), and the second fraction (0.072 g, 28%) was adduct **20a** (mp 159–160 °C). **20a**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.6–7.1 (m, PhH), 5.7 (m, C=CH), 4.65 (m, C*H*OH), 3.60 (app t, *J* = 9 Hz, OCC*H*(C)CHSO), 3.3 (ddd, *J* = 8.9, 6.9, 1.7 Hz, OCC*H*CH_2), 2.85 (m, HC*H*C=), 2.5 (m, 2 H), 2.3 (m, 3 H). 2.0–1.7 (m, 2 H); ^{13}C NMR (125, MHz $CDCl_3$) 178.9, 177.8, 143.5, 131.9, 129.2, 128.7, 126.5, 117.3, 77.5, 47.2, 41.0, 40.5, 33.4, 27.7, 24.3 ppm; IR (film) 3541, 1694, 1397, 1210 cm^{-1}; MS (CI), *m/e* 266 ($MH^+ - H_2O$); MS (EI), *m/e* 283.1210 (12%, 283.1208 calcd for $C_{17}H_{12}NO_3$), 175 (100%), 118 (60%), 91 (72%). Anal. Calcd for $C_{17}H_{12}NO_3$: C, 72.07; H, 6.09; N, 4.94. Found: C, 72.00; H, 6.09; N, 4.91. **21**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.3 (s, NH), 7.7–7.0 (m, PhH), 5.75 (br s, C=CH), 5.0 (br t, *J* = 5.5 Hz, HOC*H*), 3.52 (dd, *J* = 6, 3.5 Hz, O_2CC*H*), 3.1 (m, 1 H), 3.06 (dt, *J* = 3.5, 9 Hz, NHCO*H*), 3.7–1.9 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 178.5, 171.7, 138.5, 137.5, 129.0, 124.1, 122.1, 119.9, 84.2, 45.7, 43.5, 41.6, 30.7, 28.5, 26.8 ppm; IR (KBr) 3326, 1740, 1694, 1600, 1544, 1441 cm^{-1}; MS (CI), *m/e* 284 (MH^+); MS (EI), *m/e* 283.1193 (100%, 283.1208 calcd for $C_{17}H_{17}NO_3$), 162 (37%), 117 (19%), 93 (88%). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.02; H, 6.05; N, 4.94; Found: C, 72.04; H, 6.09; N, 4.93.

The crude material from a similar reaction (0.256 g, ca. 0.9 mmol) was taken up in CH_2Cl_2 (5 mL), cooled to 0 °C, and treated sequentially with triethylamine (0.25 mL, 1.20 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.27 mL, 1.20 mmol). This solution was maintained at 0 °C for 30 min, diluted with ether (15 mL), and washed with saturated aqueous $NaHCO_3$ (2 × 5 mL) and brine (2 × 5 mL). The resulting organic material was dried (K_2CO_3) and concentrated. The crude product was chromatographed (radial, silica gel, hexane–ethyl acetate, 8:1), giving 0.229 g (66%) of a 1.3:1 mixture of **19c** and **20c**. Pure samples of each product were obtained by preparative HPLC (silica, hexane–ethyl acetate, 8:1). **19c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.15 (m, PhH), 5.60 (m, =CH), 4.56 (m, $CHOSiR_3$), 3.48 (dd, *J* = 8.7, 5.9 Hz, COCH), 3.21 (t, *J* = 8.3 Hz, COC*H*CH_2), 2.76 (dd, *J* = 15.3, 8.4, Hz C*H*HC=), 2.56 (br s, C*H*C$HOSiR_3$), 2.4–2.1 (m, 4 H), 1.9 (m, 1 H), 0.09 (s, 9 H), 0.09 (s, 3 H), 0.04 (m, 3 H); IR (film) 2953, 1715, 1378, 1129, 774, 614; MS (CI), *m/e* 398 (MH^+); MS (EI), *m/e* 397.2058 (0.01%, 397.2073 calcd for $C_{23}H_{31}NO_3Si$), 340.1358 (100%, M − *t*-Bu, 340.1368 calcd for $C_{19}H_{22}NO_3Si$).

Reaction of 8c and *N*-Phenylmaleimide, Preparation of 20c, A solution of NPM (0.193 g, 1.12 mmol), **8c** (0.250 g, 1.12 mmol), and toluene (0.5 mL) was maintained for 36 h at room temperature, concentrated, and chromatographed (silica gel, 240–400 mesh, 5:1 hexane–ether) to give 0.356 g (84%) of pure **20c** as a clear oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.4–7.1 (m, PhH), 5.75 (m, C=CH), 5.05 (q, *J* = 11.9, 5.7 Hz, C*H*OH), 3.45 (dd, *J* = 8.9, 7.5 Hz, OCC*H*CH), 3.29 (ddd, *J* = 8.6, 7.1, 1.4 Hz, OCC*H*CH_2), 2.81 (ddd, *J* = 14.9, 7.06, 1.4 Hz, HC*H*C=), 2.45–1.6 (m, 5 H), 0.90 (s, $C(CH_3)_3$), 0.15 (s, $SiCH_3$), 0.10 (s, $SiCH_3$); IR (film) 2955, 2929, 1711, 1499, 1348, 837 cm^{-1}; MS (CI), *m/e* 398 (MH^+); MS (EI), *m/e* 397.1997 (33%, 397.2067 calcd for $C_{23}H_{31}NO_3Si$), 340 (100%).

Deprotection of 20c, A solution of acetic acid, THF, water (1:1:1, 1 mL), and **20c** (56 mg, 0.14 mmol) was maintained at room temperature for 72 h. This solution was poured into water (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic extracts were dried ($MgSO_4$), concentrated, and chromatographed (silica gel, 240–400 mesh, 25:1 hexane–EtOAc) to give 30 mg (75%) of **20a** as a white solid (mp 159–160 °C).

Reaction of 8b and *N*-Phenylmaleimide, Preparation of 20b, A solution of NPM (0.140 g, 0.807 mmol), **8c** (0.100 g, 0.140 mmol), and toluene (0.8 mL) was maintained at room temperature for 24 h and then concentrated. ^{1}H NMR analysis of this crude product indicated the presence of only one adduct (single methoxy singlet at δ 3.46). The crude material was purified by chromatography (radial, silica gel, hexane–ethyl acetate, 6:1), giving 0.174 g of **20b** (73%, 86% based on recovered NPM) as a white powder (mp 118.5–120.5 °C) and 0.023 g of recovered NPM. **20b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.2 (m, Ph*H*), 5.72 (m, C=CH), 4.59 (dd, *J* = 4.87, 9.98 Hz, C*H*OMe), 3.55 (dd, *J* = 7.78, 8.86 Hz, COC*H*), 3.46 (s, OCH_3), 3.32 (m, COC*H*), 2.85 (m, C*H*HC=), 2.5–2.44 (m, 2 H), 2.29–2.19 (m, 2 H), 1.95–1.74 (m, 2 H); IR (KBr) 1700, 1501, 1455, 1382, 1206, 1183, 1093, 693 cm^{-1}; MS (CI), *m/e* 298 (MH^+); MS (EI), *m/e* 297.1350 (2%, 297.1365 calcd for $C_{18}H_{19}NO_3$), 123 (100%). Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.82; H, 6.47; N, 4.69.

Conversion of 20a to 20b, Ag_2O (10 mg, 0.035 mmol) was added to a suspension of K_2CO_3 (5.0 mg, 0.035 mmol), **20a** (10 mg, 0.035 mmol), MeI (0.10 mL, 5.7 mmol), and $CHCl_3$ (0.5 mL). This mixture was stirred at room temperature for 4 days, filtered, and then concentrated. The crude material was chromatographed (radial, silica gel, hexane–ethyl acetate, 3:1), giving 4.6 mg of **20b** (95% based on recovered **20a**) and 5.5 mg of recovered **20a**.

Reaction of 8a with Tetracyanoethylene, TCNE (0.060 g, 0.470 mmol) was added to a solution of **8a** (0.052 g, 0.470 mmol) and THF (0.5 mL). The resulting dark orange material was maintained at room temperature for 2 h and then concentrated. Quick filtration of the crude mixture through silica gel (CH_2Cl_2–THF, 50:1) gave two fractions. ^{1}H

NMR analysis indicated that the first fraction contained the cyclic imidate **24** along with a small amount of uncharacterized material and the second fraction contained adduct **22a**. The fraction containing **22a** was further purified by flash chromatography (silica gel, 200–400 mesh, hexane–ethyl acetate, 1:1), giving 0.047 g (42%) of pure **22a** as a white powder (mp 155.5–157 °C). **22a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.6 (m, C=CH), 4.35 (m, C*H*OH), 3.15 (m, $C(CN)_2CHCHOH$), 2.65 (m, C*H*HC=), 2.4 (m, CH*H*C=), 2.3 (m, 1 H), 2.21 (d, J = 5.36 Hz, O*H*), 1.35 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 136.6, 114.1, 111.1, 110.6, 110.5, 108.7, 74.7, 51.3, 41.2, 38.7, 33.6, 32.0, 26.4 ppm; IR (KBr) 3569, 2949, 1453, 1272, 1116, 1087, 1025, 674 cm^{-1}; MS (EI), m/e 238.0850 (24%, 238.0854 calcd for $C_{13}H_{10}N_4O$) 183 (91%), 156 (100%). Anal. Calcd for $C_{13}H_{10}N_4O$: C, 65.26; H, 4.21; N, 23.42. Found: C, 65.37, H, 4.29, N, 23.44.

Isolation of **24** was difficult but could be accomplished by combining and chromatographing (silica gel, 200–400 mesh, CH_2Cl_2) fractions enriched in **24** obtained from several different runs of similar scale. **24**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (br s, =NH), 5.67 (br s, =CH), 5.18 (t, J = 5.08 Hz, CHO), 3.55 (br s, C*H*CHO), 3.16–3.03 (m, CH_2C=), 2.61–2.57 (m, 2 H), 2.32–2.25 (m, 1 H); ^{13}C NMR ($CDCl_3$, 500 mHz) 158.7, 136.2, 116.4, 114.0, 113.4, 111.8, 83.9, 48.8, 47.0, 34.7, 32.1, 30.8, 27.8 ppm; IR (KBr) 3300, 1700, 1480, 1365, 1270, 1235, 945, 870, 860 cm^{-1}; MS (EI), m/e 238.0847 (65%, 238.0854 calcd for $C_{13}H_{10}N_4O$), 221 (70%), 194 (100%), 168 (92%).

The reaction of **8a** and TCNE was quantified in the following manner. TCNE (0.058 g, 0.455 mmol) was added to a solution of **8a** (0.050 g, 0.455 mmol) and THF (0.5 mL). The resulting dark orange solution was maintained at room temperature for 4 h, during which time the color faded from orange to yellow. The entire reaction mixture was then passed through a small plug of silica gel. The silica gel was washed with hexane–ethyl acetate, 1:1 (50 mL), and the combined organic material was concentrated, giving 0.092 g (85% of the expected mass) of crude material. ^{1}H NMR analysis (500 MHz) of the crude material revealed the presence of **22a**, **24**, and the syn addition product **23a** (methine hydrogen α to the OH appeared as characteristic multiplet at δ 4.12). Integration of the vinyl proton of **22a**, the methine hydrogen α to the O of **24**, and the methine hydrogen α to the OH of **23a** gave a ratio of 12.5:1.88:1, respectively. In addition to these three major products, two minor components (<5%) giving signals at δ 6.85 and 6.55, with multiplicities characteristic of terminal vinyl groups, were detected. The appearance of new terminal vinyl groups suggests that these impurities are products of ene reaction of TCNE with **8a**.

Reaction of 8c with Tetracyanoethylene, A solution of TCNE (0.086 g, 0.670 mmol), **8c** (0.150 g, 0.670 mmol), and THF (0.7 mL) was maintained at room temperature for 3 h. Concentration afforded the crude product as a mixture of isomers (3:1, by GLC analysis). Recrystallization of the crude material from hexane gave 0.202 g (86%) of material composed of the same ratio of isomers. The major adduct **22c** was isolated by fractional crystallization from hexane (mp 121–122 °C) while the minor adduct **23c** (mp 128–129.5 °C) was isolated by preparative HPLC (silica gel, hexane–ethyl acetate, 5:1). **23c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (m, C=CH), 4.75 (dd, J = 4.1, 9.6 Hz, CHOSiR_3), 3.2 (m, $CH_2C(CN)_2$ and $C(CN)_2CHCHOSiR_3$), 2.65 (m, C=CCH*H*), 2.45 (m, C=CC*H*H), 2.0 (m, 1 H), 1.85 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 139.0, 112.8, 111.4, 111.4, 109.6, 72.8, 49.3, 39.8, 39.2, 34.3, 34.0, 28.9, 25.9, 18.2, −4.6, −4.8 ppm; IR (film) 2957, 2931, 2253, 1258, 1068, 856, 831, 813 cm^{-1}; MS (CI), m/e (352, MH^+); MS (EI), m/e 337.1484 (60%, M − Me), 337.1484 calcd for $C_{18}H_{21}N_4OSi$), 295 (50%), 100 (100%). **22c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.56 (m, C=CH), 4.17 (ddd, J = 9.4, 9.4, 6.8 Hz, $CHOSiR_3$), 3.15 (m, $CH_2C(CN)_2$ and $C(CN)_2CHCHOSiR_3$), 2.2 (m, C=CCH*H*), 2.38 (m, C=CC*H*H), 2.2 (m, 1 H), 1.8 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 137.6, 115.1, 112.6, 112.0, 112.0, 110.2, 76.7, 52.8, 42.5, 40.3, 34.8, 33.3, 27.5, 27.1, 19.2, −3.0, −3.4 ppm; IR (KBr) 2950, 2936, 2850, 1140, 849, 838, 778 cm^{-1}; MS (CI), m/e 353 (MH^+); MS (EI), m/e 295.1026 (100%, (M − t-Bu), 295.1014 calcd for $C_{15}H_{15}N_4OSi$). Anal. Calcd for $C_{18}H_{21}N_4OSi$: C, 64.74; H, 6.86; N, 15.89. Found: C, 64.68; H, 6.89; N, 15.86.

DNOE Experiments for 22c and 23c, Irradiation of the bridgehead methine hydrogen of **22c** (δ 3.15) gave a 1.5% enhancement of the methine hydrogen α to the siloxy group (δ 4.17). Irradiation of the methine hydrogen α to the siloxy group of **22c** gave no enhancement of the bridgehead methine hydrogen. Irradiation of the bridgehead methine hydrogen of **23c** (δ 3.20) gave an 8.2% enhancement of the methine hydrogen α to the siloxy group (δ 4.75). Irradiation of the methine hydrogen α to the siloxy group of **23c** gave a 15.5% enhancement of the bridgehead methine hydrogen.

Deprotection of 22c, HF (40% aqueous, 5 drops) was added to a solution of **22c** (0.010 g, 0.028 mmol) and CH_3CN (0.75 mL). The resulting solution was maintained at room temperature for 4 days. Sodium bicarbonate (saturated aqueous solution, 10 mL) was added, and the resulting solution was extracted with CH_2Cl_2 (4 × 7 mL). The combined extracts were dried (K_2CO_3) and concentrated to give 7.0 mg (~100%) of **22a** as an essentially pure amorphous solid.

Deprotection of 23c. HF (40% aqueous, 5 drops) was added to a solution of **23c** (4.8 mg, 0.014 mmol) and CH_3CN (0.5 mL). The resulting solution was maintained at room temperature for 8 days, diluted with saturated aqueous $NaHCO_3$ (7 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (K_2CO_3) and concentrated. Chromatography (silica gel, 240–400 mesh, CH_2Cl_2) of the crude material gave 2.8 mg (86%) of **25** as a pure clear oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.7 (br s, C=CH), 5.3 (dd, J = 5.2, 5.7 Hz, CHCO), 3.6 (br s, C*H*CHO), 3.2–2.9 (m, $C(CN)_2CH_2$), 2.6 (m, CH_2C=), 2.5–2.0 (m, CH_2CH_2C=); ^{13}C NMR (125 MHz, $CDCl_3$) 164.2, 137.4, 118.6, 114.1, 113.5, 112.6, 84.9, 49.2, 48.9, 35.2, 33.7, 32.2, 28.8 ppm; IR (film) 2495, 1764, 1438, 1237, 1169, 957, 868 cm^{-1}; MS (CI), m/e 240 (MH^+); MS (EI), m/e 239.0704 (17%, 239.0695 calcd for $C_{13}H_9N_3O_2$), 194 (82%), 168 (100%).

Reaction of 8b with Tetracyanoethylene, A solution of TCNE (0.103 g, 0.807 mmol), **8b** (0.100 g, 0.807 mmol), and THF (0.8 mL) was maintained at room temperature for 5 h and then concentrated. ^{1}H NMR analysis of the crude material (500 MHz) revealed two OMe signals (δ 3.5 and 3.44) in a ratio of 6.8:1. Recrystallization of the crude mixture from hexane gave 0.173 g (85%) of material composed of the same ratio of isomers. Preparative GLC ($^1/_4$ in. × 6 ft column containing 3% SP-2100, oven temperature 147 °C) allowed isolation of a pure sample of the major isomer **22b** and a highly enriched sample (76% pure) of the minor isomer **23b**. **22b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.6 (m, C=C*H*), 3.88 (ddd, J = 8.74, 8.74, 6.82 Hz, C*H*OMe), 3.50 (s, OCH_3), 3.22–3.09 (m, CH_2C=, $C(CN)_2CH$), 2.7–2.6 (m, 1 H), 2.5–2.2 (m, 2 H), 1.85–1.75 (m, 1 H). **23b**: ^{1}H NMR (500 MHz $CDCl_3$) δ 5.66 (m, C=C*H*), 4.3–4.26 (m, C*H*OMe), 3.44 (s, OCH_3), 3.3–3.1 (m, CH_2C=, $C(CN)_2CH$), 2.7–2.48 (m, 2 H), 2.17–2.10 (m, 1 H), 1.9–1.8 (m, 1 H). Characteristic data for the product mixture: IR (KBr) 2948, 1455, 1381, 1208, 11134, 1121, 1112, 1099 cm^{-1}; MS (EI), m/e 252.1022 (100%, 252.1011 calcd for $C_{14}H_{12}N_4O$), 187 (47%), 155 (79%).

DNOE Experiments for 22b and 23b, Irradiation of the bridgehead methine hydrogen of **22b** (δ 3.10) gave a 6% enhancement of the methine hydrogen α to the methoxy group (δ 3.88). Irradiation of the methine hydrogen α to the methoxy group of **22b** gave an 8% enhancement of the bridgehead methine hydrogen. Irradiation of the bridgehead methine hydrogen of **23b** (δ 3.20) gave a 15% enhancement of the methine hydrogen α to the methoxy group (δ 4.30). Irradiation of the methine hydrogen α to the methoxy group of **23b** gave a 14.8% enhancement of the bridgehead methine hydrogen.

Reaction of 10 with *N*-Phenylmaleimide, A solution of NPM (0.037 g, 0.213 mmol), **10** (0.047 g of the enriched fraction (bp 50–65 °C containing ca. 50% hexanes), ca. 0.023 g of **10**, 0.213 mmol), and toluene (0.21 mL) was maintained at room temperature for 18 h and then concentrated. ^{1}H NMR analysis of the crude material revealed two methyl doublets (δ 1.45 and 1.21) in a ratio of 1:4.8 (**29**:**28**). Radial chromatography (silica gel, hexane–ethyl acetate, 10:1) gave 0.035 g (57%, 75% based on recovered NPM) of material composed of the same ratio of isomers and 0.008 g of recovered NPM. Preparative HPLC allowed the isolation of pure samples of **28** and **29**. **28**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.15 (m, Ph*H*), 5.67 (m, C=CH), 3.42 (t, J = 8.55 Hz, COCH), 3.29 (ddd, J = 8.52, 6.52, 1.75 Hz, $COCHCH_2$), 2.86 (ddd, J = 1.70, 7.02, 14.58 Hz, C*H*HC=), 2.55 (m, $CHCH_3$), 2.35 (m, 1 H), 2.25 (m, 2 H), 2.12 (m, $CHCCH_3$), 1.95 (m, 1 H), 1.33 (m, 1 H), 1.21 (d, J = 6.6 Hz, CH_3). **29**: ^{1}H NMR (500 MHz, $CDCl_3$) 7.5–7.1 (m, PhH), 5.65 (m, C=CH), 3.4 (dd, J = 5.25, 8.48 Hz, COCH), 3.24 (dt, J = 0.9, 8.4 Hz, $COCHCH_2$), 2.75 (ddd, J = 1.0, 7.0, 14.50 Hz, C*H*HC=), 2.50 (m, $CHCCH_3$), 2.4–2.3 (m, 2 H), 2.3–2.2 (m, 2 H), 1.8–1.7 (m, 2 H), (d, J = 7.0 Hz, CH_3). Characteristic data for the product mixture: IR (KBr) 2953, 1702, 1499, 1455, 1386, 1190, 893 cm^{-1}; MS (CI), m/e 282 (MH^+): MS (EI), m/e 281.1404 (24%, 281.1416 calcd for $C_{18}H_{19}NO_2$), 175 (65%), 107 (100%).

Reaction of 10 with Tetracyanoethylene, A solution of TCNE (0.027 g, 0.208 mmol), **10** (0.045 g of the enriched fraction (bp 50–65 °C containing approximately 50% hexanes), ca. 0.023 g of **10**, 0.208 mmol), and THF (0.20 mL) was maintained at room temperature for 18 h and then concentrated. The crude material was passed through a small plug of silica (hexane–ethyl acetate, 5:1), giving 0.045 g (91%) of material. ^{1}H NMR (500 MHz) analysis revealed two vinyl resonances (δ 5.68 and 5.58) in a ratio of 1:6.17 (**26**:**25**). The major isomer **26** was isolated by fractional crystallization from hexane, while an enriched (90%) sample of the minor isomer **27** could be obtained by preparative GLC ($^1/_4$ in. × 6 ft column containing 3% SP-2100, oven temperature 150 °C). **26**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.58 (m, C=CH), 3.20–3.10 (m, $C(CN_2)CH_2$), 2.74 (m, $CHCCH_3$), 2.60–2.40 (m, 2 H), 2.20–2.10 (m, 2

H), 1.6–1.5 (m, 1 H), 1.42 (d, J = 6.13 Hz, CH_3). **27**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.64 (m, C=CH), 3.30 (m, C*H*CCH_3), 3.20 (m, C(CN_2)CH_2), 2.82 (m, C*H*CH_3), 2.60–2.40 (m, 2 H), 2.00–1.90 (m, 1 H), 1.75–1.65 (m, 1 H), 1.28 (d, J = 7.3 Hz, CH_3). Characteristic data for the product mixture: IR (KBr) 2973, 2256, 1463, 1455, 1438, 1385, 1256, 847 cm^{-1}; MS (EI), m/e 236.1053 (100%, 236.1062 calcd for $C_{14}H_{12}N_4$), 171 (53%), 108 (64%).

DNOE Experiments for 26 and 27. Irradiation of the bridgehead methine hydrogen of **26** (δ 2.15) gave a 2.1% enhancement of the methine hydrogen α to the methyl group (δ 2.74). Irradiation of the methine hydrogen α to the methyl group of **26** gave a 2% enhancement of the bridgehead methine hydrogen. Irradiation of the bridgehead methine hydrogen of **27** (δ 3.30) gave an 9.0% enhancement of the methine hydrogen α to the methyl group (δ 2.82). Irradiation of the methine hydrogen α to the methyl group of **27** gave a 11.4% enhancement of the bridgehead methine hydrogen.

Reaction of 16 and *N*-Phenylmaleimide, Preparation of 30. A solution of NPM (140 mg 0.810 mmol), **16** (104 mg 0.810 mmol), and dry toluene (1 mL) was maintained at 80 °C for 48 h, allowed to cool to room temperature, and concentrated. The resulting crude solid was recrystallized from ethyl acetate–hexane to afford 175 mg (72%) of pure **30** (mp 179–181 °C) as a single isomer: ^{1}H NMR (250 MHz, acetone-d_6) δ 7.49–7.39 (m, PhH), 7.21–7.18 (m, PhH), 6.03–5.99 (m, C=CH), 4.3 (dd, J = 8.9, 6.4 Hz, OCC*H*CH), 3.57 (dt, J = 8.7, 1.34 Hz, OCC*H*CH_2), 3.43 (m, 1 H), 3.35–3.25 (m, 1 H), 3.1–2.9 (m, 4 H), 2.71 (ddd, J = 15.5, 7.2, 1.34 Hz, HC*H*C=), 2.65–2.3 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 177.9, 176.4, 142.2, 131.5, 129.2, 128.9, 126.1, 118.9, 68.3, 50.9, 42.0, 38.5, 30.8, 25.5 ppm; IR (KBr) 1704, 1393, 1210, 1186, 1175, 1060, 1021, 762 cm^{-1}; MS (CI), m/e 302 (MH^+); MS (EI), m/e 301.0769 (55%, 301.0772 calcd for $C_{16}H_{15}NO_3S$), 253 (49%), 92 (100%). Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.76; H, 5.02; N, 4.65. Found: C, 63.71; H, 5.07; N, 4.62.

Reduction of 30 to 33. A solution of **30** (20.0 mg, 0.066 mmol in 4 mL of dry CH_2Cl_2) was added to a rapidly stirred suspension of P_2I_4[24] (37.8 mg, 0.064 mmol) in dry CH_2Cl_2 (4 mL). This mixture was allowed to stir for 10 min, diluted with 10 mL of CH_2Cl_2, and washed with $Na_2S_2O_4$ (2 × 8 mL). The organic portion was dried (Na_2SO_4) and concentrated to give 15.6 mg (85%) of **33** as a yellow crystalline solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.55–7.15 (m, PhH), 5.91–5.88 (m, C=CH), 3.99–3.96 (m, CHCS), 3.50 (dd, J = 9.0, 7.3 Hz, COCHCS), 3.32 (dt, J = 8.6, 1.6 Hz, COCHCH_2), 3.0–2.7 (m, 5 H), 2.4–2.2 (m, 1 H); IR (KBr) 2973, 1704, 1387, 1168, 781 cm^{-1}; MS (CI), m/e 286 (MH^+); MS (EI), m/e 285.030 (60%, 285.0830 calcd for $C_{16}H_{15}NO_2S$), 112 (100%).

Reaction of 17 and *N*-Phenylmaleimide, Preparation of 31. A solution of NPM (0.034 g, 0.198 mmol), **17** (0.026 g, 0.198 mmol), and toluene (0.19 mL) was maintained at 70 °C for 7 days. The reaction mixture was concentrated, and the crude material was chromatographed (silica gel, 240–400 mesh, 30:1 CH_2Cl_2–EtOH), giving 0.054 g (89%) of **30** as an essentially pure yellow solid. An analytical sample was prepared by recrystallization from EtOAc–hexane (mp 178–180 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.3 (m, Ph*H*), 7.2–7.1 (m, Ph*H*), 5.34 (dt, J = 2.91, 7.7 Hz, =CH), 5.14 (dd, J = 1.25, 9.6 Hz, OC*H*HSO), 4.62 (d, J = 9.6 Hz, OCH*H*SO), 4.18 (dd, J = 5.5, 8.8 Hz, OCCHCS), 3.63 (m, CHCSO), 3.38 (dt, J = 9.0, 1.0 Hz, COC*H*CH_2), 2.84 (ddd, J = 15.8, 7.8, 1.0 Hz, C*H*HC=), 2.45 (m, CH*H*C=); ^{13}C NMR (125 MHz, $CDCl_3$) 177.5, 176.7, 154.2, 131.2, 129.4, 129.2, 126.1, 95.8, 96.0, 67.1, 42.6, 38.7, 24.8 ppm; IR (KBr) 2984, 1702, 1500, 1212, 1045 cm^{-1}; MS (CI), m/e 304 (MH^+); MS (EI), m/e 303.0566 (3%, 303.0565 calcd for $C_{15}H_{13}NO_4S$), 273 (60%), 94 (100%). Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.39; H, 4.32; N, 4.62. Found: C, 59.44; H, 4.38; N, 4.60.

Reaction of 18 and *N*-Phenylmaleimide, Preparation of 32. A solution of NPM (0.034 g, 0.198 mmol), **18** (0.029 g, 0.198 mmol), and toluene (0.2 mL) was maintained at 70 °C for 7 days. The reaction mixture was concentrated, and the crude material was chromatographed (silica gel, 240–400 mesh, CH_2Cl_2–EtOH, 50:1, for 5 column volumes and then 30:1 CH_2Cl_2–EtOH), giving 0.060 g (95%) of **32** as a white solid (mp 194–196 °C): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.35 (m, Ph*H*), 7.1–7.2 (m, Ph*H*), 5.11 (dd, J = 1.28, 9.63 Hz, OC*H*HSO), 4.52 (d, J = 9.62 Hz, OCH*H*SO), 4.11 (dd, J = 5.54, 8.89 Hz, OCCHCSO), 3.60 (m, 1 H), 3.36 (m, 1 H), 2.66 (dd, J = 1.26, 14.32 Hz, CH_3), 2.5 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 177.6, 176.8, 146.7, 131.2, 129.4, 129.2, 126.1, 106.6, 90.3, 67.0, 42.6, 38.8, 30.9, 16.4 ppm; IR (KBr) 2990, 1702, 1694, 1398, 1166, 1045, 1017, 696 cm^{-1}; MS (CI), m/e 318 (MH^+); MS (EI), m/e 317.0723 (33%, 317.0722 calcd for $C_{16}H_{15}NO_4S$), 225 (75%), 108 (100%). Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.55; H, 4.76; N, 4.41. Found: C, 60.45; H, 4.83; N, 4.40.

Control Experiments. The isolated adduct (or an enriched sample thereof) was dissolved in the reaction solvent and maintained at room temperature while being monitored by ^{1}H NMR or capillary GC. In all cases no isomerization to another cycloadduct was observed. The following experiments were performed (adduct, solvent(s), time): **20a** (toluene, THF, CH_3OH, 48 h); **19c** and **20c** (a 58:42 mixture, toluene, 48 h); **22c** (THF, 24 h); **23c** (THF, 24 h); **26** and **27** (a 3:1 mixture, THF, 24 h); **29** (toluene, 24 h); **28** (toluene, 24 h); **22b** (THF, 24 h); **23b** (THF, 24 h).

Acknowledgment. We wish to thank Professor R. Taft for his insightful discussion and Dr. J. Ziller for assistance with the X-ray studies. We also wish to thank Professor A. G. Fallis for a preprint of ref 12 and for permission to quote his unpublished results reported in ref 42. The financial support of the National Science Foundation (Grant CHE-86-18451) and the NSF Shared Instrumentation program are gratefully acknowledged.

Registry No. **6**, 4683-50-5; **7**, 108264-48-8; **8a**, 114614-91-4; **8b**, 114614-87-8; **8c**, 114614-88-9; **9**, 114614-92-5; **10**, 114614-93-6; **11**, 1003-04-9; (*E*)-**12**, 114614-94-7; (*Z*)-**12**, 114614-89-0; (*E*)-**13**, 114614-95-8; (*Z*)-**13**, 114614-90-3; (*E*)-**14**, 114614-96-9; (*Z*)-**14**, 114615-10-0; (*E*)-**15**, 114614-97-0; (*Z*)-**15**, 114615-11-1; **16**, 114614-98-1; **17**, 114274-81-6; **18**, 114274-84-9; **19a**, 114614-99-2; **19c**, 114615-12-2; **20a**, 114673-90-4; **20b**, 114615-13-3; **20c**, 114673-91-5; **21**, 114633-62-4; **22a**, 114615-00-8; **22b**, 114615-14-4; **22c**, 114615-15-5; **23a**, 114615-01-9; **23b**, 114615-16-6; **23c**, 114615-17-7; **24**, 114615-02-0; **25**, 114615-03-1; **26**, 114615-04-2; **27**, 114615-05-3; **28**, 114615-06-4; **29**, 114714-88-4; **30**, 114615-07-5; **31**, 114274-89-4; **32**, 114274-92-9; **33**, 114615-08-6; **34**, 114615-09-7; **35**, 90049-64-2; NPM, 941-69-5; TCNE, 670-54-2; methyltriphenylphosphonium bromide, 1779-49-3.

Supplementary Material Available: Details of X-ray studies (12 pages). Ordering information is given on any current masthead page.