Role of Heteroatoms in Diastereofacial Control in Cycloaddition to a Dissymmetric Cyclohexa-1,3-diene Moiety in a Polycyclic Framework. Remarkable Stereodirecting Influence of Distal Protective Groups

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Diels−Alder cycloaddition to several derivatives of a facially dissymmetric diene, the hexacyclo-[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2,4-diene-7,15-dione **4a**, with a variety of dienophiles such as singlet oxygen, *N*-phenyltriazolinedione, dimethyl acetylenedicarboxylate, maleic anhydride, and *N*-methylmaleimide has been studied. The stereochemistry of the resulting adducts has been unambiguously secured by ^{1}H and ^{13}C NMR spectral data, chemical correlations, and X-ray crystal structure determination. While a variety of dienophiles undergo [4 + 2]-cycloadditions with **4a** predominantly from the carbonyl face, protection of the carbonyl groups in **4a** as simple mono- or bis-acetals **4b**−**e** or thioacetals **9a,b** leads to complete reversal in selectivity, favoring addition from the cyclobutane face, with heterodienophiles and acetylenic dienophiles. The reversal in selectivity observed in mono- and bis-acetals **4b**−**e** has been attributed to unfavorable electrostatic interaction between the oxygen atom and the incoming dienophile. Whereas, in the case of thioacetals **9a,b**, apart from unfavorable electrostatic interactions, Cieplak-type hyperconjugative interactions have to be given due consideration in order to account for the observed selectivities. Our studies highlight the role of simple protective groups (acetals in the present case) in modulating diastereoselection during [4 + 2]-cycloadditions.

Introduction and Background

Among the commonly employed methods for generating stereogenic centers,[1] [4π + 2π]-cycloadditions (Diels−Alder reaction) have attracted much attention, as they are among the most versatile and synthetically useful reactions in which four new contiguous stereogenic centers can be generated in a single laboratory operation.[2] The influence of olefin geometry, neighboring chiral centers, and transition state topology on product stereochemistry is well-established. However, the role of π-facial diastereoselection, which arises when the two faces of the reacting partners, viz. the diene or the dienophile, are nonequivalent (dissymmetric), is still a matter of ongoing debate.[3] Thus, it is important to study either newer probe systems or modify the existing ones to get better insights into the steric and electronic factors that control diastereoselection in Diels−Alder reactions of dissymmetric 1,3-dienes.

Cycloaddition studies with a number of simple cyclic dienes, wherein the conformational effects are minimal and which allow an assessment of other factors, have revealed the importance of steric,[4,5] ground-state geometric distortions,[6] product stabilities,[7] torsional effects,[8] orbital mixing/tilting,[9,10] secondary orbital interactions,[11] hyperconjugative effects,[12] electrostatic interactions,[13] and nonbonded attraction between the diene and dienophile[14] as additional factors in determining face selectivity. Attempts have been made to evaluate critically the relative importance of steric, orbital, and electrostatic effects in determining the π-face preferences. In this regard, substrates having the 1,3-diene moiety embedded in constrained, rigid polycyclic frames constitute incisive probe systems as electronic fine-tuning of the substituents can be achieved without concomitant conformational ambiguities. Several polycyclic probe systems such as **1**−**4a** have been studied in detail to glean insights into the subtle role of stereoelectronic factors in determining face selectivity in [4 + 2]-cycloadditions.[10,15−18] Among

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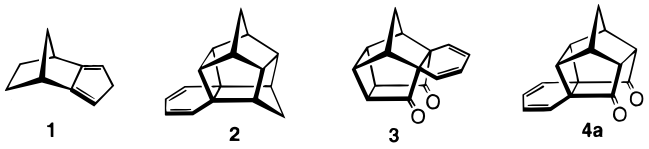
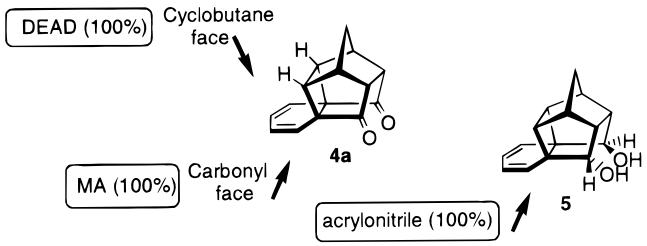
them, the hexacyclic diene **4a**, embodying a [4.4.2]-propella-2,4-diene moiety as part of its rigid structure,

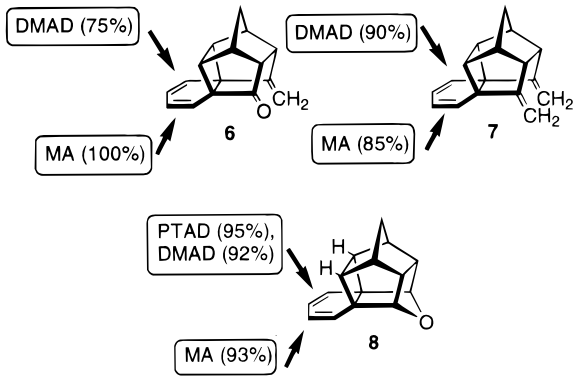


has been more enduring because of its ready availability,[19] reactivity, and ease of functional group interconversion. In addition, the planarity of the diene component was ensured on the basis of single-crystal X-ray structure[17a,d,18b] of diene **4a**, thereby ruling out ground-state geometric distortion. Furthermore, the 1,3-diene moiety in **4a** is desymmetrized by the presence of an electron-rich cyclobutane ring on one face and two carbonyl groups at the homoallylic position on the other and provides an opportunity to study the effect of heteroatoms[20,21] on Diels−Alder diastereoselection and also the subtle steric and electronic factors associated with them. Apart from the intrinsic nonequivalence in the steric environment, the functionalities can also exert electronic preferences such as hyperconjugative participation of the high-energy cyclobutane σ-bonds and electrostatic interaction of the two carbonyl groups in the vicinity of a polar reagent. Coxon et al.[17] and Pandey et al.[18] have independently studied the π-face selectivities exhibited by **4a** and its derivatives and have found that the diene **4a** captures a variety of dienophiles from the sterically more open carbonyl face. However, dienophiles such as maleic anhydride (MA), benzyne, singlet oxygen ($^1O_2$),[22] *N*-phenyl-1,2,4-triazolinedione (PTAD), dimethyl acetylenedicarboxylate (DMAD), and DEAD exhibit mixed selectivity with exclusive carbonyl-face attack in the case of MA and exclusive cyclobutane-face attack for DEAD.[17a] The variation in selectivity observed in the case of azo and alkyne dienophiles was qualitatively rationalized by Coxon et al.[17a] as an interplay of three factors. (i) In MA addition, steric interaction between the cyclobutane hydrogens and the dienophile directs addition exclusively from the carbonyl face. (ii) The azo and alkyne type of dienophiles do not possess protons similarly disposed to those in the olefinic dienophiles for steric interaction with the cyclobutane protons. In other words, the exclusive carbonyl-face attack observed with olefinic dienophiles is a consequence of the steric bias inherent in the diene **4a**. (iii) In the transition state for carbonyl-face attack, the π- or nonbonding orbital electron density in the alkyne and azo dienophiles can repulsively interact with the electron density of the carbonyl oxygen atoms.

To probe the role of carbonyl groups in π-facial selectivities in the diene **4a**, Pandey et al.[18a] have studied the facial selection in corresponding diol **5**, resulting from



$NaBH_4$ reduction of **4a**, with acrylonitrile to give the endo-product with addition exclusively from the hydroxy face as shown. On the basis of these findings, it was surmised that the carbonyl groups are unimportant in determining the face selectivity in **4a**.[18a] To substantiate their interpretation concerning the role of carbonyl groups, Coxon et al. replaced the carbonyl groups by methylidene groups as in **6** and **7**, thereby retaining the π-electron configuration but replacing the lone pairs of the carbonyl oxygens with hydrogen atoms, expecting that this subtle variation might increase the steric hindrance to the carbonyl-face addition and encourage reaction from the cyclobutane face of the diene.[17b]



It was shown that alkene dienophiles, MA and benzoquinone, react with the dienes **6** and **7** with strong preference for the carbonyl face, whereas, for DMAD, attack from this face decreases with successive methylidene substitution. In the case of PTAD this trend was found to be reversed. It was shown that several factors such as ground-state geometric distortion,[6] product stabilities,[7] σ/π-mixing,[10] and steric and torsional effects[8] which were earlier considered to be responsible for governing face selectivities could not explain all the observed selectivities in this system. Apart from orbital tilting and transition state steric and torsional interactions, unfavorable orbital interaction of the closed shells of the carbonyl(s) and methylidene(s) syn to the incoming orthogonal π-orbital of DMAD was also considered important.[17b]

To validate this proposition, Coxon et al.[17c] investigated the π-face preferences in a related cage ether **8**, wherein a lone pair of the ether oxygen is positioned centrally so as to interact with the π-orbital of the acetylenic dienophile or n-orbitals of an azo dienophile. It was reasoned that if this electronic effect were important, acetylenic and azo dienophiles would react from the cyclobutane face and alkene dienophiles from the less hindered ether face. Indeed, such a variation in face selectivities with

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Table 1. Product Distribution (%)[a] and Yield (%) in Cycloadditions of Various Dienophiles to 4a−e

	singlet oxygen		PTAD		DMAD		MA	
substrate	carbonyl face **10a−e**	cyclobutane face **11a−e**	carbonyl face **12a,c**	cyclobutane face **13a,c**	carbonyl face **14a−e**	cyclobutane face **15a−e**	carbonyl face **16a−e**	cyclobutane face **17a−e**
4a	78	22 (88)	64	36 (80)	55	45 (85)	100 (98)	
4b	14	86 (92)			17	83 (91)	100 (98)	
4c		100 (98)		100 (85)	05	95 (92)	100 (98)	
4d		100 (70)			06	94 (75)	100 (98)	
4e	03	97 (91)			18	82 (83)	100 (98)	

[a] The product ratios were obtained from the analyses of the ^{1}H NMR spectra of the crude reaction mixture as well as from isolated yields of pure compounds.

three representative dienophiles, viz. MA, DMAD, and PTAD, was observed. MO calculations at the AM1 level reproduced the observed selectivities. Additionally, on the basis of these calculations, an unfavorable interaction in the transition state between the filled π-orbital of acetylene (disposed orthogonal to the forming σ-bonds) and the lone pair on the ether oxygen was computed during approach from the ether face. Coxon et al. have recognized this factor for undermining addition from the ether face.[17c]

Results and Discussion

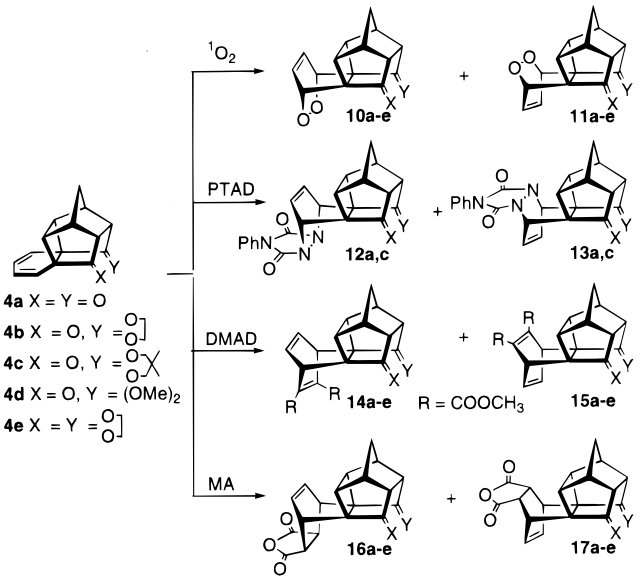
On the basis of earlier studies on system **4a**, it was reasoned that rehybridization of the carbonyl carbon(s) in **4a** and strategic disposition of hetero (O, S etc.) functionalities on the newly generated sp^3 center(s) should enable alteration of face selectivity in a profound way. In a practical sense, this expedience could be simply implemented by protecting the carbonyl groups in **4a** as corresponding acetals or thioacetals, which represents a simple modification of a carbonyl group through a protective group. Thus, without substantially altering the steric environment or sacrificing the skeletal identity of the substrate, simple protective groups could function as stereodirectors by turning on the electrostatic effects. The expectation was that with hetero and acetylenic dienophiles the speculated repulsive interactions between the acetal oxygens and the lone pair or filled π-orbital of the dienophiles would be operative and reverse the face selectivity.

Further, to make the study comprehensive, dienophiles representing three important types were employed: (a) MA and *N*-methylmaleimide (NMM), as representative alkene dienophile, wherein, the two olefinic protons could induce a steric bias; (b) DMAD, a representative acetylenic dienophile with filled π-orbitals; and (c) $^1O_2$ and PTAD, representing heterodienophiles with filled n-orbitals which can interact with the diene substrate.

Cycloadditions to Acetals 4b−e. The hexacyclic dione **4a** was readily transformed to the corresponding mono- and bis-acetals (**4b−e**) or thioacetals (**9a,b**), through simple protective group modification of the carbonyl groups.[23] The mono- and bis-acetals of **4a** were obtained using the appropriate alcohol/diol in benzene and employing PTSA as the catalyst.

The dione **4a** and acetals **4b−e** readily underwent photooxygenation when irradiated with a 500 W tungsten lamp using methylene blue as the sensitizer to furnish endoperoxides **10a−e** and **11a−e**, respectively (Scheme 1). While in the dione **4a** $^1O_2$ addition occurred predominantly from the carbonyl face,[22] in the acetals **4b−e** the addition was found to be uniformly from the cyclobutane face and the diastereomeric ratios are indicated in Table 1.

Scheme 1



Addition of PTAD, generated by the oxidation of *N*-phenylurazole to acetal **4c**, followed the same trend as observed for $^1O_2$ addition, and a single crystalline adduct **13c**, arising from cyclobutane-face attack, was realized. The carbonyl-face adduct **12c** could not be detected in the crude reaction mixture (^{1}H NMR spectrum) (Table 1). Acetals **4b**, **4d**, and **4e** did not furnish readily characterizable products on reaction with PTAD. It is known[17a] that PTAD is captured predominantly from the carbonyl face in the dione **4a** to furnish adducts **12a** and **13a** (Scheme 1).

The acetals **4b−e** underwent smooth [4 + 2]-cycloaddition with DMAD in refluxing benzene to afford adducts **14b−e** and **15b−e**, with preponderant attack from the cyclobutane face, in analogy with $^1O_2$ and PTAD additions (Scheme 1). In sharp contrast to this observation, the dione **4a** is known[17a] to afford adducts **14a** and **15a**, with modest excess of addition from the carbonyl-face (Table 1).

As a control, we also studied the addition of MA to acetals **4b−e** to rule out any significant contribution from steric factors. The addition of MA to acetals **4b−e** was effected in refluxing benzene to furnish adducts **16b−e** (Scheme 1). The series of adducts **17b−e** could not be detected in any of the reaction mixtures. We were gratified to note that the addition indeed occurred exclusively from the carbonyl face, effectively eliminating any steric intervention by the acetal groups (Table 1).

(23) A portion of this work dealing with the cycloadditions to acetals has been published as a preliminary communication, see: Mehta, G.; Uma, R. *Tetrahedron Lett.* **1995**, *36*, 4873.

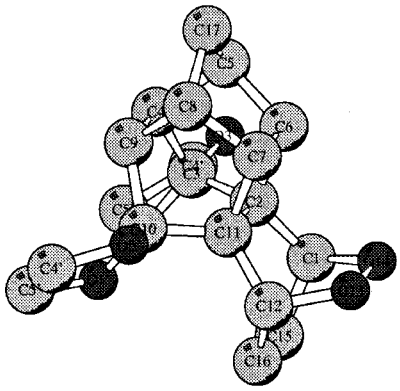


Figure 1. Molecular structure of **11e**.

The yields in the various cycloadditions studied ranged between 70 and 100% and are displayed in Table 1. The product ratios were obtained from the analyses of the ^{1}H NMR integration of the crude reaction mixture as well as from isolated yields of pure compounds and are summarized in Table 1. The diastereomers were carefully separated using silica gel column chromatography and fully characterized. Interestingly, the cyclobutane-face adducts in most of the cases eluted out first from the column.

Stereochemical Assignments of the Diastereomeric Addition Products. Stereostructures of all the cycloadducts were determined on the basis of detailed NMR spectral analyses, particularly ^{1}H NMR data; chemical correlation; and X-ray crystal structure determination of key compounds.

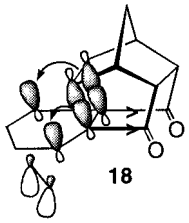
Analyses of ^{1}H NMR Spectral Data. The formation of [4 + 2]-cycloaddition products was indicated by the disappearance of signals due to cyclohexadiene moiety in the region δ 5.4−6.0 and appearance of signals due to the bicyclo[2.2.2] moiety; particularly, the allylic bridgehead protons and olefinic protons in the region δ 6.4−6.8 were of diagnostic value.

In most of the adducts, the cyclobutane protons served as a stereochemical handle, as they are deshielded by a syn transannular heteroatom bridge. On the other hand, the cyclobutane hydrogens are substantially shielded by a syn double bond. However, in the case of DMAD addition products, the cyclobutane hydrogens were no longer of any diagnostic value and hence we resorted to other methods for assigning stereostructures.

Chemical Correlation and X-ray Crystal Structure Determination. The stereostructures were unambiguously secured by chemical transformation of each of the diastereomer into a known compound whose structure was established by single-crystal X-ray diffraction studies.[17a,d,22] While the crystal structure of **11a** has been reported previously[22] by us, that of **11e** is included here and the molecular structure is shown in Figure 1. The chemical correlations involved routine protection−deprotection protocols. Unmasking the acetal groups in the adducts **11d**, **11e**, **13c**, **15c**, **15d**, **15e**, **16d**, and **16e** converted them into the adducts derived from **4a**, whose stereostructure has been previously established. Alternatively, the adducts of known derivatives of **4a** could be converted into the corresponding acetal derivatives. Thus, the endoperoxides **11d** and **11e** were hydrolyzed to dione **11a**[22] and mono-acetal **11b**, respectively. Likewise, the mono-acetal **13c** was hydrolyzed into the dione **13a**.[17a] Further, the mono-acetals **15c** and **15d** and bis-acetal **15e** were hydrolyzed to dione **15a**[17a] and mono-acetal **15b**, respectively. Alternately, the dione **14a**[17a] was acetalized to furnish **14b**, **14c**, and **14e**. In addition, mono-acetal **16d** and bis-acetal **16e** were converted to dione **16a**[17a] and mono-acetal **16b**, respectively. Last, the dione **16a**[17a] was transformed into mono-acetals **16b** and **16c**.

Interpretation of Diastereoselectivities. For acetals **4b**−**e**, addition of $^1O_2$, PTAD, and DMAD is overwhelmingly preferred from the cyclobutane face, in dramatic contrast to the carbonyl-face addition in **4a**.[17a] There is no marked change in the π-face selectivity in addition of MA to **4b**−**e**, clearly indicating that the observed preferences are dienophile specific. The fine-tuning of the face selectivity as a function of the acetal protecting group (Table 1) further reflects the effect of subtle variations in the positioning of the oxygen atoms on the extent of repulsive interactions. Interestingly, higher selectivities have been observed for the more flexible mono-acetals **4c** and **4d**. Since there is no marked change in the π-face selectivity of MA to acetals **4b**−**e** when compared with the dione **4a**, it is reasonable to rule out any steric intervention due to the acetal groups. In fact, the predominant cyclobutane-face selectivity in **4b**−**e** is a contrasteric outcome.

Several factors such as product stability,[7] ground-state geometric distortion,[6] σ/π-mixing,[10] and torsional interactions,[8] which have been previously considered to account for face selectivity in [4 + 2]-cycloaddition, are not applicable for this system. According to the Cieplak model,[12a] the addition should occur from the side opposite to the most electron rich bond, as shown for **4a**; see **18**.



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This model can readily rationalize the predominant carbonyl-face attack (addition opposite to electron rich cyclobutane bonds) in MA, but it fails to rationalize the contrasteric approach of $^1O_2$, PTAD, and DMAD in acetals **4b**−**e**. In particular, the key hyperconjugative interaction in the cycloaddition transition state should become more important when the newly formed bonds involve highly electronegative groups. Hence, addition of $^1O_2$ or PTAD to the carbonyl face of the diene is predicted to be strongly preferred on the basis of the Cieplak model; nevertheless, the observed selectivities are reversed for acetals **4b**−**e**.

The observed selectivities can be rationalized as follows: when the addition occurs from the face of the diene bearing the acetal functionality in **4b**−**e**, a repulsive nonbonded interaction between the lone pair on the acetal oxygen with the π-orbital of DMAD or n-orbitals of PTAD or $^1O_2$ (which are orthogonal to forming σ-bonds) is turned on, resulting in destabilization of the transition state. Further, the variation in diastereoselectivity, with respect to the dienophile employed (Table 1), reaffirms our surmise that the repulsive nonbonded interactions between the incoming dienophile and the acetal oxygens in **4b**−**e** govern the π-facial selectivities in these systems.

Table 2. Product Distribution (%)[a] and Yield (%) in Cycloadditions of Various Dienophiles to 9a,b

	singlet oxygen		PTAD[b]		DMAD		MA		NMM	
substrate	carb[c] face **19a,b**	cyb face **20a,b**	carb face **21a,b**	cyb face **22a,b**	carb face **23a,b**	cyb face **24a,b**	carb face **25a,b**	cyb face **26a,b**	carb face **27a,b**	cyb face **28a,b**
9a		100 (15)	09	91 (75)		100 (92)	100 (98)		100 (98)	
9b		100 (81)	11	89 (80)		100 (91)	100 (98)		100 (98)	

[a] The product ratios were obtained either from the analyses of the ^{1}H NMR spectra of the crude reaction mixture or from isolated yields of pure compounds. [b] The adducts **21a,b** and **22a,b** underwent in situ dethioacetalization to furnish **12a** and **13a**, respectively. [c] Carb face, carbonyl face; Cyb face, cyclobutane face.

In addition, these results also provide an unprecedented illustration of the stereodirecting effect of simple remote protective groups. Since acetal protection and deprotection are fairly routine manipulations, we feel that this tactic can be employed for controlling diastereoselection in certain systems.

Cycloaddition to Thioacetals 9a,b. To further extend the scope of our findings on the acetals **4b**−**e**, we directed our study to their sulfur counterparts **9a,b**, expecting to gauge the effect of the change in the heteroatom on diastereoselection in these systems. Although considerable efforts have been made to understand the influence of a heteroatom on [4 + 2]-cycloadditions, experimental data available to illustrate the role of allylic/homoallylic sulfur substituents is rather limited.[20,21] Apart from this, the following distinctive features make studies employing sulfur as a heteroatom particularly interesting:

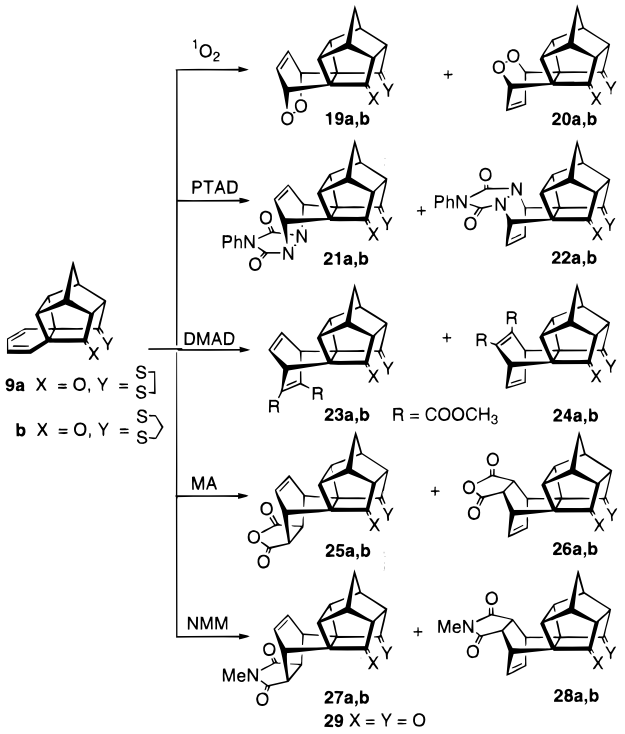
If the Cieplak hyperconjugative model[12] is operative, it is reasonable to speculate that a preference should exist for addition anti to the best σ-donor (C−S bond) when the competition is between a C−C and a C−S bond.

If the electrostatic model is the principal determinant of face selectivity, oxygen atoms will experience greater nonbonded lone pair repulsion in the vicinity of a heterodienophile such as $^1O_2$ or PTAD because of the better match in their 2p energy levels as compared to that of sulfur.[21,24] Hence, addition syn to sulfur may not be disfavored. However, progression from oxygen to sulfur is accompanied by substantial changes in atomic radii (van der Waals radii for oxygen is 1.4 Å and that of sulfur is 1.85 Å) and bond length (C−S bond is 2.0 Å and C−O bond is 1.45 Å). Taking both the bond length and atomic radii into consideration, the net steric factor favors addition opposite to sulfur.[3]

To evaluate the relative contribution of the above-mentioned effects, we ventured to investigate the π-facial selectivities of mono-thioacetals **9a,b** which were readily prepared from **4a** employing the appropriate dithiol, viz.1,2-ethanedithiol or 1,3-propanedithiol and PTSA as the catalyst. However, the bis-thioacetals were not formed under these reaction conditions. The crystalline mono-thioacetals **9a,b** were fully characterized on the basis of their ^{1}H and ^{13}C NMR spectral data. The ^{13}C NMR spectra indicated loss of symmetry in consonance with the mono-thioacetal structure.

The thioacetal **9b** readily underwent photooxygenation to furnish a single crystalline endoperoxide **20b** in near quantitative yield (Scheme 2). However, in **9a**, photooxygenation was not clean (probably due to other competing reactions such as oxidation at sulfur) and resulted in poor yield of endoperoxide **20a**. In both **9a** and **9b** $^1O_2$ addition is uniformly, exclusively from the cyclobutane-face and the adducts **19a,b** due to carbonyl face attack were not encountered (Table 2).

Scheme 2



Addition of PTAD to thioacetals **9a,b** was brought about in dichloromethane at 0−5 °C. The ^{1}H NMR spectral features of the resulting adducts clearly indicated that they were in fact PTAD addition products **12a** and **13a** of the hexacyclic dione **4a** and their identity was further confirmed by comparing the ^{1}H and ^{13}C NMR spectra with authentic samples. Our speculation was that during PTAD addition to **9a,b** the resultant [4 + 2]-adducts **21a,b** and **22a,b** underwent smooth in situ dethioacetalization to furnish adducts **12a** and **13a**, respectively, corresponding to those derived from hexacyclic dione **4a**. The issue that needed to be settled at this juncture was whether dethioacetalization preceded or followed the addition of PTAD to thioacetals **9a,b**. The answer was forthcoming from the fact that the major (~90%) diastereomer obtained in the case of **9a,b** corresponded to **22a,b** (not isolated) through the cyclobutane-face addition (cf. ~36% observed in the case of hexacyclic dione **4a**), which established beyond doubt that dethioacetalization followed PTAD addition (Scheme 2). Therefore, the diastereoselectivities observed during PTAD additions reported herein correspond to that of thioacetals **9a,b**.[25] Addition of PTAD to thioacetals **9a,b** follows the same trend as in $^1O_2$ addition, albeit with slight decrease in selectivity (Table 2).

(24) Bohm, M.; Gleiter, R. *Tetrahedron* **1980**, *36*, 3209.

Further, thioacetals **9a,b** underwent smooth [4 + 2]-cycloaddition with DMAD exclusively from the cyclobutane face, in accord with $^1O_2$ and PTAD addition. The crude reaction mixture did not indicate the presence of carbonyl-face adducts **23a,b** (Table 2).

As a control, we also studied the addition of MA and NMM to thioacetals **9a,b**, to gauge contribution from steric bias exerted by the thioacetal functionality. The addition of MA and NMM to thioacetals **9a,b** was effected in refluxing benzene to furnish adducts **25a,b** and **27a,b**, respectively (Table 2). In each case, addition indeed occurred exclusively from the carbonyl face, without any trace of the corresponding cyclobutane-face adducts (**26a,b** and **28a,b**) (Scheme 2).

The yields in cycloadditions ranged between 90 and 100% and are displayed in Table 2. The product ratios were obtained from the analyses of the ^{1}H NMR integration of the crude reaction mixture as well as from isolated yields of pure compounds and are summarized in Table 2.

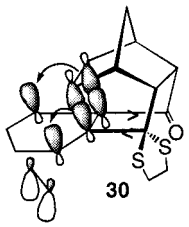
Stereochemical Assignments of the Diastereomeric Cycloaddition Products. Analyses of ^{1}H NMR Spectral Data. The formation of the [4 + 2]-cycloaddition products **19a,b**−**28a,b** was fully in consonance with the ^{1}H and ^{13}C NMR spectral data. All the cycloadditions reported herein afforded only Alder adducts. The disappearance of signals due to the cyclohexadiene moiety in the region δ 5.6−6.0 and appearance of signals due to the bicyclo[2.2.2] moiety were readily identifiable. Particularly, allylic bridgehead and olefinic protons in the region δ 6.4−6.8 were diagnostic. However, the stereostructures of adducts **24a,b**, **25a,b**, **27a,b** could not be assigned on the basis of the ^{1}H NMR spectral data alone. The signals for the diagnostic cyclobutane protons were often obscured by overlap with the multiplets due to the thioacetal group. The only exception being endoperoxide **20b**, where there was a discernible downfield shift of (ca. 0.3 ppm) for the cyclobutane protons, indicating a syn relationship to the transannular peroxo bridge.

Chemical Correlations. The stereostructures were unambiguously secured by chemical transformation of each of the diastereomer into a compound of known stereostructure. This was accomplished by either unmasking the thioacetal groups in the adducts or converting the adducts of known stereostructures into the corresponding thioacetal derivatives by protecting with appropriate dithiol. These chemical correlations involved unexceptional but tricky protection−deprotection protocols. Accordingly, the mono-thioacetals **24a,b** were dethioacetalized to the dione **15a**, whose structure has been previously established.[17a] Alternately, The dione **15a**[17a] was converted into mono-thioacetals **24a** and **24b**. Likewise, the dione **16a**[17a] was transformed into mono-thioacetals **25a** and **25b**. In addition, the dione **29**[17a] was converted into mono-thioacetals **27a** and **27b**.

Interpretation of Diastereoselectivities. The results in Table 2 clearly indicate that the thioacetal functionality has a profound bearing on the π-facial selectivity and is generally consistent with the observed trends in the acetals **4b**−**e**, most noteworthy being total selectivity in the case of MA, NMM, $^1O_2$, and DMAD with the introduction of barely a *single* thioacetal functionality. The addition of $^1O_2$ and DMAD to **9a,b** occurs exclusively from the cyclobutane face, while PTAD exhibits ~90% selectivity for this face. Last, MA and NMM almost exclusively add from the carbonyl face. For olefinic dienophiles, viz. MA and NMM, possessing an intrinsic steric bias, the addition is expected from the face of the diene which is sterically least hindered.

Considering the preferences observed for MA and NMM, it is not unreasonable to conclude that carbonyl face is still sterically less demanding as compared to cyclobutane face even after the introduction of thioacetal groups in dienes **9a,b**. Therefore, the observed preference for cyclobutane face during $^1O_2$, PTAD, and DMAD addition to thioacetals **9a,b** is a contrasteric outcome. Nonetheless, heterodienophiles do not have hydrogens, as in the case of MA or NMM, which can experience steric interaction during the cyclobutane-face attack. Considering these factors, the observed preferences during $^1O_2$, PTAD, and DMAD addition to thioacetals **9a,b** can be attributed to electronic factors such as orbital or electrostatic interactions.

The observed preferences for heterodienophiles and acetylenic dienophiles may be reconciled in terms of the Cieplak hyperconjugative model, according to which the preferred face of addition is anti to the most electron rich bond. In the substrates **9a,b**, the choice is between cyclobutane bonds and C−C bonds α to a thioacetal and a carbonyl group, as we are dealing with unsymmetrical mono-thioacetals; see **30**. Interestingly, it is evident from the trends in Table 2 that such a hyperconjugative contribution should be operative. On the other hand, unfavorable nonbonded interactions between the heterodienophiles and the lone pairs on sulfur should also encourage addition from the cyclobutane face. However, in thioacetals **9a,b** the relative contribution from such interactions is expected to decrease as compared to their oxygen variants **4b**−**e**, where there is better match of 2p energy levels. If this were the major determining factor, it is reasonable to speculate that the observed trends for cyclobutane-face addition would be reduced or comparable with the acetal series (**4b**−**e**).



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In light of these arguments, it is reasonable to consider that both electrostatic and orbital interactions act cooperatively during addition of heterodienophiles and acetylenic dienophiles, whereas, unfavorable steric interactions between cyclobutane and the olefinic hydrogens are the principal determining factors during addition of MA and NMM to thioacetals **9a,b**.

Concluding Remarks

Employing hexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2,4-diene-7,15-dione (**4a**), a unique polycycle, embodying a [4.4.2]propella-2,4-diene moiety as part of its rigid

(25) The concomitant dethioacetalization in **21a,b** and **22a,b** can be rationalized as follows. Preparation of PTAD involved oxidation[26] of *N*-phenylurazole with "oxides of nitogen"[27] and this invariably leaves residual amounts of the oxidizing reagent dissolved in DCM along with PTAD. We have shown that DCM solution of "oxides of nitrogen" effectively effects dethioacetalizations.[28]

structure, we have illustrated the profound influence of heteroatoms, viz. oxygen and sulfur, on π-facial diastereoselection in these systems by exploiting the distal carbonyl groups as a handle for electronic fine-tuning. Employing this tactic, we have shown that simple modification of carbonyl groups into mono- or bis-acetals (**4b**−**e**) or thioacetals (**9a,b**) can reverse the carbonyl face selectivity in [4 + 2]-cycloaddition with certain dienophiles. In other words, the reversal in diastereoselectivity in these systems has been accomplished through a routine protective group maneuver. With the demonstration of an unprecedented *stereodirecting* effect of simple, remote, protecting groups, we expect that this tactic would find useful synthetic applications in achieving diastereoselection in related systems, as acetal protection and deprotection is a fairly routine manipulation. The observed reversals in diastereoselectivities has been primarily attributed to unfavorable nonbonded interactions between acetal oxygens and filled orbitals on the dienophiles.

On replacement of oxygen by sulfur, as in the thioacetal system (**9a,b**), the expectation was that the magnitude of through-space interactions would be reduced and hence attack from the carbonyl face would be promoted. However, the total selectivity for the cyclobutane face, as observed in these systems, suggests the need for Cieplak-type hyperconjugative interactions to be considered in addition to through-space electrostatic interactions.

Experimental Section

All melting points are uncorrected. Microanalyses were performed on a Perkin-Elmer 240C CHN analyzer at the University of Hyderabad. Column chromatography was performed with Acme's silica gel (100−200 mesh). All nonhalogenated solvents were dried over sodium wire. Dichloromethane and chloroform were distilled over P_2O_5.

Acetalization/Thioacetalization of Dione 4a. General Procedure. In a round-bottomed flask fitted with a Dean−Stark water separator were placed dione **4a**[19] (500 mg, 2.23 mmol), alcohol/diol/thiol (∼2.5 equiv), PTSA (5−7 mg), and dry benzene (25 mL). The contents of the flask were refluxed overnight with stirring. The reaction mixture was cooled, diluted with ethyl acetate (20 mL), washed with water (3 mL) and saturated $NaHCO_3$ solution (5 mL), and dried. Removal of solvent furnished crude acetals/thioacetals which were purified on a silica gel column.

(i) Reaction with ethylene glycol gave a mixture of **4b** and **4e**. Elution with 30% ethyl acetate−hexane initially furnished the mono-acetal spiro[dihydro[1,3]dioxolane-2,7′-hexacyclo-[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2′,4′-diene]-15′-one **(4b)** (45%), which was recrystallized from DCM−hexane: mp 128−129 °C; IR (KBr) 1734, 1585 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.96−5.84 (2H, m), 5.53−5.46 (2H, m), 3.96−3.93 (4H, m), 3.16−3.09 (1H, m), 3.01−2.94 (1H, m), 2.86 (1H, bs), 2.69−2.66 (1H, m), 2.57−2.55 (2H, m), 1.79 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.43 (1H, $^1/_2$ ABq, J = 11.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.8, 123.8 (2C), 122.4, 121.0, 113.8, 66.1, 65.8, 54.6, 53.5, 51.0, 50.0, 47.4, 45.3, 42.7, 36.9. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.17; H, 6.11.

Further elution of the column with 35% ethyl acetate−hexane furnished the bis-acetal dispiro[dihydro[1,3]dioxolane-2,7′-hexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2′,4′-diene-15′, 2″-(dihydro[1,3]dioxolane)] **(4e)** (33%), which was recrystallized from DCM−hexane: mp 148−149 °C; IR (KBr) 1581 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.89−5.84 (2H, m), 5.57−5.51 (2H, m), 4.12−4.07 (4H, m), 3.87−3.80 (4H, m), 2.84 (2H, bs), 2.69 (2H, bs), 2.29 (2H, bs), 1.52 (1H, $^1/_2$ ABq, J = 11.0 Hz), 1.07 (1H, $^1/_2$ ABq, J = 10.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 123.6 (2C), 114.6, 67.2, 63.7, 53.7, 49.3, 48.8, 45.7, 32.8. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.15; H, 6.49.

(ii) Reaction with 2,2-dimethylpropane-1,3-diol gave **4c**. Elution with 30% ethyl acetate−hexane furnished the mono-acetal 5,5-dimethylspiro[dihydro-4*H*-[1,3]dioxane-2,7′-hexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2′,4′-diene]-15′-one **(4c)** (85%), which was recrystallized from DCM−hexane: mp 203 °C; IR (KBr) 1740, 1581 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.94−5.88 (2H, m), 5.74−5.69 (1H, m), 5.50−5.44 (1H, m), 3.63 (1H, $^1/_2$ ABq, J = 11.2 Hz), 3.46−3.40 (3H, m) 3.39 (1H, $^1/_2$ ABq, J = 11.4 Hz), 3.10−3.03 (1H, m), 2.94−2.86 (1H, m), 2.77−2.73 (1H, m), 2.66−2.62 (1H, m), 2.50−2.43 (1H, m), 1.76 (1H, $^1/_2$ ABq, J = 11.6 Hz), 1.40 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.07 (3H, s), 0.71 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.5, 123.8, 123.4, 122.2, 120.8, 103.7, 73.0, 71.1, 53.7, 52.4, 49.9, 49.5, 47.0, 46.4, 45.6, 42.6, 36.7, 29.9, 22.7, 21.8. Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.45; H, 7.16.

(iii) Reaction with methanol gave **4d**. Elution with 30% ethyl acetate−hexane afforded the mono-acetal 15,15-Dimethoxyhexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]pentadeca-2,4-diene-7-one **4d** (91%): mp 88−89 °C; IR (KBr) 1734, 1580 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.91 (1H, dd, J_1 = 9.8 Hz, J_2 = 4.8 Hz), 5.84−5.71 (2H, m), 5.54 (1H, d, J = 9.8 Hz), 3.23 (3H, s), 3.13 (3H, s), 2.99−2.96 (1H, m), 2.92−2.84 (2H, m), 2.70−2.60 (2H, m), 2.53−2.46 (1H, m) 1.72 (1H, $^1/_2$ ABq, J = 11.4 Hz), 1.33 (1H, $^1/_2$ ABq, J = 11.4 Hz), ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.5, 125.0, 123.80, 121.2, 120.8, 105.9, 56.4, 51.9, 51.5, 50.4(2C), 50.1, 48.2, 46.5, 44.1, 42.3, 36.2. Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.66; H, 6.74.

(iv) Reaction with 1,2-ethanedithiol gave **9a**. Elution with 10% ethyl acetate−hexane furnished the mono-thioacetal spiro[dihydro[1,3]dithiolane-2,7′-hexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]-pentadeca-2′,4′-diene]-15′-one **(9a)** (50%), which was recrystallized from DCM−hexane: mp 157 °C; IR (KBr) 1732, 1583 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.99−5.92 (2H, series of m), 5.85−5.77 (1H, m), 5.60−5.51 (1H, m), 3.35−3.11 (4H, m), 3.08−3.01 (2H, m), 2.94−2.86 (2H, m), 2.72−2.64 (2H, m), 1.84 (1H, $^1/_2$ ABq, J = 11.1 Hz), 1.40 (1H, $^1/_2$ ABq, J = 11.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 214.1, 125.5, 124.4, 123.8, 121.4, 61.4, 56.7, 56.3, 53.4, 50.7, 49.2, 48.3, 43.2, 40.1, 39.4, 23.3; MS m/z 300 (M^+). Anal. Calcd for $C_{17}H_{16}OS_2$: C, 67.96; H, 5.37. Found: C, 67.92; H, 5.35.

(v) Reaction with 1,3-propanedithiol gave **9b.** Elution with 25% ethyl acetate−hexane furnished mono-thioacetal spiro-[dihydro-4*H*-[1,3]dithiane-2,7′-hexacyclo[7.5.1.0.^{1,6}0.^{6,13}0.^{8,12}0^{10,14}]-pentadeca-2′,4′-diene]-15-one **(9b)** (80%), which was recrystallized from DCM−hexane: mp 186 °C; IR (KBr) 1723, 1583 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.07−5.63 (4H, series of m), 3.41−3.35 (1H, m), 3.21−3.17 (2H, m), 3.07−2.76 (5H, m), 2.71−2.59 (2H, m), 2.10−1.73 (2H, series of m), 1.81 (1H, $^1/_2$ ABq, J = 11.2 Hz), 1.37 (1H, $^1/_2$ ABq, J = 11.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.4, 124.2, 123.9, 123.3, 122.2, 62.2, 57.6, 56.4, 55.9, 51.4, 48.9, 48.5, 48.3, 43.0, 35.1, 27.9, 27.1, 24.6; MS m/z 314 (M^+). Anal. Calcd for $C_{18}H_{18}OS_2$: C, 68.75; H, 5.77. Found: C, 68.82; H, 5.74.

Photooxygenation of dienes. General Procedure. In a small irradiation vessel fitted with an outer jacket for cold water circulation were placed diene (0.35 mmol), methylene blue (5 mg), and 25 mL of dry chloroform. The solution was irradiated with a 500 W tungsten lamp, placed about a foot away, under a slow stream of bubbling oxygen for 3−6 h. Reactions were continuously monitored by TLC and continued until most of the starting material was consumed. At the end of the reaction, chloroform was removed under vacuum at room temperature to give a diastereomeric mixture of endoperoxides in good yield. The product ratios were determined by ^{1}H NMR analyses of the crude reaction mixture by comparing the integrations of appropriate protons.

Photooxygenation of 4a. The reaction was performed as described in the general procedure to furnish **10a**:**11a** (78:22) in 88% yield (based on starting material recovery). The minor isomer **11a** had almost the same R_f as that of the starting material. Therefore, monitoring the completion of reaction and separation were done carefully. The isomers were separated

by column chromatography using silica gel, and elution with 20% ethyl acetate−hexane initially provided unreacted **4a** and further elution gave minor isomer **11a**, which was recrystallized from DCM−hexane: mp 240 °C (chars); IR (KBr) 1726, 1298, 1105, 908 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.78 (2H, dd as t, $J = 3.9$ Hz), 4.70 (2H, dd as t, $J = 3.9$ Hz), 3.45 (2H, bs), 3.09−3.07 (2H, m), 2.72 (2H, bs), 2.11 (2H, bs); ^{13}C NMR (50 MHz, $CDCl_3$) δ 208.4, 131.6, 70.9, 55.3, 44.3, 42.0, 39.2; MS *m/z* 256 (M^+). Anal. Calcd for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72. Found: C, 69.52; H, 4.62.

Further elution with 50% ethyl acetate−hexane furnished the pure major isomer **10a**, which was recrystallized from DCM−hexane: mp 243 °C; IR (KBr) 1728, 1225, 1105 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.83 (2H, dd, $J_1 = 4.5$ Hz, $J_2 = 3.4$ Hz), 4.94 (2H, dd, $J_1 = 4.4$ Hz, $J_2 = 3.4$ Hz), 2.94 (2H, bs), 2.86 (2H, bs), 2.73 (2H, bs), 2.03 (1H, $^1/_2$ ABq, $J = 11.3$ Hz), 1.82 (1H, $^1/_2$ ABq, $J = 11.5$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 208.1, 131.4, 69.5, 55.4, 48.0, 43.6, 40.6, 40.4; MS *m/z* 256 (M^+). Anal. Cald for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72. Found: C, 70.22; H, 4.75.

Photooxygenation of 4b. The reaction was performed as described in the general procedure to furnish **10b**:**11b** (14:86) in 92% yield. The two stereoisomers were separated by column chromatography using silica gel and elution with 35% ethyl acetate−hexane. **10b:** mp 133−134 °C (from DCM−hexane); IR (KBr) 1744, 1319, 1051 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.88−6.73 (2H, m), 4.98−4.91 (1H, m), 4.82−4.77 (1H, m), 4.18−3.90 (4H, m), 2.75−2.71 (1H, m), 2.63 (3H, bs), 2.51−2.44(1H, m), 2.37−2.30 (1H, m), 1.83 (1H, $^1/_2$ ABq, $J = 11.2$ Hz), 1.50 (1H, $^1/_2$ ABq, $J = 10.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.9, 132.5, 131.1, 113.3, 70.9, 69.4, 66.4, 66.1, 55.6, 51.7, 48.1, 45.9, 43.4(2C), 42.1, 39.0, 38.7; MS *m/z* 300 (M^+). Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 68.15; H, 5.40. **11b:** mp 150−151 °C (DCM−hexane); IR (KBr) 1738, 1321, 1069 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.83−6.75 (1H, m), 6.67−6.59 (1H, m), 4.69 (2H, t, $J = 5.8$ Hz), 3.96−3.77 (4H, m), 3.35−3.25 (1H, m), 3.12−3.04 (1H, m), 2.88−2.83 (1H, m), 2.78−2.73 (1H, m), 2.61−2.53, (1H, m), 2.48−2.41 (1H, m), 1.93 (1H, $^1/_2$ ABq, $J = 10.9$ Hz), 1.79 (1H, $^1/_2$ ABq, $J = 11.3$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.2, 131.0, 130.9, 111.4, 71.8, 71.1, 65.8, 65.1, 54.8, 52.9, 51.5, 50.9, 43.9, 42.3, 42.1, 40.1, 36.9. MS *m/z* 300 (M^+). Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.85; H, 5.35.

Photooxygenation of 4c. The reaction was performed as described in the general procedure to furnish **11c** (single isomer) in 98% yield and was purified by column chromatography over silica gel with 30% ethyl acetate−hexane as the solvent system. **11c:** mp 222−223 °C (DCM−hexane); IR (KBr) 1744, 1325, 1121, 1032 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.69 (2H, t, $J = 3.7$ Hz), 4.84−4.79 (1H, m), 4.68−4.65 (1H, m), 3.59 (1H, d, $J = 11.4$ Hz), 3.49−3.23 (5H, m), 3.06−2.98 (1H, m), 2.78−2.71 (2H, m), 2.40−2.32 (1H, m), 1.90 (1H, $^1/_2$ ABq, $J = 11.2$ Hz), 1.76 (1H, $^1/_2$ ABq, $J = 10.9$ Hz), 1.06 (3H, s), 0.69 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.6, 132.0, 129.5, 101.4, 72.9, 71.8, 71.2, 71.0, 54.6, 50.2, 48.0, 44.0, 42.0, 41.9, 39.8, 36.9, 29.8, 22.8, 21.7. Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.20; H, 6.50.

Photooxygenation of 4d. The reaction was performed as described in the general procedure to furnish **4d** (single isomer) in 70% yield (based on starting material recovery) and was purified by column chromatography over silica gel with 25% ethyl acetate−hexane as the solvent system. **4d:** mp 151 °C (DCM−hexane); IR (KBr) 1738, 1121, 1059 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.78−6.64 (2H, m), 4.83 (1H, d, $J = 5.7$ Hz), 4.66 (1H, d with st, $J = 5.7$ Hz), 3.26 (4H, bs), 3.16 (3H, s), 3.08−3.00 (1H, m), 2.87−2.69 (3H, m), 2.41−2.33 (1H, m), 1.89 (1H, $^1/_2$ ABq, $J = 10.8$ Hz), 1.75 (1H, $^1/_2$ ABq, $J = 11.3$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.6, 130.8, 130.5, 105.2, 72.8, 70.9, 55.6, 53.8, 52.4, 50.9, 50.5, 49.5, 44.1, 42.9, 42.0, 39.8, 36.7. Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.58; H, 6.02.

Photooxygenation of 4e. The reaction was performed as described in the general procedure to furnish **10e**:**11e** (3:97) in 91% yield. The major diastereomer **11e** was separated by column chromatography using silica gel and elution with 35% ethyl acetate−hexane. **11e:** mp >230 °C (sublimes); IR (KBr) 1316, 1157, 1026 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.73 (2H, dd as t, $J = 3.5$ Hz), 4.65 (2H, dd as t, $J = 3.5$ Hz), 3.99−3.91 (4H, m), 3.87−3.73 (4H, m), 2.95 (2H, bs), 2.67 (2H, bs), 2.26 (2H, bs), 1.63 (1H, $^1/_2$ ABq, $J = 10.7$ Hz), 1.42 (1H, $^1/_2$ ABq, $J = 10.7$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 131.1, 112.5, 72.3, 66.6, 63.1, 50.9, 48.9, 44.1, 40.4, 36.0; MS *m/z* 344 (M^+). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.35; H, 5.88.

Photooxygenation of 9b. The reaction was performed as described in the general procedure to furnish **20b** (single isomer) in 81% yield, and it was purified by column chromatography over silica gel with 25% ethyl acetate−hexane as the solvent system: mp 213 °C (DCM−hexane); IR (KBr) 1728, 1277, 737 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.81 (2H, dd as t, $J = 3.8$ Hz), 4.95−4.88 (1H, m), 4.78−4.75 (1H, m), 3.71−3.62 (1H, m), 3.47−3.39 (1H, m), 3.22−2.58 (8H, series of m), 2.11−2.01 (1H, m), 2.00 (1H, $^1/_2$ ABq, $J = 12.4$ Hz), 1.85−1.60 (1H, m), 1.77 (1H, $^1/_2$ ABq, $J = 10.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.2, 132.0, 131.2, 73.2, 71.0, 58.1, 57.9, 52.0, 51.1, 46.9, 44.4, 42.1, 38.9, 36.2, 28.6, 26.5, 24.8; MS *m/z* 346 (M^+). Anal. Calcd for $C_{18}H_{18}O_3S_2$: C, 62.40; H, 5.24. Found: C, 62.50; H, 5.28.

[4 + 2]-Cycloadditions with PTAD. General Procedure. PTAD was prepared as follows: To a stirred suspension of *N*-phenylurazole (0.5 mmol) in DCM cooled in an ice bath (0−5 °C) was added a solution of "oxides of nitrogen" (usually regarded as a mixture of N_2O_4, N_2O_3 and NO_2)[27] in DCM. This was prepared according to the literature procedure[26] by treating arsenious oxide with concentrated HNO_3, and the resulting gaseous mixture was bubbled through a DCM solution cooled in an ice bath (0−5 °C). The reaction mixture turned red and was stirred for additional 30 min to get a clear homogeneous red solution of *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD) in DCM, which was used for the cycloadditions.

To an ice-cooled solution of diene (0.35 mmol) in DCM (10 mL) was slowly added, dropwise, a solution of PTAD (0.40 mmol) in DCM (5 mL). The solution was stirred at 0−5 °C for 1 h until the red color had disappeared and completion of the reaction was monitored by TLC analysis. DCM was removed at room temperature under reduced pressure to give a solid residue, which was analyzed using ^1H NMR spectroscopy to determine the product ratios.

PTAD Addition to 4c. The reaction was performed as described in the general procedure to furnish **13c** (single isomer) in 85% yield and was purified by column chromatography over silica gel with 25% ethyl acetate−hexane as the solvent system. **13c:** mp 240 °C (DCM−hexane); IR (KBr) 1750, 1715, 1399, 1125 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.47−7.38 (5H, m), 6.53 (2H, t, $J = 4.0$ Hz), 5.26 (1H, t, $J = 4$ Hz), 5.03 (1H, t, $J = 4$ Hz), 3.64 (1H, d, $J = 11.2$ Hz), 3.53−3.30 (4H, m), 3.27−3.20 (1H, m), 3.03−2.97 (1H, m), 2.83−2.72 (2H, m), 2.49−2.42 (1H, m), 1.94 (1H, $^1/_2$ ABq, $J = 12.8$ Hz), 1.75 (1H, $^1/_2$ ABq, $J = 10.9$ Hz), 1.10 (3H, s), 0.73 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.1, 156.2(2C), 131.5, 130.4, 129.1(2C), 128.2, 127.8, 125.6 (2C), 101.5, 73.0, 71.1, 56.1, 51.7, 51.5, 51.0, 50.2, 47.9, 44.3, 42.8, 42.0, 39.7, 37.7, 29.8, 22.9, 21.7. Anal. Calcd for $C_{28}H_{27}N_3O_5$: C, 69.26; H, 5.61; N, 8.65. Found: C, 69.31; H, 5.59; N, 8.70.

PTAD Addition to 9a and 9b. The reaction was performed as described in the general procedure to furnish **12a**:**13a** (9:91) in 75% overall yield in the case of **9a** and (11:89) in 80% overall yield for **9b**. Addition of PTAD accompanied by concomitant dethioacetalization furnished **12a** and **13a**, which were separated by column chromatography using neutral alumina and elution with 70% ethyl acetate−chloroform. The two products **12a** and **13a** were found to be identical with the products obtained from PTAD addition to **4a**.[17a]

[4 + 2]-Cycloadditions with DMAD. General Procedure. A solution of diene (0.30 mmol) and DMAD (0.31 mmol)

(26) Dox, A. W. *Organic Synthesis*; Wiley: New York, 1941; Collect. Vol. 1, p 266.

(27) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John-Wiley: New York, 1967; p 737.

in dry benzene was refluxed for 12−18 h. Benzene was removed under vacuum to give a diastereomeric mixture of adducts. The product ratios were determined by ^{1}H NMR analyses of the crude reaction mixture by comparing the integrations of appropriate protons.

DMAD Addition to 4b. The reaction was performed as described in the general procedure to furnish **14b**:**15b** (17:83) in 91% yield. The diastereomers were separated by column chromatography using silica gel and elution with 35% ethyl acetate−hexane. **14b:** mp 184 °C; IR (KBr) 1742, 1711, 1437, 1265, 1065 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.63 (2H, t, J = 2.7 Hz), 4.10−3.90 (6H, m), 3.82 (3H, s), 3.69 (3H, s), 2.75−2.14 (6H, series of multiplets), 1.78 (1H, $^1/_2$ ABq, J = 10.9 Hz), 1.55 (1H, $^1/_2$ ABq, J = 10.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.7, 166.3, 166.1, 143.2, 142.5, 135.2, 135.0, 112.4, 66.1, 64.9, 59.0, 56.1, 53.1, 52.2, 51.9, 50.8, 44.0, 43.0, 42.2, 40.2, 39.6, 39.3, 38.2. Anal. Calcd for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.45; H, 5.40. **15b:** mp 159 °C; IR (KBr) 1738, 1262, 1076 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.52 (1H, t, J = 6.4 Hz), 6.32 (1H, t, J = 6.4 Hz), 3.98−3.72 (6H, m), 3.77 (3H, s), 3.75 (3H, s), 2.68−2.25 (6H, series of multiplets), 1.75 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.54 (1H, $^1/_2$ ABq, J = 10.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.7, 166.4, 166.2, 143.7, 143.1, 133.2, 132.6, 113.0, 65.8, 65.1, 58.3, 55.5, 53.9, 52.3(2C), 50.9, 43.7, 43.1, 42.1, 40.1, 39.7, 39.0, 38.0. Anal. Calcd for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.35; H, 5.40.

DMAD Addition to 4c. The reaction was performed as described in the general procedure to furnish **14c**:**15c** (5:95) in 92% yield. The diastereomers were separated by column chromatography using silica gel and elution with 30% ethyl acetate−hexane. **14c:** mp 190−191 °C; IR (KBr) 1748, 1709, 1281, 1119 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.70−6.59 (2H, m), 4.34 (1H, d, J = 4.5 Hz), 3.94 (1H, d, J = 4.5 Hz), 3.80 (3H, s), 3.69 (3H, s), 3.67 (1H, d, J = 9.3 Hz), 3.43−3.31 (4H, m), 2.62−2.57 (2H, m), 2.45 (1H, t, J = 6 Hz), 2.33 (1H, dd, J_1 = 10 Hz, J_2 = 2 Hz), 2.12 (1H, t, J = 6.5 Hz), 1.77 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.52 (1H, $^1/_2$ ABq, J = 10.9 Hz), 1.05 (3H, s), 0.70 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.2, 166.7, 165.5, 144.2, 142.1, 135.9, 135.2, 102.8, 73.2, 70.8, 60.7, 54.8, 52.1, 51.7, 49.6, 46.6, 43.8, 43.3, 42.0, 39.7, 39.3, 39.1, 38.4, 29.5, 23.4, 22.5. Anal. Calcd for $C_{26}H_{28}O_7$: C, 69.01; H, 6.24. Found: C, 69.12; H, 6.28. **15c:** mp 181−182 °C; IR (KBr) 1730, 1709, 1260, 1082 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.51−6.41 (2H, m), 4.20 (1H, dd, J_1 = 4.0 Hz, J_2 = 2.0 Hz), 3.98−3.94 (1H, m), 3.79 (3H, s), 3.77 (3H, s), 3.61 (1H, d, J = 11.2 Hz), 3.44−3.36 (4H, m), 2.61−2.53 (3H, m), 2.34−2.27 (2H, m), 1.76 (1H, $^1/_2$ ABq, J = 11.1 Hz), 1.55 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.12 (3H, s), 0.70 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.1, 166.4(2C), 143.8, 143.7, 134.0, 131.7, 102.8, 72.9, 71.0, 60.1, 54.8, 52.2(2C), 49.9, 47.1, 43.8, 43.1, 41.9, 40.0, 39.4, 38.9, 38.0, 29.8, 22.9, 21.7. Anal. Calcd for $C_{26}H_{28}O_7$: C, 69.01; H, 6.24. Found: C, 69.00; H, 6.28.

DMAD Addition to 4d. The reaction was performed as described in the general procedure to furnish **14d**:**15d** (4:96) in 75% yield. The diastereomers were separated by column chromatography using silica gel and elution with 30% ethyl acetate−hexane. **14d:** mp 134 °C; IR (KBr) 1742, 1707, 1282, 1123, 1059 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.68−6.58 (2H, m), 4.26−4.23 (1H, m), 3.98−3.94 (1H, m), 3.81 (3H, s), 3.72 (3H, s), 3.44 (3H, s), 3.17 (3H, s), 2.78−2.69 (2H, m), 2.58−2.53 (1H, m), 2.47−2.39 (1H, m), 2.32−2.25 (1H, m), 2.13−2.04 (1H, m), 1.75 (1H, $^1/_2$ ABq, J = 10.9 Hz), 1.52 (1H, $^1/_2$ ABq, J = 11.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.5, 166.3 (2C), 143.3, 142.5, 135.7, 135.0, 106.2, 62.0, 55.5, 53.1, 52.3, 52.1, 51.9, 50.8, 50.2, 44.7, 44.0, 42.0, 41.0, 39.24, 39.18, 38.1. Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 67.00; H, 5.90. **15d:** mp 119−120 °C; IR (KBr) 1736, 1271, 1123, 1074 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.49−6.34 (2H, m), 4.13 (1H, d, J = 5.8 Hz), 3.89 (1H, d, J = 5.8 Hz), 3.76 (3H, s), 3.74 (3H, s), 3.37 (3H, s), 3.10 (3H, s), 2.71−2.65 (2H, m), 2.53−2.47 (2H, m), 2.27−2.17 (2H, m), 1.71 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.51 (1H, $^1/_2$ ABq, J = 11.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.7, 166.4, 166.1, 144.8, 142.2, 133.3, 131.8, 106.4, 60.4, 54.7, 52.9, 52.4, 52.2 (2C), 50.3(2C), 44.0(2C), 41.7, 40.9, 39.4, 38.7, 37.8. Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 67.05; H, 5.90.

DMAD Addition to 4e. The reaction was performed as described in the general procedure to furnish **14e**:**15e** (18:82) in 83% yield. The diastereomers were separated by column chromatography using silica gel and elution with 40% ethyl acetate−hexane. **14e:** mp 247 °C (darkens), 253 °C (melts); IR (KBr) 1728, 1437, 1254, 1063 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.63 (2H, t, J = 4 Hz), 4.07−3.81 (10H, series of m), 3.74 (6H, s), 2.53 (2H, bs), 2.14 (2H, bs), 2.07 (2H, bs), 1.51 (1H, $^1/_2$ ABq, J = 10.8 Hz), 1.19 (1H, $^1/_2$ ABq, J = 10.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.5, 143.7, 135.7, 113.8, 66.9, 63.4, 56.8, 51.9, 48.4, 44.1, 41.6, 40.5, 35.7. Anal. Calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77. Found: C, 66.14; H, 5.80. **15e:** mp 192−193 °C; IR (KBr) 1721, 1645, 1260, 1073 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.53 (2H, t, J = 3.2 Hz), 4.03−3.83 (10H, series of m), 3.80 (6H, s), 2.55 (2H, bs), 2.19 (4H, bs), 1.51 (1H, $^1/_2$ ABq, J = 11.0 Hz), 1.22 (1H, $^1/_2$ ABq, J = 11.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.6, 144.3, 133.3, 114.1, 66.7, 63.1, 55.8, 52.2, 48.7, 44.1, 41.7, 40.3, 35.7. Anal. Calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77. Found: C, 66.00; H, 5.79.

DMAD Addition to 9a. The reaction was performed as described in the general procedure to furnish **24a** (single isomer) in 93% yield and was purified by column chromatography over silica gel with 20% ethyl acetate−hexane as the solvent system. **24a:** mp 139 °C (DCM−hexane); IR (KBr) 1736, 1709, 1333, 1254, 1057 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.56 (2H, t, J = 3.6 Hz), 4.39 (1H, dd, J_1 = 4.6 Hz, J_2 = 3.1 Hz), 4.02 (1H, dd, J_1 = 4.6 Hz, J_2 = 3.1 Hz), 3.84 (3H, s), 3.81 (3H, s), 3.32−3.15 (4H, m), 3.06−2.97 (1H, m), 2.92−2.86(1H, m), 2.70−2.45 (3H, m), 2.31−2.24 (1H, m), 1.86 (1H, $^1/_2$ ABq, J = 10.9 Hz), 1.58 (1H, $^1/_2$ ABq, J = 10.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 213.7, 166.4, 166.3, 144.6, 143.3, 135.6, 131.7, 64.2, 64.0, 57.9, 52.9, 52.4 (2C), 47.0, 45.9, 43.5, 42.4, 39.8, 39.3 (2C), 38.9, 37.5; MS m/z 442 (M^+). Anal. Calcd for $C_{23}H_{22}O_5S_2$: C, 62.42; H, 5.01. Found: C, 62.52; H, 5.05.

DMAD Addition to 9b. The reaction was performed as described in the general procedure to furnish **24b** (single isomer) in 91% yield and was purified by column chromatography over silica gel with 15% ethyl acetate−hexane as the solvent system. **24b:** mp 204−205 °C (DCM−hexane); IR (KBr) 1736, 1717, 1337, 1254, 1057 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.61−6.56 (2H, m), 4.35 (1H, dd, J_1 = 5.0 Hz, J_2 = 1.8 Hz), 4.05 (1H, dd, J_1 = 5.1 Hz, J_2 = 2.2 Hz), 3.81 (3H, s), 3.78 (3H, s), 3.61−3.52 (1H, m), 3.18−2.50 (8H, series of multiplets), 2.27−2.19 (1H, m), 2.11−2.01 (1H, m), 1.88−1.73 (1H, m), 1.85 (1H, $^1/_2$ ABq, J = 11.4 Hz), 1.56 (1H, $^1/_2$ ABq, J = 11.3 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.7, 166.4, 166.0, 144.8, 142.3, 134.8, 133.1, 63.7, 60.9, 57.3, 55.8, 52.4 (2C), 51.5, 47.1, 45.7, 42.0 (2C), 38.9, 38.7, 37.5, 29.0, 26.6, 25.0; MS m/z 456 (M^+). Anal. Calcd for $C_{24}H_{24}O_5S_2$: C, 63.13; H, 5.30. Found: C, 63.10; H, 5.29.

[4 + 2]-Cycloadditions with MA. General Procedure. A solution of diene (0.40 mmol) and MA (0.41 mmol) in dry benzene was refluxed for 12−18 h. Benzene was removed under vacuum to give a single diastereomer and was further confirmed by analyzing the ^{1}H NMR of crude reaction mixture.

MA Addition to 4b. The reaction was performed as described in the general procedure to furnish **16b** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **16b:** mp 279−280 °C; IR (KBr) 1860, 1834, 1779,1736, 1229, 1078 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.55−6.41 (2H, m), 4.09−3.92 (4H, m), 3.62 (1H, dd, J_1 = 4.4 Hz, J_2 = 2.9 Hz), 3.50 (1H, dd, J_1 = 8.8 Hz, J_2 = 3.3 Hz), 3.42−3.37 (1H, m), 3.32−3.27 (1H, m), 2.70−2.59 (3H, m), 2.53−2.44 (2H, m), 2.31−2.23 (1H, m), 1.80 (1H, $^1/_2$ ABq, J = 11.1 Hz), 1.52 (1H, $^1/_2$ ABq, J = 11.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 212.5, 173.2, 172.6, 134.0, 132.6, 113.1, 65.4, 64.9, 54.2, 51.7, 51.5, 49.3, 44.3, 43.5, 42.0, 40.8, 40.3, 39.8, 39.0, 32.8, 32.4. Anal. Calcd for $C_{21}H_{18}O_6$: C, 68.85; H, 4.95. Found: C, 68.90; H, 4.98.

MA Addition to 4c. The reaction was performed as described in the general procedure to furnish **16c** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **16c:** mp 251 °C; IR

(KBr) 1860, 1836, 1777,1738, 1227, 1086 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.55−6.40 (2H, m), 3.95 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 3.7$ Hz), 3.70 (1H, d, $J = 11.6$ Hz), 3.60−3.39 (6H, m), 3.32−3.26 (1H, m), 2.66−2.58 (2H, m), 2.50−2.39 (2H, m), 2.27−2.19 (1H, m), 1.80 (1H, $^1/_2$ ABq, $J = 11.2$ Hz), 1.51 (1H, $^1/_2$ ABq, $J = 10.8$ Hz), 1.18 (3H, s), 0.77 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.7, 173.2, 172.9, 134.2, 132.5, 103.6, 73.6, 70.9, 54.1, 50.2, 48.5, 48.3, 44.3, 43.6, 41.9, 40.8, 40.5, 39.7, 38.7, 32.5, 32.4, 29.9, 23.7, 21.9. Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.58; H, 5.92. Found: C, 70.65; H, 5.95.

MA Addition to 4d. The reaction was performed as described in the general procedure to furnish **16d** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **16d:** mp 241−242 °C; IR (KBr) 1856, 1833, 1771, 1738, 1231, 1086 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.45−6.41 (2H, m), 3.81 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 3.1$ Hz), 3.55−3.47 (2H, m), 3.46 (3H, s), 3.31 (3H, s), 3.26−3.21 (1H, m), 2.93−2.85 (1H, m), 2.77−2.72 (1H, m), 2.60−2.55 (1H, m), 2.48−2.36 (2H, m), 2.22−2.16 (1H, m), 1.77 (1H, $^1/_2$ ABq, $J = 11.3$ Hz), 1.49 (1H, $^1/_2$ ABq, $J = 11.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.9, 173.2, 172.6, 133.7, 132.7, 107.3, 56.0, 53.7, 53.4, 50.9, 50.6, 49.4, 45.1, 44.2, 41.8, 41.1, 40.5, 39.4, 38.7, 33.8, 32.1. Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.55; H, 5.42.

MA Addition to 4e. The reaction was performed as described in the general procedure to furnish **16e** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **16e:** mp 268 °C; IR (KBr) 1860, 1834, 1775, 1236, 1074 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.48−6.42 (2H, m), 4.09−3.89 (8H, m), 3.77 (2H, bs), 3.35 (2H, bs), 2.51 (2H, bs), 2.28 (2H, bs), 2.12 (2H, bs), 1.51 (1H, $^1/_2$ ABq, $J = 10.8$ Hz), 1.14 (1H, $^1/_2$ ABq, $J = 10.7$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.8, 133.6, 114.5, 66.6, 63.2, 49.4, 48.9, 43.8, 43.0, 41.0, 34.8, 33.3. Anal. Calcd for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.25; H, 5.42.

MA Addition to 9a. The reaction was performed as described in the general procedure to furnish **25a** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **25a:** mp > 280 °C; IR (KBr) 1860, 1777, 1725, 1225, 1084 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.62−6.45 (2H, m), 4.21 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 3.9$ Hz), 3.72−3.63 (2H, m), 3.43−3.27 (5H, m), 3.13−3.06 (1H, m), 2.83−2.78 (1H, m), 2.66−2.52 (3H, m), 2.24−2.17 (1H, m), 1.87 (1H, $^1/_2$ ABq, $J = 11.5$ Hz), 1.49 (1H, $^1/_2$ ABq, $J = 11.7$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 213.9, 172.9, 172.3, 134.9, 133.0, 75.0, 66.1, 56.9, 53.7, 52.5, 47.0, 46.4, 42.3, 41.4(2C), 40.4, 38.9, 38.6, 38.3, 36.1, 32.4; MS *m*/*z* 398 (M^+). Anal. Calcd for $C_{21}H_{18}O_4S_2$: C, 63.29; H, 4.55. Found: C, 63.35; H, 4.58.

MA Addition to 9b. The reaction was performed as described in the general procedure to furnish **25b** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **25b:** mp >280 °C; IR (KBr) 1838, 1775, 1721, 1231, 1096 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.58−6.45 (2H, m), 4.30 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 3.7$ Hz), 3.73−3.62 (2H, m), 3.49 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 2.9$ Hz), 3.40−3.35 (1H, m), 3.19−3.00 (3H, m), 2.84−2.57 (5H, m), 2.21−2.10 (2H, m), 1.98−1.76 (1H, m), 1.88 (1H, $^1/_2$ ABq, $J = 11.1$ Hz), 1.50 (1H, $^1/_2$ ABq, $J = 11.0$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.6, 172.4, 172.2, 134.6, 132.9, 59.5, 59.0, 56.9, 52.1, 50.7, 47.2, 46.1, 42.1, 41.5, 40.6, 39.4, 37.5, 35.0, 32.1, 28.9, 26.4, 24.7; MS *m*/*z* 412 (M^+). Anal. Calcd for $C_{22}H_{20}O_4S_2$: C, 64.05; H, 4.89. Found: C, 64.10; H, 4.87.

[4 + 2]-Cycloadditions with NMM. General Procedure. A solution of diene (0.30 mmol) and NMM (0.31 mmol) in dry benzene was refluxed for 12−18 h. Benzene was removed under vacuum to give a single diastereomer (> 96%) and was further confirmed by analyzing the ^1H NMR of crude reaction mixture.

NMM Addition to 9a. The reaction was performed as described in the general procedure to furnish **27a** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **27a:** mp 280 °C; IR (KBr) 1769, 1728, 1694, 1277 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.44−6.27 (2H, m), 3.86 (1H, dd, $J_1 = 7.9$ Hz, $J_2 = 3.2$ Hz), 3.65−3.60 (1H, m), 3.43−3.25 (6H, m), 3.09−3.03 (1H, m), 2.88 (3H, s), 2.80−2.75 (1H, m), 2.62−2.48 (3H, m), 2.20−2.13 (1H, m), 1.84 (1H, $^1/_2$ ABq, $J = 11.3$ Hz), 1.46 (1H, $^1/_2$ ABq, $J = 11.1$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 214.3, 178.9, 178.5, 133.7, 132.3, 75.2, 66.0, 57.7, 53.9, 53.1, 47.0, 46.4, 42.3, 41.4, 40.5, 39.7, 38.9, 38.5, 38.3, 36.2, 32.4, 24.5. Anal. Calcd for $C_{22}H_{21}NO_3S_2$: C, 64.20; H, 5.14; N, 3.40. Found: C, 64.25; H, 5.12; N, 3.98.

NMM Addition to 9b. The reaction was performed as described in the general procedure to furnish **27b** (single isomer) in near quantitative yield, and the crude adduct was directly crystallized from DCM−hexane. **27b:** mp >280 °C; IR (KBr) 1775, 1725, 1696, 1279 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.41−6.28 (2H, m), 4.03−3.96 (1H, m), 3.73−3.58 (2H, m), 3.32−3.28 (1H, m), 3.24−2.99 (4H, series of multiplets), 2.89 (3H, s), 2.80−2.53 (5H, series of multiplets), 2.18−2.05 (2H, m), 1.96−1.81 (1H, m), 1.86 (1H, $^1/_2$ ABq, $J = 10.5$ Hz), 1.48 (1H, $^1/_2$ ABq, $J = 10.8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.1, 178.5, 178.4, 133.5, 132.3, 59.8, 59.0, 57.5, 52.3, 51.3, 47.3, 46.0, 42.2, 40.5, 40.0, 39.4, 37.6, 35.2, 32.0, 28.9, 26.4, 24.8, 24.6; MS *m*/*z* 425 (M^+). Anal. Calcd for $C_{23}H_{23}NO_3S_2$: C, 64.91; H, 5.45; N, 3.29. Found: C, 65.00; H, 5.46; N, 3.29.

Hydrolysis of Ethylene Acetal of 11e; Conversion of 11e to 11b. A mixture of bis-acetal **11e** (30 mg, 0.09 mmol) and CSA (catalytic, 2 mg) in moist acetone (2 mL) was stirred at room temperature for 30 min. Acetone was removed under vacuum to furnish a residue which was charged on a silica gel column. Elution with 30% ethyl acetate−hexane furnished mono-acetal **11b** (25 mg, 95%). This was found to be identical (mp, IR, and ^1H NMR) to the sample **11b** derived from mono-acetal **4b**.

Hydrolysis of Dimethyl Acetal of 11d; Conversion of 11d to 11a. A mixture of mono-acetal **11d** (25 mg, 0.08 mmol) and Amberlyst-15 (10 mg) in moist acetone (2 mL) was stirred at room temperature for 15 min. Amberlyst resin was filtered and the solvent was removed under vacuum to furnish a residue which was charged on a silica gel column. Elution with chloroform furnished dione **11a** (20 mg, 94%). This was found to be identical (mp, IR, and ^1H NMR) to the sample **11a** derived from dione **4a**.

Acetalization of 14a; Conversion of 14a to 14b and 14e. A mixture of dione **14a** (60 mg, 0.16 mmol), ethylene glycol (0.03 mL, 0.49 mmol), PTSA (3 mg), and benzene (20 mL) was refluxed for 12 h with a Dean−Stark water separator. The reaction was cooled and quenched by adding saturated $NaHCO_3$ solution (2 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic extract was washed and dried. Removal of solvent furnished a mixture of acetals, which were separated by column chromatography using silica gel. Elution with 40% ethyl acetate−hexane first furnished mono-acetal **14b** (30 mg, 45%), and on further elution pure bis-acetal **14e** (26 mg, 35%) was obtained. Both **14b** and **14e** were found to be identical (mp, IR, and ^1H NMR) to the sample derived from mono-acetal **4b** and bis-acetal **4e**, respectively.

Acetalization of 14a; Conversion of 14a to 14c. A mixture of dione **14a** (30 mg, 0.08 mmol), 2,2-dimethylpropane-1,3-diol (25 mg, 0.24 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 12 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 35% ethyl acetate−hexane furnished mono-acetal **14c** (35 mg, 95%). This sample was found to be identical (mp, IR, and ^1H NMR) to the sample **14c** derived from mono-acetal **4c**.

Hydrolysis of Neopentyl Acetal of 15c; Conversion of 15c to 15a. To a stirred solution of NaI (25 mg, 0.17 mmol) in dry acetonitrile (2 mL) was added successively trimethylchlorosilane (0.02 mL, 0.16 mmol) and mono-acetal **15c** (30 mg, 0.07 mmol) under a dry nitrogen atmosphere. Iodine color formation appeared instantaneously. The reaction was stirred for 45 min and then quenched with water and extracted with DCM (3 × 10 mL), and the organic layer was washed successively with aqueous sodium thiosulfate, water, and brine and was dried. Removal of solvent and filtration through silica gel (elution with 25% ethyl acetate−hexane) afforded the dione **15a** (17

mg, 70%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **15a** derived from dione **4a**.

Hydrolysis of Dimethyl Acetal of 15d; Conversion of 15d to 15a. A mixture of mono-acetal **15d** (33 mg, 0.08 mmol) and Amberlyst-15 (10 mg) in moist acetone (2 mL) was stirred at room temperature for 30 min. Amberlyst resin was filtered and the solvent was removed under vacuum to furnish a residue, which was charged on a silica gel column. Elution with 25% ethyl acetate−hexane furnished dione **15a** (28 mg, 95%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **15a** derived from dione **4a**.

Hydrolysis of Ethylene Acetal of 15e; Conversion of 15e to 15b. A mixture of bis-acetal **15e** (35 mg, 0.08 mmol) and Amberlyst-15 (10 mg) in moist acetone (3 mL) was stirred at room temperature for 45 min. Amberlyst resin was filtered and the solvent was removed under vacuum to furnish a residue which was charged on a silica gel column. Elution with 30% ethyl acetate−hexane furnished mono-acetal **15b** (30 mg, 95%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **15b** derived from mono-acetal **4b**.

Thioacetalization of 15a; Conversion of 15a to 24a. A mixture of dione **15a** (37 mg, 0.1 mmol), 1,2-ethanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg) in DCM (10 mL) was stirred for 4 h. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 20% ethyl acetate−hexane furnished mono-thioacetal **24a** (38 mg, 85%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **24a** derived from mono-thioacetal **9a**.

Thioacetalization of 15a; Conversion of 15a to 24b. A mixture of dione **15a** (37 mg, 0.1 mmol), 1,3-propanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 12 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 30% ethyl acetate−hexane furnished mono-thioacetal **24b** (41 mg, 90%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **24b** derived from mono-thioacetal **9b**.

Dethioacetalization of 24a; Conversion of 24a to 15a. [Bis(trifluroacetoxy)iodo]benzene (47 mg, 0.11 mmol) was added at room temperature to a stirred solution of mono-thioacetal **24a** (30 mg, 0.07 mmol) in MeOH:H_2O (10 mL, 9:1). The mixture was stirred for an additional 10 min and quenched with saturated solution of $NaHCO_3$ and extracted with DCM (3 × 5 mL). Removal of solvent and filtration through silica gel pad (elution with 25% ethyl acetate−hexane) furnished dione **15a** (15 mg, 60%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **15a** derived from dione **4a**.

Dethioacetalization of 24b; Conversion of 24b to 15a. To a stirred solution of the mono-thioacetal **24b** (30 mg, 0.07 mmol) in DCM (10 mL), cooled in an ice bath (0−5 °C), was added dropwise a solution of "nitrogen oxides" in DCM until the pink color was discharged. After stirring for 5 min, the reaction was quenched with ice-cold aqueous $NaHCO_3$ and extracted with DCM (3 × 5 mL). Removal of solvent and filtration through silica gel pad (elution with 25% ethyl acetate−hexane) furnished dione **15a** (17 mg, 70%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **15a** derived from dione **4a**.

Hydrolysis of Neopentyl Acetal of 13c; Conversion of 13c to 13a. To a stirred solution of NaI (12 mg, 0.08 mmol) in dry acetonitrile (2 mL) was added successively trimethylchlorosilane (0.01 mL, 0.08 mmol) and mono-acetal **13c** (15 mg, 0.03 mmol) under a dry nitrogen atmosphere. The reaction was stirred for 45 min and then quenched with water and extracted with DCM (3 × 10 mL), and the organic layer was washed successively with aqueous sodium thiosulfate, water, and brine and then dried. Removal of solvent and filtration through neutral alumina (elution with 70% ethyl acetate-chloroform) afforded the dione **13a** (8 mg, 65%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **13a** derived from dione **4a**.

Acetalization of 16a; Conversion of 16a to 16b. A mixture of dione **16a** (33 mg, 0.1 mmol), ethylene glycol (0.01 mL, 0.20 mmol), PPTS (3 mg), and benzene (10 mL) was refluxed for 6 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 40% ethyl acetate−hexane furnished mono-acetal **16b** (30 mg, 80%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **16b** derived from mono-acetal **4b**.

Acetalization of 16a; Conversion of 16a to 16c. A mixture of dione **16a** (20 mg, 0.06 mmol), 2,2-dimethylpropane-1,3-diol (8 mg, 0.08 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 12 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 35% ethyl acetate−hexane furnished mono-acetal **16c** (23 mg, 91%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **16c** derived from mono-acetal **4c**.

Hydrolysis of Dimethyl Acetal of 16d; Conversion of 16d to 16a. A mixture of mono-acetal **16d** (30 mg, 0.08 mmol) and Amberlyst-15 (10 mg) in moist acetone (3 mL) was stirred at room temperature for 30 min. Amberlyst resin was filtered and the solvent was removed under vacuum to furnish a residue which was charged on a silica gel column. Elution with 40% ethyl acetate−hexane furnished dione **16a** (25 mg, 96%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **16a** derived from dione **4a**.

Hydrolysis of Ethylene Acetal of 16e; Conversion of 16e to 16b. A mixture of bis-acetal **16e** (29 mg, 0.07 mmol) and PTSA (catalytic, 2 mg) in moist acetone (2 mL) was stirred at room temperature for 30 min. Acetone was removed under vacuum to furnish a residue, which was charged on a silica gel column. Elution with 40% ethyl acetate−hexane furnished mono-acetal **16b** (24 mg, 93%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **16b** derived from mono-acetal **4b**.

Thioacetalization of 16a; Conversion of 16a to 25a. A mixture of dione **16a** (29 mg, 0.09 mmol), 1,2-ethanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 6 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 30% ethyl acetate−hexane furnished mono-thioacetal **25a** (30 mg, 84%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **25a** derived from mono-thioacetal **9a**.

Thioacetalization of 16a; Conversion of 16a to 25b. A mixture of dione **16a** (32 mg, 0.1 mmol), 1,3-propanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 6 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 35% ethyl acetate−hexane furnished mono-thioacetal **25b** (37 mg, 90%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **25b** derived from mono-thioacetal **9b**.

Thioacetalization of 29; Conversion of 29 to 27a. A mixture of dione **29** (34 mg, 0.1 mmol), 1,2-ethanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 6 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 40% ethyl acetate−hexane furnished mono-thioacetal **27a** (38 mg, 90%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **27a** derived from mono-thioacetal **9a**.

Thioacetalization of 29; Conversion of 29 to 27b. A mixture of dione **29** (34 mg, 0.1 mmol), 1,3-propanedithiol (0.02 mL, 0.2 mmol), PTSA (3 mg), and benzene (10 mL) was refluxed for 6 h with a Dean−Stark water separator. Usual workup and removal of solvent furnished a residue, which was purified by column chromatography using silica gel. Elution with 40% ethyl acetate−hexane furnished mono-thioacetal **27b** (41 mg,

95%). This sample was found to be identical (mp, IR, and ^{1}H NMR) to the sample **27b** derived from mono-thioacetal **9b**.

X-ray crystal structure data of 11e: $C_{19}H_{20}O_6$, M_r = 344.40, colorless crystals from DCM−hexane, orthorhombic, space group $P2_12_12_1$, a = 8.889(2) Å, b = 9.011(4) Å, c = 19.369(6) Å, V = 1551.4(9) Å^3, Z = 4, D_{calcd} = 1.731 Mg m^{-3}, T = 293 °K, $F(000)$ = 848, μ(Mo Kα) = 0.125 mm$^{-1.}$ Data were collected on Enraf-Nonius CAD-4 diffractometer, with graphite-monochromated Mo−Kα radiation (λ = 0.71070 Å), by the $\omega/2\theta$ scan method in the range $2 \leq \theta \leq 25°$. At final convergence R_1 [$I > 2\sigma(I)$] = 0.0517, wR_2 = 0.1491 for 306 parameters, GOF = 1.393, $\Delta\rho_{max}$ = 0.293 e Å^{-3}, $\Delta\rho_{min}$ = −0.252 e Å^{-3}. The structure was solved by direct methods,[29a] refined by full-matrix least-squares on F^2 with all non-H atoms anisotropic and H atoms isotropic.[29b]

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Supporting Information Available: All the chemical correlations in a schematic form and Crystallographic experimental sections and tables of X-ray crystal data, bond lengths and angles, final fractional coordinates, and thermal parameters for **11e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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