Heteroatomic Influences on the π-Facial Selectivity of Diels−Alder Cycloadditions to Dispiro[4.0.4.4]tetradeca-11,13-dienes

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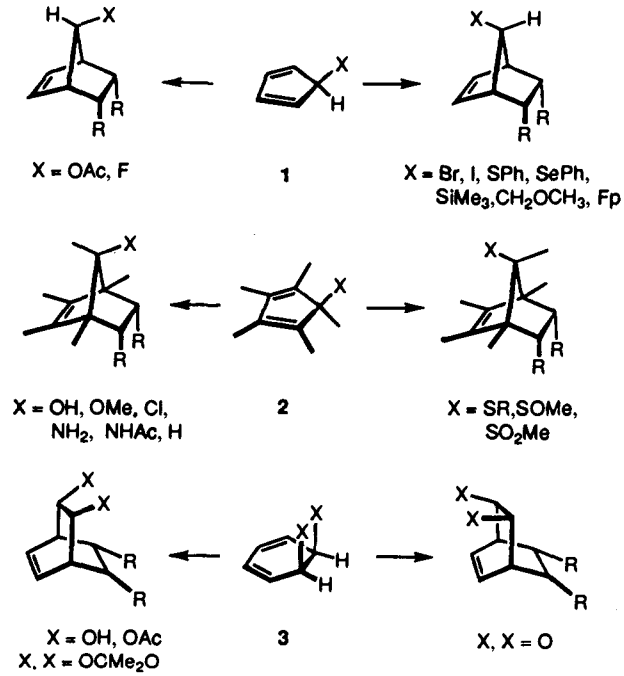
Abstract: Derivatives of the title structure bearing one or two heteroatoms adjacent to the spirocyclic carbons have been reacted principally with *N*-phenylmaleimide and *N*-methyltriazolinedione. The distributions of [4 + 2] cycloadducts have been quantified and, where mixtures have resulted, the stereoisomeric adducts have been isolated in a pure state following chromatographic separation. The stereochemical assignments follow principally from NOE measurements and X-ray crystallographic determinations. A relative reactivity ordering was established for the triazolinedione cycloadditions since this dienophile reacted with all of the available dienes. The stereoselectivities observed for these reactions suggested the intermediacy of aziridinium imide intermediates, and calculations of the AM1 type were carried out in order to examine the steric, electronic, and electrostatic properties of the reactants. Our analysis shows that electrostatic effects dominate in the syn dioxa system, whereas steric factors must be accorded proper consideration when accounting for the π-facial selectivity exhibited by the oxa/thia and dithia compounds.

The recent dramatic advances in organic synthesis have been accompanied by ever-increasing pressures to attain greater levels of stereochemical control. This heightened expectation has impacted every segment of our science, including many of the more venerable reactions. The Diels−Alder cycloaddition is a case in point. For many years, the capture of a diene by a dienophile was recognized to be capable of generating as many as four contiguous stereogenic centers in a single laboratory step.[1,2] Subsequently, asymmetric[3] and intramolecular variants[4] of this process came to the fore and have been accorded widespread attention. To a substantial degree, the controlling factors that are operational in these modifications are quite well understood.

In the last decade, an ability to enhance the scaffolding power of [4 + 2] cycloadditions has come to be specifically recognized. Should π-facial diastereoselectivity be controllable in those circumstances when at least one of the reactants possesses two different π-faces, the number of centers of asymmetry being simultaneously introduced is capable of growing to five or more. Of the results reported to date, heteroatoms have been noted to exert a stereodirecting influence that is often impressively high.[5]



For instance, when simple cyclopentadienes such as **1** are involved, the presence of a C-5 acetoxy[6] or fluoro substituent[7] induces dienophiles to react with syn-facial selectivity. All other groups including bromine,[8] iodine,[8] phenylthio,[9] phenylse-

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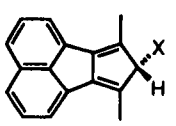
leno,[9,10] trimethylsilyl,[11] CH_2OCH_3,[12] and $(\eta^5\text{-}C_5H_5)Fe(CO)_2$[13] lead to the opposite stereochemical outcome. In many of the latter examples, the observed stereoselectivity can be simply attributed to steric control.

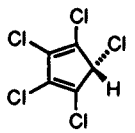
In a very extensive study of heteroatom-directed π-facial diastereoselection in permethylated cyclopentadienes **2**, Macaulay and Fallis established that those derivatives carrying the substituents OH, OMe, Cl, NH_2, and NHAc react to form syn adducts preferentially.[14] The parent hydrocarbon (X = H) behaves analogously,[15] but this behavior is not contrasteric. While a slight syn discrimination was observed with **2** (X = SH), other sulfur-containing groups gave anti adducts as the major or exclusive products.

Plane nonsymmetric 1,3-cyclohexadienes such as **3** are recognized to be somewhat less face-selective in their cycloaddition chemistry, perhaps because of inherently greater conformational flexibility.[16] Notwithstanding, the same trend is apparent when X is OH, OAc, or an acetonide. The sharply differing behavior of the epoxide can be attributed to steric shielding of the syn face in its critical midregion.

Three other cyclopentadienyl systems have emerged as important diastereoselection reference points. Adducts derived from **4a,b** arise by exclusive attack from that direction syn to



4a, X = OH
b, X = OAc



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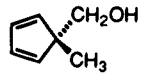


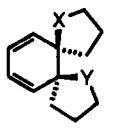
6

the oxygenated functionality.[17] The addition of dienophiles to **5** likewise proceeds with a strong kinetic preference from the syn direction.[18] Finally, the presence of an hydroxymethyl group in **6** does not exert a favorable syn influence despite its latent ability for possible hydrogen bonding to the incoming dienophile.[19]

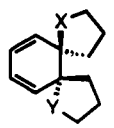
A number of theories have been advanced in explanation of the origin of the syn selectivity phenomenon observed for hydroxyl, amino, chloro, and fluoro substituents. One of the earliest to be formulated was the orbital mixing rule of Fukui,[10,20] wherein a group X from the above subset was suggested to be conducive to syn capture of the dienophile because of stabilizing orbital interactions on that surface. Kahn and Hehre later concluded that electrostatic interactions are the important determinant in governing π-facial selectivity, with the more nucleophilic diene face reacting preferentially.[21] As pointed out elsewhere,[5] however, this simple model necessarily must include –SH, at variance with the experimental results. Ahn called attention to the possibility that nonbonded attraction between the heteroatom and dienophile might well serve as a stabilizing transition state factor.[22] Somewhat later, Cieplak applied hyperconjugative σ-assistance in a generic way to this problem.[23] Predictions concerning facial selec-tivity can, according to this model, be made by using the Baker-Nathan ordering of σ-donor ability: $\sigma_{C-O} < \sigma_{C-N} < \sigma_{C-Cl} < \sigma_{C-C} < \sigma_{C-H} < \sigma_{C-S}$.[24] On this basis, a preference should exist for addition on that face opposite to the antiperiplanar σ bond that is better able to donate hyperconjugatively into the σ* orbital of the forming bonds.[14]

In conjugated diene systems more diverse in structure than those recognized here, other factors could be controlling. The most widely recognized theories that define their π-facially-selective responses are π-orbital tilting[25,26] and filled-orbital repulsion.[27,28]

Dispiro 1,3-cyclohexadienes possessing a pair of syn heteroatoms as in **A** bear a structural similarity to **3** while offering a considerable reduction in the steric imbalance across the diastereotopic faces. Furthermore, the extensive control available over the nature of substituents X and Y[29] makes feasible a direct comparison of the σ-donating effects of both C–O and C–S bonds. Furthermore, when these same heteroatoms are oriented anti as in **B**, a direct one-on-one competition becomes



A



B

available. To our knowledge, the interesting issue of two different heteroatoms vying for control of an incoming dienophile has not previously been investigated. Since the monoheterocyclic analogues, viz., Y = CH_2, are also available, the possibility remains open for establishing whether the progression from one to two heteroatomic centers gives rise to an additive or a multiplicative effect.

This paper presents the details of a systematic study of Diels–Alder cycloadditions to dispiro[4.0.4.4]tetradeca-11,13-dienes containing one or two heteroatoms. In every case, product stereochemistry was corroborated either by NOE analysis following COSY and HETCOR measurements or by X-ray crystallographic determinations. We have also sought to develop a general conceptual solution to the problem of which features contribute to making the two faces different. Since

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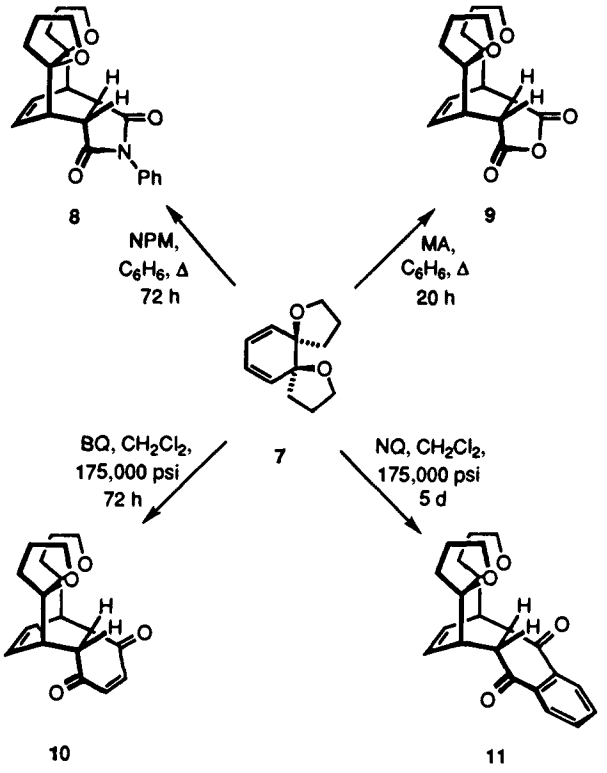
Scheme 1

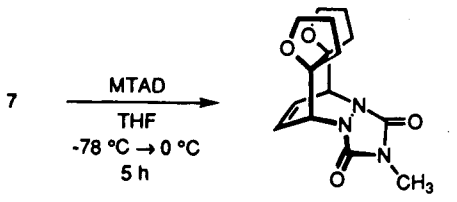


no evidence was uncovered for reversibility, we have concluded that the stereochemical outcomes materialize under kinetic control. Fortunately, since single-bond rotations are significantly restricted in **A** and **B**, the relative positions of the heteroatoms in the transition states are definable with reasonable confidence. As the trajectory of the attacking reagent unfolds, it becomes necessary to distinguish between steric contributions and electronic factors, the latter in its myriad of forms.

Results

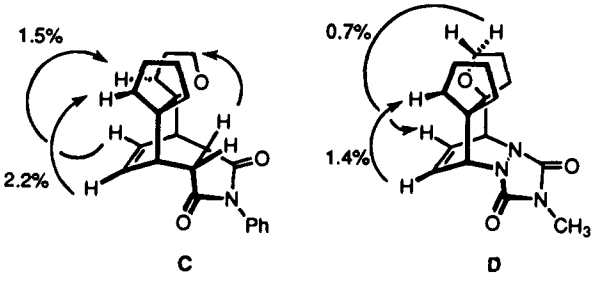
Oxygen-Containing Systems. The first line of investigation involved the syn dioxa diene **7**. Heating benzene (or C_6D_6) solutions of **7** with *N*-phenylmaleimide (NPM) or with maleic anhydride (MA) at the reflux temperature for 20−72 h made possible direct examination of the reaction mixtures by high-field ^{1}H NMR (Scheme 1). *p*-Benzoquinone (BQ) and 1,4-naphthoquinone (NQ) were less reactive toward **7**. These cycloadditions were therefore carried out on CH_2Cl_2 solutions at 175 000 psi in a high pressure reactor. In all four instances, a single adduct was produced within reasonable limits of detectability. The assignment of syn stereochemistry to **8**−**11** was made possible by the measurement of NOE interactions. The magnitude of the enhancement between the newly formed bridgehead protons and the $-CH_2O-$ hydrogens in the spiro rings was utilized as internal calibration against which the level of interaction (or absence thereof) exhibited by the olefinic protons and the same $-CH_2O-$ units were compared. On the basis of this criterion, all four adducts failed to give a measurable result. Other long-range effects served to confirm the distal relationship of the oxygen atoms to the double bond. As a consequence of their nonplanar disposition within the adducts, the tetrahydrofuran rings project one γ-methylene proton above the π cloud of the double bond and the second to the interior of the molecule. The shielding provided to the external protons is adequate to shift them upfield of the absorption range of their geminal neighbors. As a consequence, a two-proton multiplet located at δ 1.6−1.5 was evident in the majority of the cycloadducts produced in this study. When the olefinic proton signals in **8**−**11** were saturated, the following respective enhancements of this upfield absorption were noted: 3.5%, 2.7%, 3.1%, and 3.3%, respectively. Endo entry of the dienophile in the case of **8** was similarly confirmed by a 1.7% NOE between the vinyl protons and those of the aromatic ring.

N-Methyltriazolinedione (MTAD) is one of the more reactive dienophiles known,[30] and exposure of **7** to this reagent in THF solution at −78 °C led to complete reaction within 5 h. The



resulting crystalline adduct **12** displayed no diagnostic NOE enhancements and was therefore examined by X-ray diffraction. By this means, it proved possible to establish that addition had occurred in this instance from that direction anti to the heteroatoms (Figure 1). The contrasting selectivity of MTAD relative to the other dienophiles is noteworthy.

Our attention next focused on the lesser oxygenated analog **13**. Of the two dienophiles examined, NPM was considered to be representative of the "classical" 2π reagents. On the other hand, MTAD was investigated because of the stereochemical crossover observed with **7**. As summarized in Scheme 2, **13** proved not to react with NPM under the conditions previously utilized. However, in CH_2Cl_2 solution buffered with Hunig's base (to preclude acid-catalyzed rearrangement[29a]) at 150 000 psi for 72 h, smooth condensation occurred to afford a 13:1 mixture of **14** and **15** in 85% yield. Following chromatographic separation of these diastereomers, it proved possible to establish the entire connectivity of the protons and carbons in **14** by ^{1}H−^{1}H and ^{1}H−^{13}C COSY analysis. The positive NOE enhancements exhibited by this adduct, which are illustrated in **C**, clearly define it to be the product of syn addition.



In contrast, the stereochemical characteristics of the MTAD cycloaddition are such that only anti product **16** is produced. When simple inspection of the ^{1}H NMR spectrum of **16** revealed the presence of a single alkene-shielded methylene proton on a spiro ring, the possibility of syn attack was ruled out. This conclusion was substantiated by the NOE effects given in **D**.

Further penetration into the relative rates of these reactions required that the trans dioxa diene **17** also be given consideration (see below). Since the π faces in **17** are homotopic, exposure of this diene to MTAD can only give rise to **18** (Scheme 3).

Sulfur-Containing Dienes. Limited prior experience by others with **2**[14] provided a provocative backdrop for analysis of the cycloaddition behavior of the syn dithia analog **19**. Much

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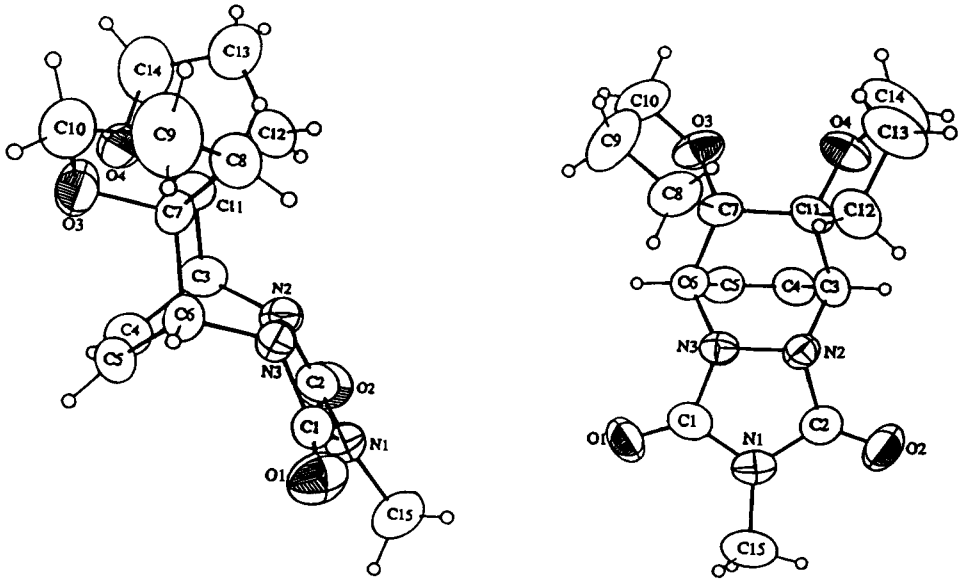
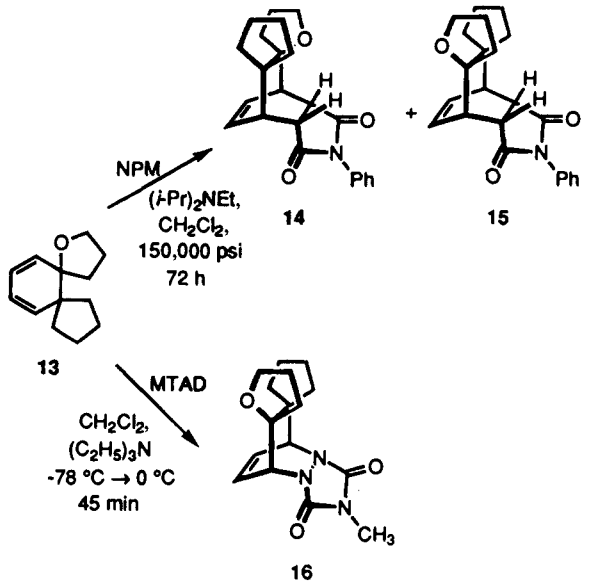
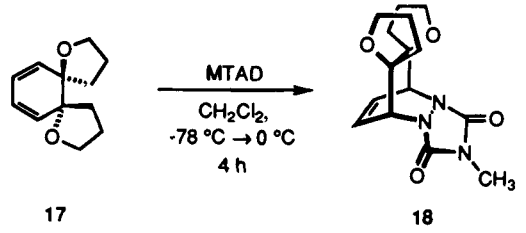


Figure 1. Computer-generated perspective drawings of **12** as determined by X-ray crystallography: left, side view; right, front view.

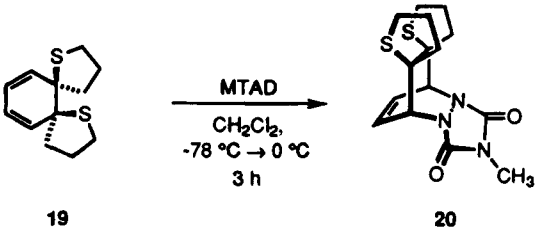
Scheme 2



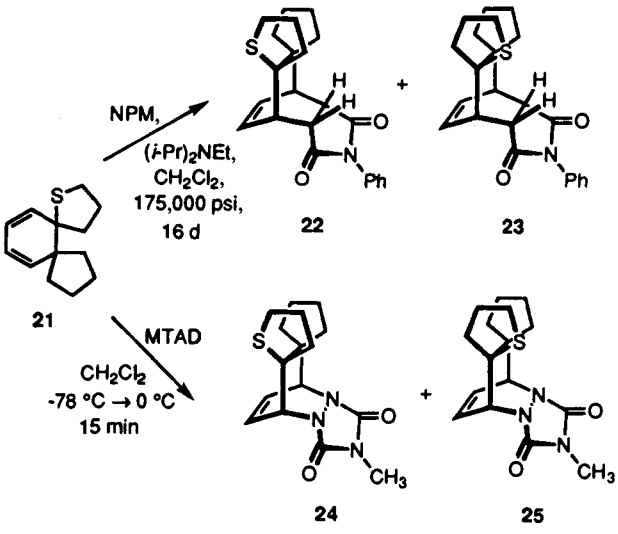
Scheme 3



Scheme 4



Scheme 5

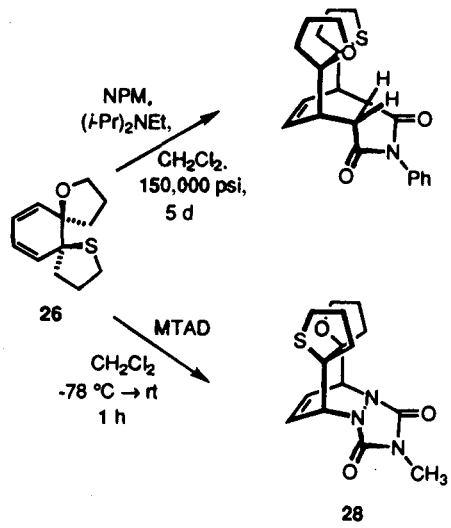


to our disappointment, however, **19** proved unreactive to NPM and MA even under forcing conditions (175 000 psi, >30 days). This dropoff in reactivity is not a new phenomenon, it having been observed as well with **2**-SPh and **2**-SMe.[14] Notwithstanding this apparent kinetic disadvantage, **19** entered efficiently into Diels–Alder reaction with MTAD under ordinary conditions (Scheme 4). The stereochemistry of **20** manifested itself by the absence of any upfield γ-tetrahydrothiophene protons and the existence of positive NOE contributions between the olefinic protons and those α to sulfur (0.6%). In fact, the high-field NMR spectra of **12** and **20** feature a great many similarities.

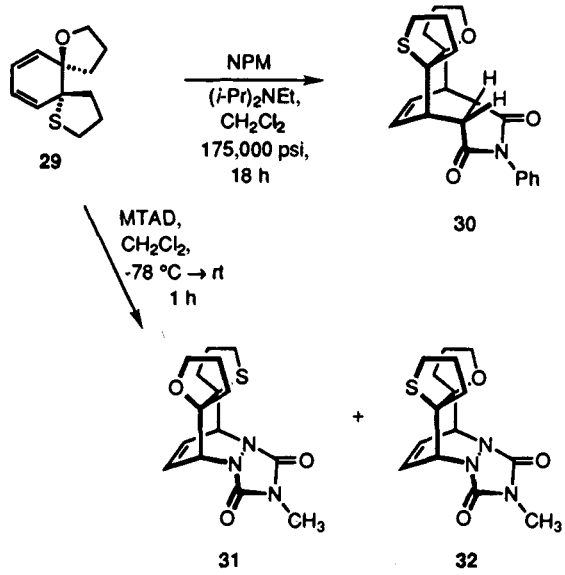
The instability of diene **21** has previously been noted.[29] Accordingly, all reactions involving **21** were performed with freshly prepared material. Its condensation with NPM proved to be very sluggish. After 16 days at 175 000 psi, two isomeric crystalline adducts were produced in only 14% and 12% yield (Scheme 5). The remaining additional material was found by ^{1}H and ^{13}C NMR to be a polymer of **21**. Although **22** and **23** displayed spectroscopic parameters fully compatible with the anticipated gross structural features, NOE experiments were inconclusive and their specific relative stereochemistry was not assigned. This was not a major issue, since these adducts were formed in approximately equivalent amounts.

The cycloaddition of MTAD to **21** is considerably more stereoselective, anti capture to give **24** occurring 10 times faster than syn approach to afford **25**. The major adduct exhibited an absorption at δ 1.38–1.31 with an integral area of 1, representing the exo proton on the δ carbon of the spirocyclo-

Scheme 6



Scheme 7



pentane ring positioned directly above the alkene. Double irradiation of the olefinic proton multiplet (δ 6.52−6.42) gave rise to an NOE effect for this signal as well as for the somewhat more remote α-sulfido protons.

Mixed Oxygen/Sulfur Heteroatom Combinations. The results gained from the mixed oxa/thia dienes were expected to be particularly informative. The cumulative rate-retarding effect of two sulfur atoms was expected to be offset to some degree by replacement with one oxygen such that normal reactivity toward "classical" dienophiles would return. Beyond that, a trans disposition of the heteroatoms could establish the extent to which the oxygen and sulfur centers might be capable of exerting effects in the same direction. When placed in a cis arrangement, however, these same heteroatoms are necessarily forced to act in direct competition for the incoming dienophile.

Diene **26** reacted with NPM and MTAD to give a single cycloadduct in each instance (Scheme 6). That syn stereoselectivity had operated during the formation of **27** was immediately apparent from the presence in its ^{1}H NMR spectrum of a multiplet of area 2 at δ 1.65−1.56 for the two exo protons bonded to the γ carbons of the spirocyclic rings. Measurable NOE enhancements of this absorption were observed when either of the olefinic protons were irradiated. Additional confirmation of the indicated stereochemistry was secured from those NOE enhancements evident between the protons α to the

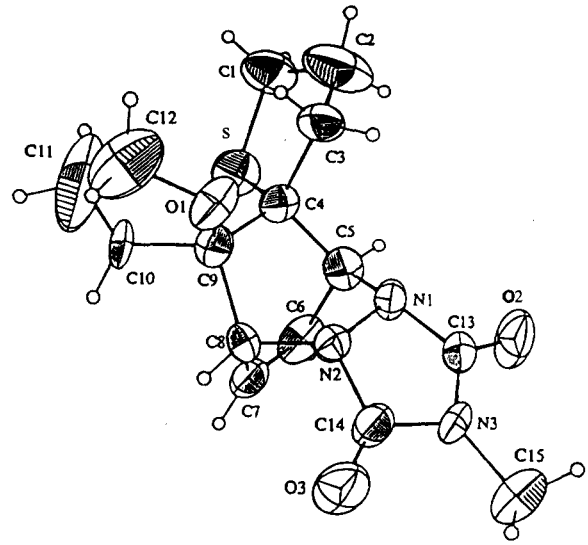
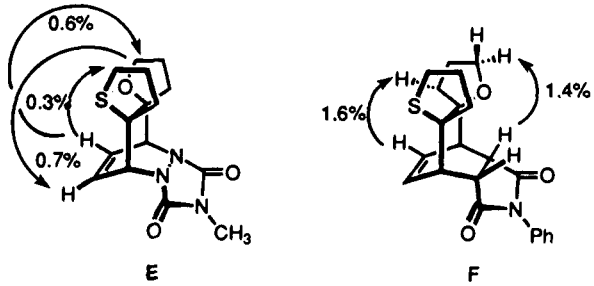


Figure 2. Computer-generated perspective drawing of **32** as determined by X-ray crystallography.

imide carbonyls and those α to the ether oxygen. The differing anisotropic shielding of the α-carbonyl protons is also striking. As a consequence of their proximity to different heteroatoms, the one positioned below the oxygen resonates further downfield (δ 3.84) than that situated adjacent to the sulfur (δ 3.69).

The spectral data for **28** reflect a reversal of its stereochemistry relative to **27**. No upfield methylene absorptions were evident. The NOE data compiled in **E** proved telltale of the fact that the heteroatoms were indeed situated above the double bond as a consequence of anti addition.



The anti oxa/thia diene **29** underwent cycloaddition to NPM in a high-pressure reactor to furnish **30** as the only detectable product in 70% yield after chromatography (Scheme 7). The facial selectivity exercised during the formation of this adduct was again deduced on the basis of NOE results. Structure **F** illustrates two of the more important enhancements measured. No effects were observed on the $-CH_2O-$ absorption when the olefinic protons were saturated. However, the 1.6% enhancement seen for the lone upfield exo proton (δ 1.86−1.71) belonging to the γ carbon of the tetrahydrofuran ring confirmed that the oxygen atom was oriented syn to the maleimide subunit.

Diene **29** reacted quite rapidly with MTAD to generate the pair of adducts **31** and **32**, which were isolated in 35% and 50% yield, respectively. In these examples, NOE measurements were of little assistance in making the necessary unequivocal distinction concerning the face selectivity. Urazole **32** was sufficiently crystalline, however, to allow its structure to be determined by means of X-ray diffraction. As seen in Figure 2, the more prevalent pathway involves dienophile approach syn to oxygen and anti to sulfur. With MTAD as the dienophilic reagent, however, this trajectory is hardly overwhelming.

Competition Experiments. A requirement subjectively imposed on the competition experiments was that all of the

Table 1. Results of Competition Experiments

expt. no.	diene pair	adducts: major	adducts: minor	adduct ratio
1	**7, 17**	18	12	100:1
2	**7, 19**	20	12	2.4:1
3	**7, 13**	16	12	100:0
4	**7, 29**	31/32	12	8.4:1
5	**7, 26**	28	12	8.3:1
6	**13, 29**	16	31/32	2:1
7	**17, 13**	18	16	1.5:1
8	**13, 26**	16	28	1.6:1
9	**26, 29**	28	31/32	1.3:1
10	**26, 19**	28	20	4:1

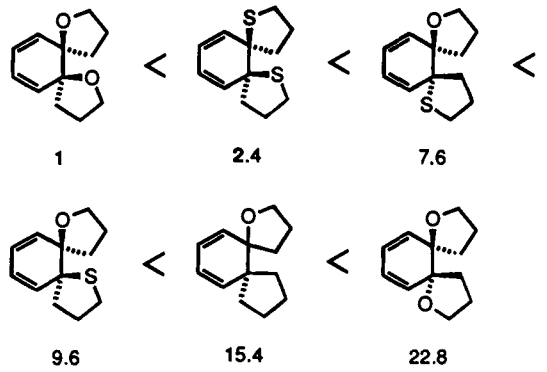


Figure 3. Order of reactivity for the cycloaddition of MTAD with the dispiro dienes.

dienes be suitably reactive in order to elucidate their relative ranking as comprehensively as possible. The limited reactivity of the syn dithia system **19** immediately restricted our considerations to the use of MTAD. Although this course of action was somewhat less than desirable because the triazolinedione need not react via a classical Diels–Alder mechanism but via the intermediacy of aziridinium imide intermediates,[31-34] this aspect of the investigation was certain to provide added insight into those factors that enhance, or detract from, the π-facial stereoselectivity exhibited by these hetero dispiro[4.0.4.4]-tetradecadienes.

The generalized procedure consisted of treating an equimolar mixture of two dispiro dienes with slightly less than 0.5 mol equiv of MTAD. The color of the dienophile was completely discharged within 30 min. Careful ^{1}H NMR integration of the product mixtures at 300 MHz allowed for direct determination of the product ratios (Table 1). On the basis of these data, the assignment of a relative reactivity order toward MTAD was possible (Figure 3). The syn dioxa diene **7**, the most sluggish substrate toward this dienophile, provides one end of a continuum that features the trans dioxa isomer **17** at the other (22.8-fold more reactive).

Theoretical Evaluation of the Problem. For reasons of simplification, NPM was supplanted by *N*-methylmaleimide (NMM) in all calculations. The geometric parameters of the dienophiles NMM and MTAD as well as of the dienes **7**, **19**, **26**, and **29** were optimized using the AM1 procedure.[35] In order to rationalize the differences in reactivity, electronic, electrostatic, and steric properties were accorded particular attention.

NMM and TMAD differ significantly in their frontier orbital energies. NMM is less reactive and therefore more stereoselective than MTAD. This is in good agreement with the lower lying LUMO of TMAD ($E_{LUMO} = -1.74$ eV) with respect to NMM ($E_{LUMO} = -1.14$ eV). Since the LUMO energy of NPM is −1.23 eV, the substitution of phenyl by methyl is not expected to lead to significant changes in the properties under discussion. The dienes **19**, **26**, and **29** have comparable HOMO energies (**19**, −8.66 eV; **26**, −8.84 eV; **29**, −8.79 eV). On this basis, one is led to assume that steric and electrostatic factors will dominate throughout the series. The low reactivity of **7** fits well in the frontier orbital picture, for its HOMO lies lower in energy ($E_{HOMO} = -9.03$ eV) relative to the other three dienes.

Table 2. π-Facial Selectivity Anticipated Solely on the Basis of Electrostatic Considerations

diene	dienophile: NMM or NPM, electrost.	NMM or NPM, expt	MTAD, electrost.	MTAD, expt.
7	syn to O	syn to O	anti to O	anti to O
19	anti to S	no reaction	syn to S	anti to S
26	syn to O	syn to O	anti to O	anti to O
29	syn to O	syn to O	anti to O	syn/anti O (1.5:1)

The electrostatic properties are very important in order to explain the π-facial selectivity. NMM has a positive Mulliken partial charge on the hydrogen and carbon atoms of the carbon–carbon double bond, whereas MTAD has a slightly positive partial charge on the doubly bonded nitrogens but a negative charge density in the region where the lone pairs are located. In contrast to that, NMM reveals a positive charge density at the sp^2 hydrogens. This region is of importance during the reaction since approach of the dienophiles then leads to electrostatic interactions with the heteroatoms of the dienes.

The partial charges on the dienes may be summarized as follows:

$$O \approx -0.25 \qquad S \approx +0.14 \qquad CH_2 \approx +0.10$$

Consequently, the π-facial selectivities given in Table 2 should be favored. As we see, steric factors must also be included to complete the picture. The large sulfur atom forces MTAD to the opposite side, leading to the anti product which would be unexpected for purely electrostatic reasons (**19** + MTAD). MA reacts very poorly with sulfur-containing dienes or, as in the case of **19** + MA, not at all. This low reactivity can also be attributed to the steric demands of the sulfur atom. The present experiments can be rationalized by taking into account the following rules of thumb: (1) proximity to oxygen results in the onset of electrostatic factors; (2) in the competition between sulfur and CH_2, the steric factor dominates, with S being larger than CH_2. Only the **29** + MTAD cycloaddition appears not to follow these "rules". For steric reasons, the attack should occur syn to oxygen, whereas electrostatic effects should cause the anti product to be favored. The slight dominance of the syn product points out the existence of a modest steric override.

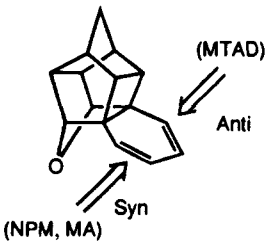
Discussion

Conventional concertedness can be considered plausible for those processes involving NPM as the dienophile. The π-facial stereoselectivity of its [4 + 2] cycloaddition to **7**, **13**, **21**, **26**, and **29** gives evidence of being governed principally by steric and electrostatic factors. The constitution of the resultant adducts is such that approach syn to one or two oxygens or to one oxygen and one sulfur is kinetically more favorable than reaction on that π surface proximal to a pair of CH_2 groups. With **29**, NPM attacks syn to oxygen in order to avoid

(31) Seymour, C. A.; Greene, F. D. *J. Am. Chem. Soc.* **1980**, *102*, 6384.
(32) Nelsen, S. F.; Kapp, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 5548.
(33) Jensen, F.; Foote, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6376.
(34) Clennan, E. L.; Earlywine, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 7104.
(35) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

interaction with the larger sulfur atom. When only one sulfur is present as in **21**, the S/CH_2 combination compares somewhat more favorably in size with the CH_2/CH_2 array on the opposite face and the two possible adducts are formed in approximately equal amounts. Disappointingly, the lack of reactivity of **19** toward NPM did not permit implementation of a classical test of the Cieplak model.

The obvious contrasteric behavior of MTAD can be rationalized in terms of the repulsive interactions that come into play between the nonbonded electron pairs on the heteroatoms present in the dienes and on the nitrogen atoms of the dienophile. Coxon has previously encountered similar behavior with diene **33**.[28a] Whereas NPM and MA are captured from the less

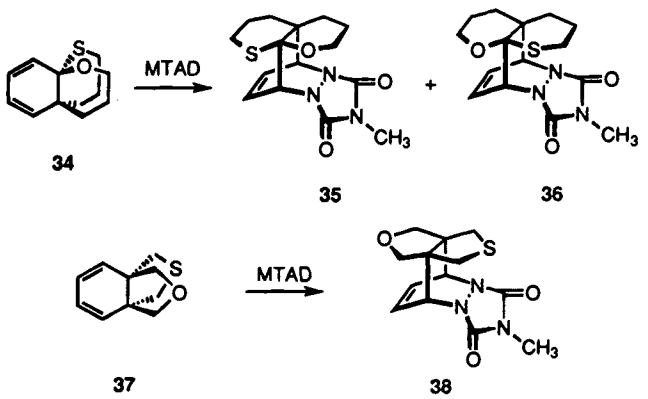


33

sterically congested face of the diene syn to the ether oxygen, MTAD and dimethyl acetylenedicarboxylate add from the more crowded anti direction. Replacement of the oxygen in **33** with a methylene bridge results in exclusive syn attack in all cases including MTAD.[28b,c]

Despite its attractiveness, this electrostatic model is not followed in the case of **29**. With the oxygen and sulfur atoms residing on opposite faces, the expectation would be that the nonbonded lone pairs residing on the azo nitrogens of the MTAD would generate greater repulsion when in the proximity of the oxygen center because of the better match in their 2p energy levels.[36] However, 50% more **32** was produced than **31**; consequently, cycloaddition syn to oxygen is clearly preferred.

This result might be construed by some as an anomaly. To the contrary, two allied observations indicate that the behavior of **29** should not be dismissed. The first finding concerns diene **34**, which reacts with MTAD to deliver a 20:1 mixture of **35** and **36**.[29a] The predominant formation of **35** requires that the



34 **35** **36**

37 **38**

dienophile approach the unsaturated ring from that direction syn to oxygen. In contrast, propelladiene **37** (and its related sulfone) experiences addition solely from that direction syn to sulfur to furnish **38**.[27] The almost complete crossover observed with the two closely related dienes **34** and **37** is quite remarkable.

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

The competition experiments were undertaken for the purpose of gaining insight into the qualitative kinetic aspects of the cycloadditions involving the spiro dienes. One striking aspect of Table 1 and Figure 3 is the fact that syn dithia system **19** is more reactive toward MTAD than its syn dioxa analogue **7**, especially when proper consideration is given to the total inertness of **19** to NPM, MA, and other conventional dienophiles. Attention is also called to the >20-fold rate difference that materializes when the oxygen atoms are positioned anti rather than syn. This appreciable sensitivity to spatial orientation serves to dismiss purely inductive effects as being contributory in a primary way to the relative ability of MTAD to cycloadd to these dienes.

Also deserving special comment is the increased reactivity of **17** relative to **13**. Predictions based on the electrostatic repulsion theory advanced above would necessarily support **13** as the more reactive of the two dienes, in contradiction to experimental fact. In the transition state involving **13** and MTAD, all heteroatomic interactions resulting from proximity considerations can be skirted, while this is not possible with **17**. Nonetheless, **17** is 1.5 times more reactive than **13** toward this dienophile.

Ginsburg has attributed the maverick behavior of MTAD toward **37** and related unsaturated propellanes to secondary orbital effects.[27b] The results obtained in the course of this study seem not to follow that explanation, nor do they adhere completely to the repulsive model of Coxon.[28a] An explanation founded totally on steric effects is equally untenable.[37,38] On the other hand, our observations are not inconsistent with precedent if the mechanism followed by MTAD involves initial formation of an aziridinium imide intermediate which rearranges via a 1,4-zwitterion to deliver the urazole products.[33,34]

Experimental Section

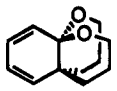
Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at the indicated field strengths. High-resolution mass spectra were recorded at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All reactions were carried out under a nitrogen atmosphere, and the ensuing separations were effected under flash chromatography conditions on Merck silica gel HG_{254}. The organic extracts were dried over anhydrous magnesium sulfate. Solvents were reagent grade and in many cases dried before use.

(1′*R*,2*S*,3′*R*,4′*S*,5′*R*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-phenyldispiro[furan-2(3*H*),2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-furan]-5′,6′-dicarboximide (8). A magnetically stirred solution of **7** (53 mg, 0.28 mmol), *N*-phenylmaleimide (95 mg, 0.55 mmol), and benzene (2 mL) was refluxed for 72 h, cooled, and concentrated to leave an oil which was purified by MPLC (silica gel, elution with 1:1 ethyl acetate−hexanes) to afford 83 mg (83%) of **8** as the only product; as colorless crystals: mp 222−224 °C (from hexanes); IR (KBr, cm^{-1}) 1710, 1500, 1385, 1180, 1055; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.30 (m, 3 H), 7.18−7.14 (m, 2 H), 6.21 (dd, J = 4.4, 3.4 Hz, 2 H), 3.99−3.87 (m, 4 H), 3.62 (d, J = 1.3 Hz, 2 H), 3.14−3.12 (m, 2 H), 2.08−1.80 (m, 6 H), 1.60−1.50 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 132.0, 131.9, 128.9, 128.4, 126.5, 84.9, 67.9, 44.7, 39.6, 36.1, 25.6; MS *m/z* (M^+) calcd 365.1627, obsd 365.1623. Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.31; H, 6.34. Found: C, 72.19; H, 6.24.

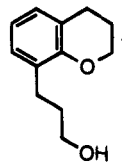
(1′*R*,2*S*,3′*R*,4′*S*,5′*R*,6′*S*)-4,4″,5,5″-Tetrahydrodispiro[furan-2(3*H*),2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-furan]-5′,6′-dicarboxylic Anhydride (9). A magnetically stirred solution of **7** (73 mg, 0.38 mmol), maleic anhydride (41 mg, 0.42 mmol), and benzene (5 mL) was refluxed for 20 h, cooled, and concentrated. The residue was chromatographed

(37) Gillard, J. R.; Burnell, D. J. *Can. J. Chem.* **1992**, *70*, 1296.
(38) Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625.

on silica gel (elution with 40% ethyl acetate in hexanes) to furnish in order of elution propelladiene **i** (9 mg, 12%),[29a] benzopyran **ii** (4 mg,



i



ii

5%),[29a] unreacted **7** (7 mg, 9%), and cycloadduct **9** (51 mg, 46%) as colorless crystals: mp 253–256 °C (from ethyl acetate); IR (KBr, cm^{-1}) 1785, 1230, 1090, 1060, 1040, 925, 770; ^1H NMR (300 MHz, $CDCl_3$) δ 6.23 (dd, J = 4.5, 3.3 Hz, 2 H), 3.94–3.83 (m, 4 H), 3.72–3.70 (t, J = 1.7 Hz, 2 H), 3.08–3.04 (m, 2 H), 2.06–1.79 (m, 6 H), 1.58–1.48 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 132.5, 84.4, 68.0, 44.4, 40.4, 35.9, 25.6; FAB MS m/z (M^+) calcd 290.12, obsd 290.10. Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25. Found: C, 66.13; H, 6.29.

(1′*R*,2*R*,4′*S*,4′a*R*,8′a*S*,10′*S*)-1′,4,4′,4″,4′a,5,5″,8′a-Octahydrodispiro[furan-2(3*H*),9′-[1,4]ethanonaphthalene-10′,2″(3″*H*)-furan]-5′,8′-dione (10). A solution of **7** (51 mg, 0.26 mmol), benzoquinone (28 mg, 0.26 mmol), and CH_2Cl_2 (3 mL) was subjected to high-pressure conditions (175 000 psi) for 3 d. The solvent was evaporated, and the residue was purified by MPLC (silica gel, elution with 3:1 ethyl acetate in hexanes) to yield 53 mg (67%) of **10** as an off-white solid: mp 160–162 °C (from ether); IR (KBr, cm^{-1}) 1750, 1665, 1345, 1305, 1255, 1140, 1060; ^1H NMR (300 MHz, $CDCl_3$) δ 6.64 (s, 2 H), 6.15 (dd, J = 4.6, 3.3 Hz, 2 H), 3.98–3.87 (m, 4 H), 3.64 (t, J = 1 Hz, 2 H), 3.18–3.14 (m, 2 H), 2.10–1.93 (m, 2 H), 1.93–1.79 (m, 4 H), 1.58-1.46 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.9, 141.9, 133.1, 84.8, 67.6, 46.9, 44.0, 35.9, 25.5; MS m/z (M^+) calcd 300.1362, obsd 300.1362. Anal. Calcd for $C_{18}H_{12}O_4$: C, 71.98; H, 6.71. Found: C, 71.98; H, 6.78.

(1′*R*,2*R*,4′*S*,4′a*R*,9′a*S*,12′*S*)-1′,4,4′,4″,4′a,5,5″,9′a-Octahydrodispiro[furan-2(3*H*),11′-[1,4]ethanoanthracene-12′,2″(3″*H*)-furan]-9′,10′-dione (11). A solution of **7** (56 mg, 0.29 mmol) and naphthoquinone (47 mg, 0.30 mmol) in CH_2Cl_2 (2 mL) was subjected to high-pressure conditions (175 000 psi) for 5 d. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 40% ethyl acetate in hexanes) to afford 70 mg (69%) of **11** as a colorless solid: mp 219–220 °C (from ethyl acetate); IR (KBr, cm^{-1}) 1675, 1275, 1065, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02–7.96 (m, 2 H), 7.68–7.62 (m, 2 H), 6.10 (dd, J = 4.6, 3.3 Hz, 2 H), 4.00–3.85 (m, 4 H), 3.84 (t, J = 1.1 Hz, 2 H), 3.32–3.28 (m, 2 H), 2.11–1.75 (m, 6 H), 1.58–1.50 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 135.7, 133.8, 133.5, 126.6, 85.0, 67.6, 47.1, 45.0, 35.9, 25.6; MS m/z (M^+) calcd 350.1518, obsd 350.1524. Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.37; H, 6.37.

(1′*R*,2*R*,4′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[furan-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)-furan]-2′,3′-dicarboximide (12). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (3.5 mg, 0.31 mmol) in CH_2Cl_2 (2 mL) was added via cannula to a magnetically stirred solution of **7** (60 mg, 0.31 mmol) in CH_2Cl_2 (3 mL) cooled to −78 °C. The reaction mixture was allowed to warm to room temperature (rt) during 45 min, at which time the red color was no longer present. Additional triazolinedione (10 mg) was added as a solid when TLC analysis indicated that a trace of **7** remained. The reaction mixture was stirred for 4 h, concentrated, and purified by MPLC (silica gel, elution with 1:1 ethyl acetate-hexanes) to furnish 78 mg (82%) of **12** as colorless crystals: mp 178–181 °C (from ethyl acetate); IR (KBr, cm^{-1}) 1775, 1760, 1455, 1395, 1220, 1075, 1020, 780, 750; ^1H NMR (300 MHz, $CDCl_3$) δ 6.44–6.40 (m, 2 H), 4.45–4.43 (m, 2 H), 3.92–3.71 (m, 4 H), 2.95 (s, 3 H), 2.16-1.97 (m, 6 H), 195–1.83 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 129.7, 85.3, 68.7, 58.2, 33.1, 25.4 (2 C); MS m/z (M^+) calcd 305.1376, obsd 305.1365. Anal. Calcd for $C_{15}H_{19}N_3O_4$: C, 59.01; H, 6.27. Found: C, 59.04; H, 6.41.

(1′*S*,3′*S*,4′*R*,5′*S*,6′*R*)-4″,5″-Dihydro-*N*-phenyldispiro[cyclopentane-1,2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-furan]-5′,6′-dicarboximide (14) and (1′*R*,3′*S*,4′*R*,5′*R*,6′*S*)-4″,5″-Dihydro-*N*-phenyldispiro[cyclopentane-1,2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-furan]-5′,6′-dicarboximide (15). A solution of **13** (64 mg, 0.34 mmol), *N*-phenylmaleimide (60 mg, 0.34 mmol), and diisopropylethylamine (4.4 mg, 0.034 mmol) in CH_2Cl_2 (2 mL) was submitted to high pressure (150 000 psi) for 3 d. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 20% ethyl acetate in hexanes). The first compound to elute was **14** (97 mg, 79%) as colorless crystals: mp 199.5–200.5 °C (from 1:1 ethyl acetate–hexanes); IR (KBr, cm^{-1}) 1770, 1705, 1495, 1380, 1170, 1050, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.28 (m, 3 H), 7.11 (d, J = 8.2 Hz, 2 H), 6.33–6.28 (m, 1 H), 6.12–6.07 (m, 1 H), 3.90–3.83 (m, 1 H), 3.80–3.72 (m, 1 H), 3.50 (dd, J = 8.2, 3.1 Hz, 1 H), 3.20 (dd, J = 8.2, 2.9 Hz, 1 H), 3.07–3.04 (m, 1 H), 2.86–2.84 (m, 1 H), 1.97–1.79 (m, 3 H), 1.76–1.36 (m, 10 H), 1.26–1.17 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.2, 178.6, 134.7, 132.1, 130.2, 128.9, 128.3, 126.5, 87.6, 67.3, 52.9, 44.8, 43.9, 41.1, 39.8, 38.6, 34.7, 33.3, 25.1, 24.7, 24.3; MS m/z (M^+) calcd 363.1834, obsd 363.1841. Anal. Calcd for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93. Found: C, 75.91; H, 6.89.

The second compound to elute was **15** (7 mg, 6%), a colorless solid of mp 229–230 °C (from 1:1 ethyl acetate–hexanes); IR (KBr, cm^{-1}) 1710, 1500, 1380, 1175, 1050, 735; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.34 (m, 3 H), 7.16 (br d, J = 7.2 Hz, 2 H), 6.42–6.38 (m, 1 H), 6.30–6.25 (m, 1 H), 3.87–3.79 (m, 2 H), 3.19 (dd, J = 8.2, 3.2 Hz, 1 H), 3.12 (br d, J = 5.9 Hz, 1 H), 3.06 (dd, J = 8.2, 2.8 Hz, 1 H), 2.98–2.95 (m, 1 H), 2.12–1.42 (m, 10 H), 1.38–1.25 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 177.8, 132.8, 131.9, 131.2, 129.1, 128.6, 126.5, 88.7, 67.5, 54.1, 44.4, 43.2, 41.0, 40.8, 35.7, 32.9, 26.1, 24.2, 23.7; MS m/z (M^+) calcd 363.1834, obsd 363.1839.

(1′*R*,4′*S*,6′*R*)-4″,5″-Dihydro-*N*-methyldispiro[cyclopentane-1,5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)-furan]-2′,3′-dicarboximide (16). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (34 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) was added via cannula to a stirred solution of **13** (56 mg, 0.29 mmol) and triethylamine (420 μL, 0.030 mmol) in CH_2Cl_2 (5 mL) at −78 °C. The reaction mixture was stirred at rt for 45 min and then concentrated. Chromatography of the residue on silica gel (elution with 1:1 ethyl acetate in hexanes) furnished 40 mg (45%) of **16** as a colorless solid: mp 153–155 °C (from 20% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1775, 1710, 1460, 1215, 1065, 1020; ^1H NMR (300 MHz, $CDCl_3$) δ 6.51–6.46 (m, 1 H), 6.38–6.33 (m, 1 H), 4.43 (dd, J = 5.5, 1.5 Hz, 1 H), 4.36 (dd, J = 5.6, 1.5 Hz, 1 H), 3.89–3.82 (m, 1 H), 3.79–3.71 (m, 1 H), 2.97 (s, 3 H), 2.18–2.11 (m, 1 H), 2.10–1.86 (m, 3 H), 1.85–1.71 (m, 3 H), 1.69–1.53 (m, 4 H), 1.27–1.19 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 157.6, 130.7, 129.5, 85.7, 68.5, 58.4, 58.1, 53.7, 34.8, 33.5, 32.2, 25.4, 25.4, 24.2, 23.7; MS m/z (M^+) calcd 303.1583, obsd 303.1581. Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.35; H, 6.98. Found: C, 63.43; H, 7.12.

(1′*R*,2*R*,4′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[thiophene-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)-thiophene]-2′,3′-dicarboximide (20). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (31 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) was added via cannula to a magnetically stirred solution of **19** (57 mg, 0.25 mmol) in CH_2Cl_2 (3 mL) at −78 °C. The solution was allowed to warm to rt, stirred for 3 h, and concentrated. Chromatography of the residue on silica gel (elution with 1:1 ethyl acetate in hexanes) afforded 74 mg (87%) of **20** as colorless crystals: mp 156–157 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1775, 1710, 1445, 1390, 1260, 1205, 1020, 915, 765; ^1H NMR (300 MHz, $CDCl_3$) δ 6.55 (dd, J = 3.9, 3.3 Hz, 2 H), 4.65–4.63 (m, 2 H), 2.94 (s, 3 H), 2.94–2.79 (m, 4 H), 2.25–2.08 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 131.0, 66.7, 59.1, 37.2, 32.2, 29.7, 25.4; MS m/z (M^+) calcd 337.0919, obsd 337.0917. Anal. Calcd for $C_{15}H_{19}N_3O_2S_2$: C, 53.39; H, 5.67. Found: C, 53.40; H, 5.76.

(1′*R*,3′*S*,4′*S*,5′*R*,6′*S*)-4″,5″-Dihydro-*N*-phenyldispiro[cyclopentane-1,2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-thiophene]-5′,6′-dicarboximide (22) and (1′*S*,3′*S*,4′*R*,5′*R*,6′*R*)-4″,5″-Dihydro-*N*-phenyldispiro[cyclopentane-1,2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-thiophene]-5′,6′-dicarboximide (23). A solution of **21** (37 mg, 0.18 mmol), *N*-phenylmaleimide (34 mg, 0.20 mmol), and diisopropylethylamine (2.9 mg, 0.022 mmol) in CH_2Cl_2 (2 mL) was subjected to high-pressure conditions (175 000 psi) for 16 d. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 20% ethyl acetate and 1% triethylamine in hexanes) to furnish polymerized starting

material (23 mg, 62%) followed by 10 mg (14%) of one cycloadduct and then 8 mg (12%) of its facial isomer (relative stereochemistry not determined).

For the less polar imide: colorless crystals, mp 203−204 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1800, 1710, 1470, 1385, 1100, 915, 790; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47−7.33 (m, 3 H), 7.18−7.14 (m, 2 H), 6.38−6.24 (m, 2 H), 3.87 (dd, J = 8.3, 3.2 Hz, 1 H), 3.21 (dd, J = 8.3, 3.2 Hz, 1 H), 3.18−3.15 (m, 1 H), 2.95−2.89 (m, 3 H), 2.14−1.97 (m, 3 H), 1.89−1.51 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9, 178.5, 133.5, 132.0, 131.9, 129.1, 128.5, 126.5, 68.4, 52.5, 46.5, 44.0, 41.6, 41.4, 40.8, 39.3, 37.0, 31.4, 28.8, 23.6, 23.5; MS m/z (M^+) calcd 379.1606, obsd 379.1603.

For the minor polar imide: colorless crystals, mp 226−227 °C (from 1:1 ethyl acetate-hexanes); IR (KBr, cm^{-1}) 1715, 1385, 1180; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47−7.33 (m, 3 H), 7.17−7.13 (m, 2 H), 6.44−6.35 (m, 2 H), 3.36−3.32 (m, 1 H), 3.24 (dd, J = 8.2, 3.1 Hz, 1 H), 3.19 (dd, J = 8.2, 2.8 Hz, 1 H), 2.98−2.95 (m, 1 H), 2.89−2.81 (m, 2 H), 2.23−2.03 (m, 2 H), 2.00−1.91 (m, 3 H), 1.84−1.58 (m, 6 H), 1.49−1.43 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 177.7, 133.5, 133.4, 131.9, 129.1, 128.6, 126.5, 67.4, 54.0, 47.1, 42.4, 42.0, 41.2, 41.0, 38.8, 33.8, 31.8, 30.2, 23.2, 23.1; MS m/z (M^+) calcd 379.1606, obsd 379.1602. Anal. Calcd for $C_{23}H_{25}NO_2S$: C, 72.79; H, 6.64. Found: C, 72.47; H, 6.57.

(1′*R*,4′*S*,6′*R*)-4″,5″-Dihydro-*N*-methyldispiro[cyclopentane-1,5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′2″(3″*H*)-thiophene]-2′,3′-dicarboximide (24) and (1′*S*,4′*R*,6′*R*)-4″,5″-Dihydro-*N*-methyldispiro-[cyclopentane-1,5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′2″(3″*H*)-thiophene]-2′,3′-dicarboximide (25). A solution of *N*-methyltriazoline-3,5-dione (34 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was added via cannula to a stirred solution of **21** (57 mg, 0.27 mmol) in CH_2Cl_2 (4 mL) at −78 °C. The cooling bath was removed, the reaction mixture was stirred at rt for 15 min, the solvent was evaporated, and the residue was chromatographed on silica gel (elution with 30% ethyl acetate and 1% triethylamine in hexanes). The first adduct to elute was **24** (40 mg, 45%), a colorless solid of mp 166−167 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1770, 1720 , 1455, 1400, 1210, 1035, 1020, 1010, 770; ^1H NMR (300 MHz, $CDCl_3$) δ 6.52−6.42 (m, 2 H), 4.62 (dd, J = 5.3, 1.5 Hz, 1 H), 4.38 (dd, J = 5.4, 1.7 Hz, 1 H), 2.97 (s, 3 H), 2.84 (dd, J = 7.4, 5.6 Hz, 2 H), 2.30−2.23 (m, 1 H), 2.14−2.02 (m, 2 H), 2.00−1.58 (m, 8 H), 1.38−1.31 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 157.6, 131.2, 130.5, 64.6, 59.8, 57.7, 53.7, 39.6, 38.0, 33.4, 32.6, 29.5, 25.4, 23.1, 23.0; MS m/z (M^+) calcd 319.1355, obsd 319.1360. Anal. Calcd for $C_{16}H_{21}N_3O_2S$: C, 60.16; H, 6.63. Found: C, 60.43; H, 6.74.

The second product to elute was **25** (4 mg, 4%), a colorless solid of mp 188−190 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 6.54−6.43 (m, 2 H), 4.52 (dd, J = 5.4, 1.7 Hz, 1 H), 4.27 (dd, J = 5.4, 1.7 Hz, 1 H), 3.00 (s, 3 H), 2.79−2.58 (m, 2 H), 2.47−2.25 (m, 2 H), 2.11−1.92 (m, 2 H), 1.91−1.78 (m, 1 H), 1.78−1.64 (m, 3 H), 1.63−1.50 (m, 4 H); MS m/z (M^+) calcd 319.1355, obsd 319.1352.

(1′*R*,2*S*,3′*R*,4′*S*,5′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-phenyldispiro[furan-2(3*H*),2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-thiophene]-5′,6′-dicarboximide (27). A solution of **26** (51 mg, 0.24 mmol), N-phenylmaleimide (47 mg, 0.27 mmol), and diisopropylethylamine (3.2 mg, 0.025 mmol) in CH_2Cl_2 (2 mL) was subjected to high-pressure conditions (150 000 psi) for 5 d. The solvent was evaporated, and the residue was chromatographed on silica gel (gradient elution with 20% ethyl acetate in hexanes, then 30% ethyl acetate in hexanes) to afford 13 mg (25%) of unreacted **26** and 39 mg (56% based on unrecovered diene) of **27** as colorless crystals: mp 221−222 °C (from 1:1 ethyl acetate−hexanes); IR (KBr, cm^{-1}) 1780, 1705, 1500, 1385, 1175, 1065, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.32 (m, 3 H), 7.19−7.15 (m, 2 H), 6.37−6.31 (m, 1 H), 6.24−6.19 (m, 1 H), 3.98−3.88 (m, 2 H), 3.84 (dd, J = 8.2, 3.0 Hz, 1 H), 3.69 (dd, J = 8.3, 3.5 Hz, 1 H), 3.20−3.13 (m, 2 H), 2.87−2.79 (m, 2 H), 2.17−2.05 (m, 2 H), 2.04−1.92 (m, 4 H), 1.65−1.56 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.8, 178.8, 134.1, 132.1, 130.6, 129.0, 128.4, 126.5, 86.0, 70.0, 68.2, 46.4, 45.2, 41.8, 41.2, 40.2, 34.6, 30.0, 29.6, 25.9; MS m/z (M^+) calcd 381.1399, obsd 381.1394. Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.27; H, 6.08. Found: C, 69.08; H, 5.99.

(1′*R*,2*R*,4′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[furan-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)thiophene]-2′,3′-dicarboximide (28). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (28 mg, 0.24 mmol) in CH_2Cl_2 (3 mL) was added via cannula to a magnetically stirred solution of **26** (48 mg, 0.23 mmol) in CH_2Cl_2 (4 mL) at −78 °C. The cooling bath was removed, and the reaction mixture was stirred at rt for 30 min before being treated with more dienophile (9 mg). Stirring was maintained for an additional 30 min, after which the solvent was evaporated. Chromatography of the residue on silica gel (elution with 1:1 ethyl acetate-hexanes) furnished **28** in quantitative yield as a colorless solid: mp 140.5−142 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1775, 1715, 1445, 1395, 1205, 1075, 775; ^1H NMR (300 MHz, $CDCl_3$) δ 6.56−6.51 (m, 1 H), 6.39−6.34 (m, 1 H), 4.57 (dd, J = 5.6, 1.5 Hz, 1 H), 4.42 (dd, J = 5.6, 1.6 Hz, 1 H), 3.82 (br t, J = 6.6 Hz, 2 H), 2.93 (s, 3 H), 2.84−2.75 (m, 2 H), 2.19−2.06 (m, 5 H), 2.05−1.90 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 156.9, 130.7, 129.6, 86.0, 68.8, 66.8, 59.1, 59.0, 38.1, 31.8, 31.1, 29.9, 25.6, 25.3; MS m/z (M^+) calcd 321.1147, obsd 321.1149. Anal. Calcd for $C_{15}H_{19}N_3O_3S$: C, 56.06; H, 5.96. Found: C, 56.14; H, 5.97.

(1′*R*,2*S*,3′*S*,4′*S*,5′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-phenyldispiro[furan-2(3*H*),2′-bicyclo[2.2.2]oct[7]ene-3′,2″(3″*H*)-thiophene]-5′,6′-dicarboximide (30). A solution of **29** (50 mg, 0.24 mmol), *N*-phenylmaleimide (45 mg, 0.26 mmol), and diisopropylethylamine (3.5 mg, 0.026 mmol) in CH_2Cl_2 (1.5 mL) was subjected to high-pressure conditions (175 000 psi) for 18 h. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 20% ethyl acetate-hexanes) to furnish 63 mg (70%) of **30** as a colorless solid: mp 189−190 °C (from 1:1 ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1710, 1500, 1380, 1180, 1055; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.32 (m, 3 H), 7.17−7.13 (m, 2 H), 6.47−6.42 (m, 1 H), 6.25−6.19 (m, 1 H), 4.01−3.94 (m, 1 H), 3.90−3.82 (m,1 H), 3.59 (dd, J = 8.2, 3.4 Hz, 1 H), 3.37−3.34 (m, 1 H), 3.25 (dd, J = 8.2, 3.0 Hz, 1 H), 3.18−3.14 (m, 1 H), 2.93−2.76 (m, 2 H), 2.39−2.28 (m, 1 H), 2.20−1.88 (m, 6 H), 1.86−1.71 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.8, 177.6, 135.1, 131.9, 131.2, 129.0, 128.4, 126.4, 89.0, 68.6, 68.1, 46.8, 43.9, 41.3, 40.0, 39.2, 36.9, 33.2, 30.2, 25.2; MS m/z (M^+) calcd 381.1399, obsd 381.1393. Anal. Calcd for $C_{22}H_{23}NO_3S$: C, 69.27; H, 6.08. Found: C, 69.28; H, 6.08.

(1′*S*,2*S*,4′*R*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[furan-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)thiophene]-2′,3′-dicarboximide (31) and (1′*R*,2*S*,4′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[furan-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)thiophene]-2′,3′-dicarboximide (32). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (38 mg, 0.34 mmol) in CH_2Cl_2 (4 mL) was added via cannula to a magnetically stirred solution of **29** (64 mg, 0.31 mmol) in CH_2Cl_2 (3 mL) at −78 °C. After being warmed slowly to rt over 60 min, the reaction mixture was concentrated and the residue was chromatographed on silica gel (elution with 75% ether in hexanes). The first adduct to elute was **31** (35 mg, 35%), a colorless crystalline solid, mp 159.5−162 °C; IR (KBr, cm^{-1}) 1775, 1715, 1450, 1395, 1205, 1055, 1025, 780, 750; ^1H NMR (300 MHz, $CDCl_3$) δ 6.49−6.36 (m, 2 H), 4.64 (dd, J = 5.5, 1.8 Hz, 1 H), 4.47 (dd, J = 5.4, 1.8 Hz, 1 H), 3.93−3.78 (m, 2 H), 2.98 (s, 3 H), 2.96−2.86 (m, 2 H), 2.57 (dt, J = 13.5, 7.9 Hz, 1 H), 2.25−2.17 (m, 1 H), 2.10−1.92 (m, 5 H), 1.68−1.54 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 157.2, 130.1, 130.0, 86.2, 69.6, 68.1, 62.6, 58.0, 38.4, 36.9, 32.9, 30.1, 25.6, 25.4; MS m/z (M^+) calcd 321.1147, obsd 321.1151.

The second product to elute was **32** (50 mg, 50%), a colorless crystalline solid: mp 206−207 °C (from 1:1 ethyl acetate−hexanes); IR (KBr, cm^{-1}) 1770, 1715, 1455, 1400, 1210, 1055, 775; ^1H NMR (300 MHz, $CDCl_3$) δ 6.59−6.54 (m, 1 H), 6.42−6.35 (m, 1 H), 4.69 (dd, J = 5.6, 1.5 Hz, 1 H), 4.53 (dd, J = 5.9, 1.5 Hz, 1 H), 4.04−3.87 (m, 2 H), 2.98 (s, 3 H), 2.92−2.78 (m, 2 H), 2.39−2.29 (m, 1 H), 2.26−2.16 (m, 1 H), 2.15−1.91 (m, 5 H), 1.69−1.60 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 156.1, 133.2, 129.2, 87.2, 69.1, 66.2, 58.9, 58.4, 37.8, 36.2, 33.9, 29.7, 25.3, 25.2; MS m/z (M^+) calcd 321.1147, obsd 321.1142. Anal. Calcd for $C_{15}H_{19}N_3O_3S$: C, 56.06; H, 5.96. Found: C, 56.08; H, 6.02.

(1′*R*,2*S*,4′*S*,6′*S*)-4,4″,5,5″-Tetrahydro-*N*-methyldispiro[furan-2(3*H*),5′-[2,3]diazabicyclo[2.2.2]oct[7]ene-6′,2″(3″*H*)-furan]-2′,3′-dicarboximide (18). Competition Experiments. A. Between 7 and 17. A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (27 mg, 0.24 mmol) in CH_2Cl_2 (5 mL) was added via cannula to a magnetically stirred solution of **7** (58 mg, 0.30 mmol) and **17** (58 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) at −78 °C. The cooling bath was

removed, and the reaction mixture was stirred at rt for 4 h. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 1:1 ethyl acetate-hexanes) to afford (in order of elution) 22 mg (38%) of **17**, 58 mg (100%) of **7**, and 55 mg (97% based on unrecovered diene) of **18** as a colorless solid: mp 165–166.5 °C (from 30% ethyl acetate in hexanes); IR (KBr, cm^{-1}) 1770, 1710, 1450, 1400, 1210, 1065, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 6.46–6.35 (m, 2 H), 4.53 (dd, $J = 5.1$, 2.3 Hz, 1 H), 4.45 (dd, $J = 4.9$, 2.3 Hz, 1 H), 4.09–3.97 (m, 1 H), 3.94–3.85 (m, 2 H), 3.76 (dd, $J = 7.9$, 6.7 Hz, 1 H), 2.96 (s, 3 H), 2.28–2.18 (m, 1 H), 2.14–2.03 (m, 2 H), 2.01–1.79 (m, 4 H), 1.52–1.44 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.1, 156.7, 131.3, 128.6, 86.8, 86.4, 69.7, 69.2, 58.4, 57.4, 32.2, 30.5, 25.5, 25.4, 25.3; MS *m/z* (M^+) calcd 305.1376, obsd 305.1371. Anal. Calcd for $C_{15}H_{19}N_3O_4$: C, 59.01; H, 6.27. Found: C, 58.93; H, 6.32.

B. Between 7 and 19 (General Procedure). A solution of freshly sublimed *N*-methyltriazoline-3,5-dione (9.5 mg, 0.084 mmol) in CH_2Cl_2 (3 mL) was added via cannula to a solution of **7** (22 mg, 0.12 mmol) and **19** (24 mg, 0.11 mmol) in CH_2Cl_2 (2.5 mL) at −78 °C. The cooling bath was removed, and the reaction mixture was stirred at rt until the red color had disappeared. The solvent was evaporated, and ^1H NMR analysis of the residue revealed the ratio of **20** to **12** to be 2.4:1. The residue was chromatographed on silica gel (gradient elution with 20–70% ethyl acetate in hexanes) to afford 11 mg (47%) of **119**, 12.5 mg (56%) of **7**, 12 mg (44%) of **20**, and 4 mg (15%) of **12**.

C. **Between 7 and 13.** The procedure was followed as before using **7** (41 mg, 0.21 mmol), **13** (41 mg, 0.21 mmol), and *N*-methyltriazoline-3,5-dione (19 mg, 0.17 mmol). Once the color had disappeared, ^1H NMR analysis of the reaction mixture revealed that only **13** had reacted. The mixture was chromatographed on silica gel to afford **13** (14 mg, 34%), **7** (40 mg, 99%), and **16** (40 mg, 77%).

D. Between 7 and 29. The procedure was followed as before using **7** (38 mg, 0.20 mmol), **29** (41 mg, 0.20 mmol), and *N*-methyltriazoline-3,5-dione (19 mg, 0.16 mmol). After the color was no longer visible, ^1H NMR analysis of the reaction mixture indicated that an 8.4:1 mixture of **31/32** and **12** had been produced.

E. Between 7 and 26. The above procedure was followed with **7** (32 mg, 0.17 mmol), **26** (35 mg, 0.17 mmol), and *N*-methyltriazolinedione (15 mg, 0.14 mmol). After the color was no longer visible, ^1H NMR analysis of the reaction mixture revealed that an 8.3:1 mixture of **28** and **12** had been produced.

F. Between 13 and 29. The above procedure was followed with **13** (31 mg, 0.16 mmol), **29** (34 mg, 0.16 mmol), and *N*-methyltriazoline-3,5-dione (15 mg, 0.13 mmol). After the color was no longer visible, ^1H NMR analysis of the reaction mixture revealed a 2:1 ratio of **16** to **31/32.** Chromatographic separation of the components yielded 18 mg (46%) **16** and 10 mg (25%) of the mixture of **31** and **32.**

G. Between 13 and 17. The above procedure was followed with **13** (39 mg, 0.21 mmol), **17** (41 mg, 0.21 mmol), and *N*-methyltriazoline-3,5-dione (19 mg, 0.17 mmol). After the red color was no longer visible, ^1H NMR analysis of the reaction mixture indicated that a 1.5:1 ratio of **18** to **16** had been produced. Chromatographic separation of the components furnished 11 mg (22%) of **16** followed by 18 mg (36%) of **18.**

H. Between 13 and 26. The above procedure was followed with **13** (34 mg, 0.18 mmol), **26** (37 mg, 0.18 mmol), and *N*-methyltriazolinedione (17 mg, 0.15 mmol). After the red color was no longer visible, ^1H NMR analysis of the reaction mixture revealed a 1.6:1 ratio of **16** to **28** to have been produced. Chromatographic separation of the components afforded 29 mg (65%) of **16** followed by 19 mg (40%) of **28.**

I. Between 26 and 29. The above procedure was followed with **26** (43 mg, 0.21 mmol), **19** (43 mg, 0.21 mmol), and *N*-methyltriazoline-3,5-dione (19 mg, 0.17 mmol). After the red color was no longer visible, ^1H NMR analysis of the reaction mixture disclosed the ratio of **28** to **31/32** to be 1.3:1.

J. Between 26 and 19. The above procedure was followed with **26** (33 mg, 0.16 mmol), **19** (36 mg, 0.16 mmol), and *N*-methyltriazoline-3,5-dione (17 mg, 0.15 mmol). After the red color was no longer visible, ^1H NMR analysis of the reaction mixture disclosed the ratio of **28** to **20** to be 4:1. Chromatographic separation of the components afforded 42 mg (88%) of **28** followed by 9 mg (18%) of **20.**

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Supplementary Material Available: Crystallographic experimental sections and tables of X-ray crystal data, bond lengths and angles, final fractional coordinates, and thermal parameters for **12** and **32** (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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