Cycloaddition Chemistry of 1,3-Thiazolium-4-olate Systems.† Reaction with Nitroalkenes and Interpretation of Results Using PM3 Calculations

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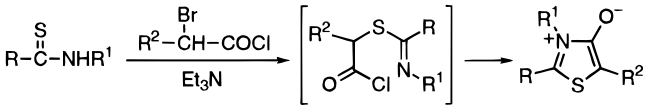
1,3-Dipolar cycloaddition of 1,3-thiazolium-4-olates, readily prepared from thioureido derivatives, and *trans*-β-nitrostyrene at room temperature in methylene chloride (48 h) resulted in two readily separable diastereomeric racemic 4,5-dihydrothiophenes via transient cycloadducts that underwent rearrangement under these reaction conditions. Using chiral carbohydrate-derived nitroalkenes, two diastereomeric dihydrothiophenes were obtained, showing that regiospecificity and facial selectivity were involved in these cycloadditions. ^{1}H NMR data and trapping experiments with isolated initial cycloadducts indicated that the cycloadditions were reversible and accounted for observed adduct and final product ratios. Single-crystal X-ray determinations established the structures of critical intermediates and products, and PM3 semiempirical MO calculations provide a rationalization for both the reactivity of the thiazolium-4-olates and the regioselectivity observed in the cycloadditions.

Introduction

Mesoionic heterocycles are receiving considerable attention as synthons in modern organic synthesis. These are five-membered, aromatic heterocycles that cannot be represented by Lewis forms not involving charge separation[1] and, although the peculiar structure and reactivity of such systems have elicited great interest in the past, the current research focuses on the uniqueness of mesoionics as masked 1,3-dipoles and their role in cycloaddition chemistry.[2]

While münchnones (1,3-oxazolium-5-olates) have been the most extensively studied class of mesoionic compounds, two types of isomeric mesoionics, isomünchnones (1,3-oxazolium-4-olates) and thioisomünchnones (1,3-thiazolium-4-olates), have received less attention despite offering rapid access to different heterocyclic compounds useful in natural product syntheses.[3] Both systems are able to react with a wide variety of alkenic and alkynic dipolarophiles, including remarkably the recent reactions of isomünchnones with buckminsterfullerene, C_{60}.[4]

Scheme 1



As a part of our ongoing program on the cycloadditions of mesoionic compounds,[5] we now report on the reactivity of thioisomünchnones toward nitroalkenes, including asymmetric syntheses with chiral nitro olefins in which the auxiliary is a carbohydrate-based template. A preliminary account of this work has appeared.[6] In addition, a theoretical study using the PM3 semiempirical method[7] agrees with the regiochemistry and selectivity observed, thus allowing us to rationalize thioisomünchnone cycloadditions.

Results and Discussion

Synthesis of Thioisomünchnones. A general synthesis of 1,3-thiazolium-4-olates was developed by Potts and co-workers by reaction of *N*-monosubstituted thioamides (1,3-binucleophiles) with α-haloacyl halides (1,2-bielectrophiles) in the presence of Et_3N (Scheme 1).[8]

This one-pot procedure also enables the preparation of thioisomünchnones arising from *N*,*N*,*N*′-trisubstituted thioureas which cannot be prepared by the older method involving the cyclodehydration of thioglycolic acids.[9] We have found, however, that *N*′-aryl-*N*-benzyl-*N*-methyl-

† IUPAC name for thioisomünchnones. The Chemical Abstracts Service indexes these substances as *anhydro*-4-hydroxythiazolium hydroxides.

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(2) (a) Potts, K. T. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2, pp 1−82. (b) Padwa, A. *Acc. Chem. Res*. **1991**, *24*, 22−28. (c) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385−5453.

(3) For excellent accounts on isomünchnones/thioisomünchnones: (a) Osterhout, M. H.; Nadler, W. R.; Padwa, A. *Synthesis* **1994**, 123−141. (b) Marino, J. P., Jr.; Osterhout, M. H.; Padwa, A. *J. Org. Chem*. **1995**, *60*, 2704−2713.

(4) González, R.; Knight, B. W.; Wudl, F.; Semones, M. A.; Padwa, A. *J. Org. Chem*. **1994**, *59*, 7949−7951.

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(6) Avalos, M.; Babiano, R.; Cabanillas, A.; Cintas, P.; Diánez, M. J.; Estrada, M. D.; Jiménez, J. L.; López-Castro, A.; Palacios, J. C.; Garrido, S. P. *J. Chem. Soc., Chem. Commun*. **1995**, 2213−2214.

(7) Stewart, J. J. P. *J. Comput. Chem*. **1989**, *10*, 209−220.

(8) Potts, K. T.; Chen, S. J.; Kane, J.; Marshall, J. L. *J. Org. Chem*. **1977**, *42*, 1633−1638.

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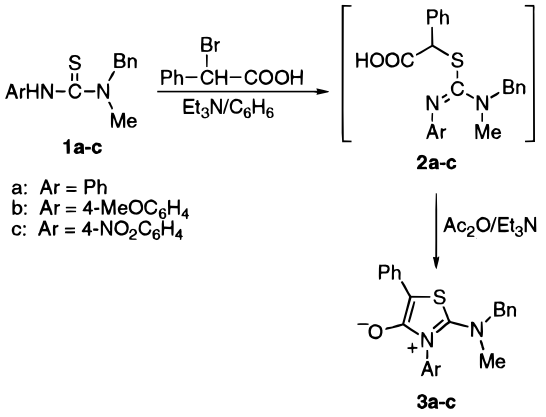
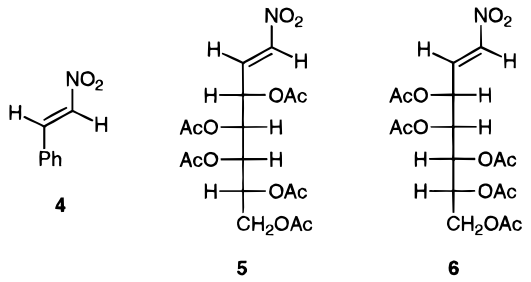
Scheme 2



thioureas (**1a**−**c**), readily prepared from aryl isothiocyanates and *N*-methylbenzylamine, reacted with α-bromophenylacetic acid in benzene/Et_3N affording the nonisolated thioglycolic acid intermediates **2a**−**c**. Further cyclodehydration with Ac_2O/Et_3N gave the thioisomünchnones **3a**−**c**, which were usually contaminated with triethylammonium salts (Scheme 2). Purification was achieved upon treatment with $KHCO_3$/18-crown-6 in CH_2Cl_2/Et_2O.

Reactions with Nitroalkenes. 1,3-Dipolar cycloadditions of thioisomünchnones with nitroalkenes have not been as extensively studied as with other asymmetrically-substituted dipolarophiles,[5a,6] and the usefulness and control exerted by a nitro group are of special interest. Our experiments with *β*-nitrostyrene (**4**) and the chiral nitroalkenes **5** and **6** are summarized in Schemes 3 and 5, respectively (*vide infra*).



Thioisomünchnone **3a** reacted smoothly with *trans*-*β*-nitrostyrene (**4**) in CH_2Cl_2 at room temperature for 48 h and gave a diastereomeric 3:1 mixture of racemic 4,5-dihydrothiophenes **9a** and **10a** in 93% overall yield. These products were readily separated by column chromatography (Scheme 3).

The formation of these dihydrothiophenes should proceed through transient cycloadducts **7a** and **8a**. ^1H NMR monitoring (400 MHz) in $CDCl_3$ at 0 °C provided evidence for the formation of these cycloadducts in a 1:3 ratio, respectively. The reaction mixture was allowed to warm at room temperature, and after 1 h, the conversion of **7a** into **9a** was complete whereas compound **8a** remained unaltered. The analogous reaction of **3b** and **4** at 0 °C resulted in the formation of **7b** and **8b** (1:3 ratio). After 1 h at room temperature, the transformation of **7b** into **9b** was complete, and the cycloadduct **8b** was isolated from the reaction mixture by precipitation with cold ether. When the reaction was conducted in CH_2Cl_2 at room temperature for 48 h, the dihydrothiophene **9b** was isolated in 90% yield. Remarkably, a sample of **8b** in $CDCl_3$ at room temperature *slowly converted into* **9b** *and not into the thiophene* **10b** *which was not detected at all in this entry*. The experiments described are consistent with the retrocycloaddition of cycloadduct **8b** occurring readily at room temperature. In order to test such a retro-dipolar process, two trapping experiments were carried out (Scheme 4).

Thus, in the presence of a stoichiometric amount of methyl propiolate, the cycloadduct **8b** gives the pyridone **11**, which was also obtained by direct cycloaddition of **3b** with methyl propiolate.[10] On the other hand, the reaction of **8b** with the thioisomünchnone **3c** gave a mixture of dihydrothiophenes **9b**, **9c**, and **10c** in the ratio 1:1:2 as determined by ^1H NMR. These compounds were separated by preparative thin-layer chromatography, and they had physical and spectroscopic properties identical to those of authentic samples. These results demonstrate the retrocycloaddition of **8b** to **3b** and *β*-nitrostyrene.

Likewise, the cycloaddition of **3c** with **4** at room temperature for 4 h afforded a 1:2 mixture of dihydrothiophenes **9c** and **10c**, separable by chromatography. Again, transient cycloadducts **7c** and **8c** could be detected at 0 °C by NMR analysis, but they readily converted into **9c** and **10c**. Structures of dihydrothiophenes **9** and **10** were determined by homo- and heteronuclear two-dimensional correlations and selective decoupling experiments. Of particular importance is the high-field chemical shift of H4 in compounds **9** ($\Delta\delta_H \sim 0.1-0.2$ ppm), while the C5 resonances of these compounds were shifted downfield ($\Delta\delta_C \sim 3.5-5.0$ ppm) with respect to those of **10**. The stereochemical assignment was confirmed finally by the single-crystal X-ray structure determination of **10a**. The diffraction data were recorded as described in the Supporting Information.[11]

The structures attributed to cycloadducts **7** and **8** are consistent with those proposed for the resulting dihydrothiophenes **9** and **10**.

Asymmetric Syntheses. Having demonstrated that thioisomünchnones **3a**−**c** undergo 1,3-dipolar cycloaddition with *β*-nitrostyrene to furnish a mixture of two diastereomeric dihydrothiophenes, we were eager to test the asymmetric version of this novel process by using a chiral and enantiomerically pure nitroalkene to induce facial selectivity in these reaction conditions. We chose as carbohydrate-based chiral auxiliaries the nitroalkenes **5** and **6** that were readily prepared from the commercially available D-galactose and D-mannose, respectively, in a three-step sequence.[12] The presence of two chiral side chains, with opposite configuration at the first stereogenic center, will be of benefit in evaluating the influence of the chiral fragment and determining the stereochemical outcome (Scheme 5).

Mesoionic compounds **3** and nitroalkene **5** in toluene at reflux or in CH_2Cl_2 at room temperature gave exclu-

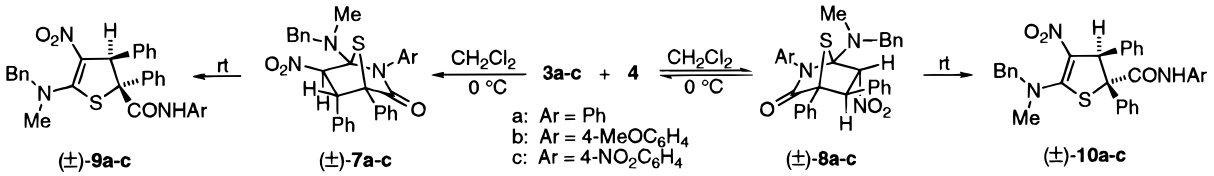
(9) (a) Duffin, G. F.; Kendall, J. D. *J. Chem. Soc.* **1951**, 734−739. (b) Ohta, M.; Chosho, H.; Shin, C.; Ichimura, K. *Nippon Kagaku Zasshi* **1964**, *85*, 440−443; *Chem. Abstr.* **1964**, *61*, 14657h.

(10) Avalos, M.; Babiano, R.; Cabanillas, A.; Cintas, P.; Jiménez, J. L.; Palacios, J. C.; Valencia, C. unpublished results on reactions of thioisomünchnones with alkynes.

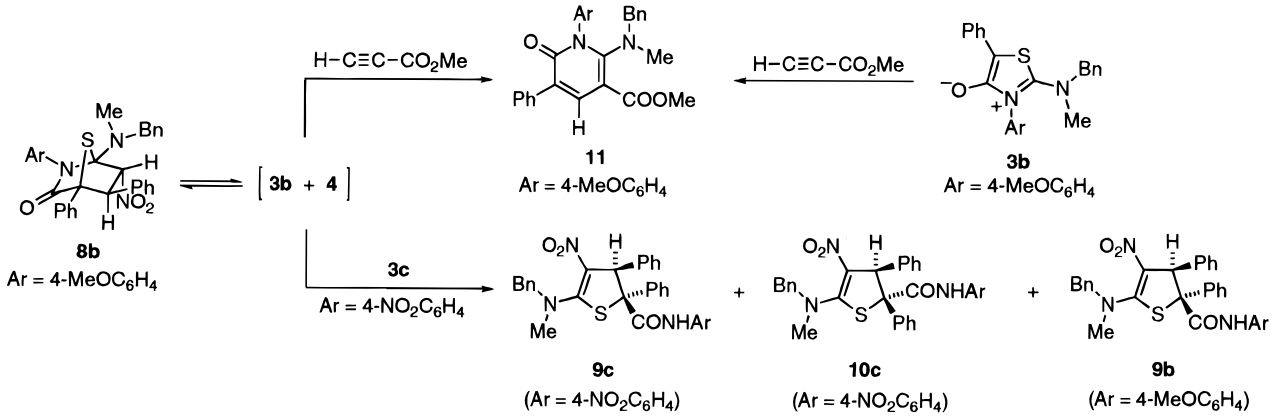
(11) The authors have deposited crystal X-ray diffraction data of this work with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(12) (a) Sowden, J. C.; Schaffer, R. *J. Am. Chem. Soc.* **1951**, *73*, 4662−4664. (b) Sowden, J. C.; Strobach, D. R. *J. Am. Chem. Soc.* **1960**, *82*, 954−955.

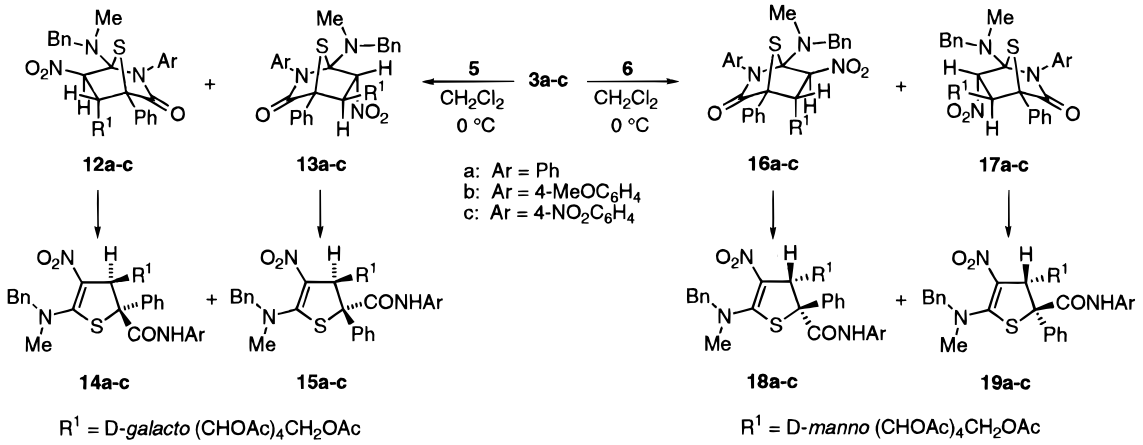
Scheme 3



Scheme 4



Scheme 5



sively the 4,5-dihydrothiophenes **14** and **15**. Structures of compounds **14a** and **15a** were unequivocally assigned by X-ray diffraction analyses.[6] When the reaction was conducted in $CDCl_3$ at 0 °C and monitored by ^1H NMR, we succeeded in detecting the intermediates **12** and **13**, whose stability follows the order **b** > **a** > **c** depending on the substitution pattern of the mesoionic ring. Again, the transformation of **12** into **14** was faster than that of **13** into **15**. This fact allowed us to isolate the cycloadduct **13b** by precipitation with cold ether. A $CDCl_3$ solution of **13b** was monitored by ^1H NMR showing, after 30 days at 25 °C, a mixture of **14b** and **15b** (1:1.4 ratio). This experiment proves again that a stable cycloadduct may undergo a retro-dipolar addition yielding starting materials that, after recombination, provide the two cycloadducts. On the other hand, on heating **13b** in CH_2Cl_2 in the presence of silica gel, compound **15b** was obtained quantitatively after 5 h.

Cycloadditions of **3** with chiral nitroalkene **6**, bearing a D-*manno* carbohydrate side chain, occurred in a way similar to those outlined above. Again, the transient cycloadducts **16** and **17** were detected spectroscopically and the 4,5-dihydrothiophenes **18** and **19** were isolated. Furthermore, the unambiguous structures of compounds **19a** and **19b** have been determined by X-ray diffraction analyses.[13]

It should be pointed out that stereocenters at C4 and C5 of compounds **18** and **19** have the configuration opposite to those of **14** and **15**, respectively. This fact accounts for the facial selectivity provided by two different and complementary carbohydrate auxiliaries and reveals the discriminating role exerted by the first stereocenter of acyclic sugar chains.

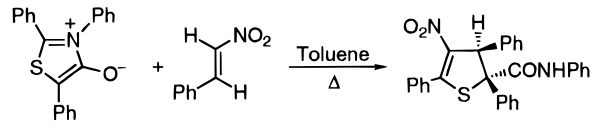
Influence of Thioisomünchnone Structure on the Reactivity. Results summarized above are unprecedented in the literature since it is known that reactions of 1,3-thiazolium-4-olates with olefinic dipolarophiles provide stable cycloadducts,[14,15] often as *endo*/*exo* mixtures, which eventually fragment into α-pyridones. In addition, Padwa and co-workers have described the preparation of nitrogen- and sulfur-containing polycyclic

(13) Diánez, M. J.; Estrada, M. D.; López-Castro, A.; Pérez-Garrido, S. Private communication.

(14) Potts, K. T.; Baum, J.; Houghton, E. *J. Org. Chem.* **1974**, *39*, 3631−3641.

(15) Robert, A.; Baudy, M.; Foucaud, A.; Golic, L.; Stanovnik, B. *Tetrahedron* **1978**, *34*, 3525−3530.

Scheme 6

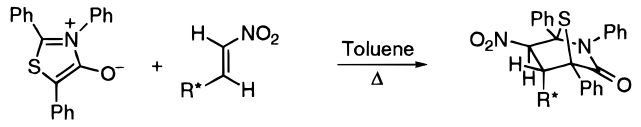


20 **4** **(±)-21**

Table 1. Comparative ^{13}C NMR Chemical Shifts for Compounds 9, 10, and 21

	trans			*cis*		
	9a	**9b**	**9c**	**10a**	**10c**	**21**
C2	166.2	166.2	165.8	161.5	162.9	150.8
C3	120.3	120.5	121.8	121.7	122.0	130.4
C4	56.7	56.4	56.1	58.4	59.8	59.1
C5	73.6	73.8	75.1	70.4	70.8	71.4

Scheme 7



20 **5** R* = D-*galacto*-$(CHOAc)_4CH_2OAc$ **22**
6 R* = D-*manno*-$(CHOAc)_4CH_2OAc$ **23**

systems by intramolecular cycloaddition of alkenes attached to 1,3-thiazolium-4-olate systems.[16]

Initially, we suspected that the difference of reactivity could likely be ascribed to the nitroalkene rather than the mesoionic heterocycle itself. In order to obtain support for this hypothesis, the reactions of thioisomünchnone **20**, the first, well-characterized 1,3-thiazolium-4-olate system,[17] with nitroalkenes were examined. The reaction of *β*-nitrostyrene (**4**) with an excess (33%) of **20** proceeded slowly, and *after 6 days in refluxing toluene*, the racemic 4,5-dihydrothiophene **21** was isolated in 43% yield (Scheme 6).

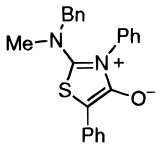
The thiophene structure for compound **21** is supported by the NMR data. Besides aromatic signals, its ^1H NMR spectrum displays two resonances shifted downfield at 7.7 and 6.0 ppm. The former, exchangeable by addition of D_2O, should be ascribed to the NH proton, while the latter is attributed to H-4. In addition, ^{13}C NMR data also support this structure because the resonances of C4 and C5 carbon atoms are similar to those of 4,5-dihydrothiophenes **10**. Table 1 shows a comparison of ^{13}C resonances for compounds **9**, **10**, and **21**, where *cis* or *trans* refers to the relative orientations of the two phenyl groups at C4 and C5.

The reaction of thioisomünchnone **20** with nitroalkenes **5** and **6** also occurred at reflux over 24−48 h, and an excess (33%) of thioisomünchnone **20** was also required. Unlike *trans*-*β*-nitrostyrene, reactions with compounds **5** and **6** afforded the cycloadducts **22** and **23**, respectively (Scheme 7).

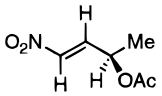
NMR data did not provide evidence for the transformation of such intermediates into the corresponding dihydrothiophenes. The structures of the cycloadducts were established by comparison of their NMR data with those of pure cycloadducts described in this work as well as with similar bicyclic systems formed by Diels−Alder reaction of nitroalkenes **5** and **6** with cyclopentadiene.[18] Unequivocal evidence of the stereostructure of these cycloadducts was obtained from the single-crystal X-ray determination of **23**.[11]

In summary, the cycloadditions of **20** proceeded slowly and required prolonged heating, while mesoionic compounds **3a**−**c** reacted with nitroalkenes at 0 °C in shorter reaction times. This distinctive behavior suggests that the presence of an amino group, instead of aryl substituents, plays a crucial role in the reactivity. In order to gain further insight into this feature as well as to explain the regiochemistry and facial selectivity observed, a theoretical study was undertaken.

Rationalization of Thioisomünchnone Cycloadditions. Semiempirical calculations using the PM3 method[7] for the cycloaddition of thioisomünchnone **3a** with **24** were carried out.



3a

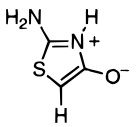


24

This model system is very close to the real reaction with chiral nitroalkenes **5** and **6**, the differences being the lack of the carbohydrate skeleton though **24** maintains the *E* disposition around the double bond and the same configuration at the first stereogenic carbon as in compound **5**. Geometrical parameters, formal charge distributions, enthalpies of formation at 298 K, and ionization potentials for **3a** and **24** are shown in Figure 1. The charge distributions of +0.122 at the mesoionic ring and −0.380 at the exocyclic oxygen reflect the mesoionic character of **3a**, thus supporting the model approach.

Table 2 also shows the values of FMO energies and coefficients for both reactants. Energy values for HOMOs/LUMOs of **3a** and **24** lead us to consider that the $HOMO_{dipole} - LUMO_{dipolarophile}$ interaction was prevalent ($\Delta E = -6.77$ eV). This agrees with Sustmann's type I reactions,[19] which are referred to as HOMO−dipole-controlled cycloadditions.

Next, we tried to rationalize the difference of reactivity found in the reactions of thioisomünchnones **3a**−**c** and **20**. PM3 semiempirical calculations were used to evaluate the MO energies of simplified models **25** and **26** (Table 3). The higher value for E_{HOMO} of **25** with respect to that of **26** ($\Delta E = 0.15$ eV) does justify its higher reactivity.



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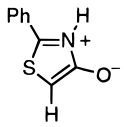


26

(a) Regiochemistry. According to FMO postulates,[20] after identifying the HOMO/LUMO pair closer in energy,

(16) Hertzog, D. L.; Nadler, W. R.; Zhang, Z. J.; Padwa, A. *Tetrahedron Lett.* **1992**, *33*, 5877−5880.
(17) Potts, K. T.; Houghton, E.; Singh, U. P. *J. Org. Chem.* **1974**, *39*, 3627−3631.
(18) Román, E.; Hodgson, D. J.; Yokomori, Y.; Eliel, E. L.; Bueno, M.; Serrano, J. A. *Carbohydr. Res.* **1988**, *180*, 263−276.
(19) (a) Sustmann, R. *Tetrahedron Lett.* **1971**, 2717−2720. (b) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 838−840.
(20) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976.

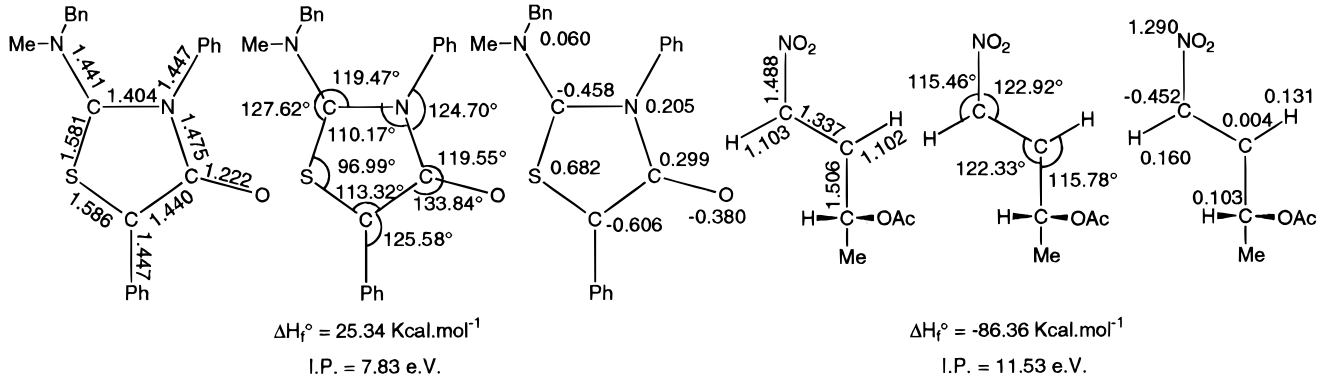


Figure 1. Molecular models of stationary structures of mesoionic compound **3a** and nitroalkene **24** describing geometrical parameters, formal charge distributions, enthalpies of formation at 298 K, and ionization potentials.

Table 2. Energy and Coefficient Values for FMOs of Compounds 3a and 24

			3a		**24**	
compd	OM	*E* (eV)	C2	C5	C1	C2
3a	HO	−7.83	−0.35	0.55		
	LU	−1.40	−0.61	−0.35		
24	HO	−11.53			0.55	0.43
	LU	−1.06			−0.50	0.67

Table 3. Energy Values for FMOs of Compounds 25 and 26

compd	E_{HOMO} (eV)	E_{LUMO} (eV)
25	−8.09	−1.09
26	−8.24	−1.49

the relative sizes of the coefficients of the atomic orbitals will predict the regioselectivity. The four approaches in which HOMO and LUMO face the coefficients with larger sizes are represented in Figure 2. In all the cases C2 and C5 carbon atoms of the 1,3-thiazolium-4-olate interact with the C1−C2 bond of the nitroalkene. This regiochemistry is in agreement with the experimental results of this 1,3-dipolar cycloaddition.

(b) Facial Diastereoselectivity. In Figure 2, the approaches a and b involve the attack of the *si*(C2)−*re*(C5) face of **3a** to *si*(C1)−*si*(C2) and *re*(C1)−*re*(C2) faces of the nitroalkene **24**, respectively. On the other hand, the approaches c and d involve the interaction of the *re*(C2)−*si*(C5) face of **3a** with *re*(C1)−*re*(C2) and *si*(C1)−*si*(C2) faces of **24**, respectively. Accordingly, Scheme 8 displays the four possible cycloadducts in which R* replaces the methyl group of **24** and denotes the chiral fragment of nitroalkenes **5** or **6**.

Opening of such cycloadducts should provide the corresponding dihydrothiophenes **31**−**34** (Scheme 9).

The experimental results with the nitroalkene **5** are consistent with cycloadducts **27** and **30** only, which would afford the 4,5-dihydrothiophenes **31** and **34**, respectively, the latter compounds having the same configuration as **15a** and **14a**. The exclusive formation of **14a** and **15a** shows that the nitroalkene **5** *reacts with complete facial diastereoselectivity*. This behavior can be ascribed to the chiral fragment (R*) which, in approaches a and d, moves away the bulkier substituent (sugar chain) from the heterocyclic ring (Scheme 10).

The same explanation is also applicable for the observed reactivity of **3a** toward D-*manno* nitroalkene **6**. The approaches depicted in Scheme 11 lead to cycloadducts **16** and **17** that afford the 4,5-dihydrothiophenes **18** and **19**, respectively. These results allow us to rule out the influence of secondary orbital or Coulombic

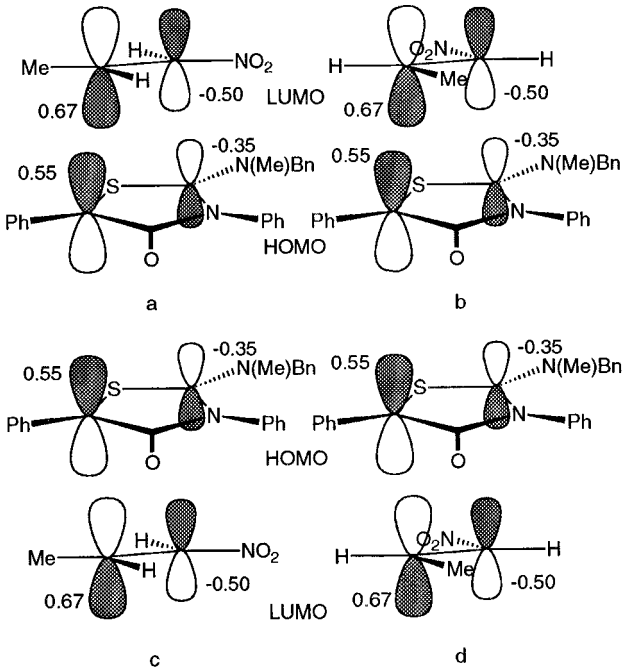
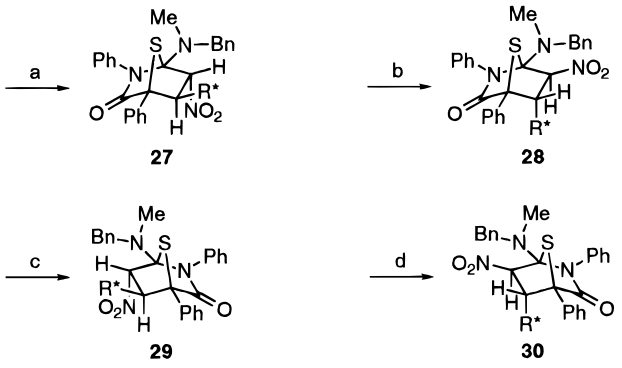


Figure 2. Schematic representation of the four possible approaches of HOMOs and LUMOs of compounds **3a** and **24**.

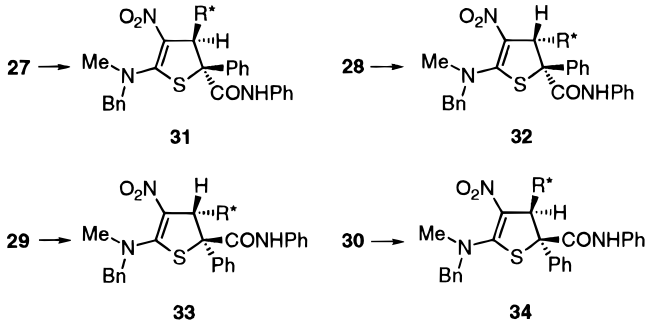
Scheme 8



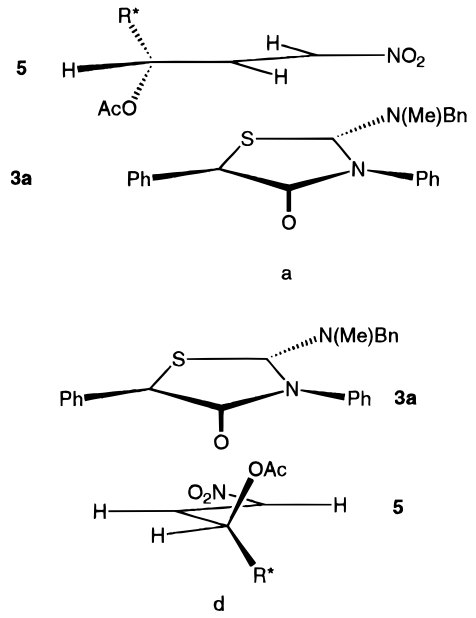
interactions on the stereochemical outcome because they should contribute at the same extent in each approach.

Opening of Cycloadducts. The particular mode of opening of the cycloadducts generated by reaction of thioisomünchones **3a**−**c** with nitroalkenes can be attributed to the presence of a dialkylamino group at the C2 atom of the mesoionic ring. Moreover, cleavage of cycloadducts to give the corresponding dihydrothiophenes proceeded rapidly with electron-withdrawing substitu-

Scheme 9



Scheme 10

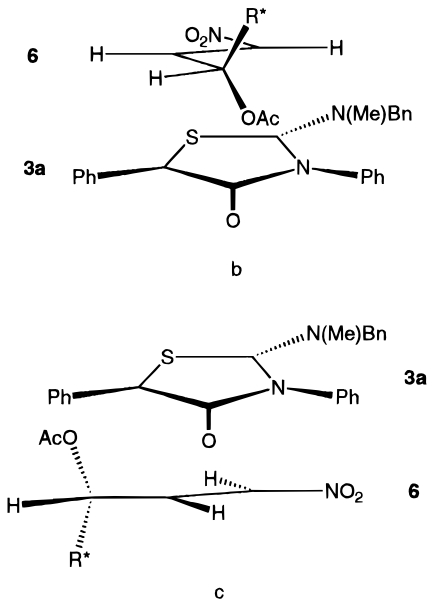


ents (4-$NO_2C_6H_4$) at the N2 atom, whereas electron-releasing groups (4-$MeOC_6H_4$) stabilize considerably such cycloadducts, which eventually can be isolated and further characterized.

At first sight, the reaction may take a dissociative pathway with the initial abstraction of the α-hydrogen to the nitro group which would provide the driving force for cycloadduct cleavage. Such a deprotonation may occur by intermolecular attack of the dialkylamino group, arising from the cycloadduct itself or the starting mesoionic system. The elimination pathway is not consistent with the E2 mechanism owing to stereoelectronic effects. Thus, cycloadducts **8**, **13**, and **17**, which do not fragment or undergo slow transformations, have the favorable arrangement between the *exo* proton (H6) and the leaving group for an *anti* elimination. However, the ease with which cycloadducts **7**, **12**, and **16** fragment into 4,5-dihydrothiophenes would be consistent with the abstraction of an *endo* proton.

It is known that the E1cB mechanism would most likely be found with substrates containing acidic protons and poor leaving groups. Among the limiting cases of this mechanism, the $(E1cB)_R$ or the $(E1cB)_{ip}$ variants for which a substantial effect on leaving groups takes place would be in agreement with our experimental results. Thus the relative rates are dependent on the substituents in the order 4-$NO_2C_6H_4$ > C_6H_5 > 4-$MeOC_6H_4$. In the $(E1cB)_R$ mechanism, the first step is a rapid and reversible proton exchange between the substrate and the base followed by the rate-determining process involving the

Scheme 11



C1−N2 heterolysis that could certainly then yield the 4,5-dihydrothiophenes. However, a sample of the stable cycloadduct **22** and Et_3N was shaken in $CDCl_3$ with D_2O, and H/D exchange was not observed. This result clearly excludes the $(E1cB)_R$ path. Furthermore, when the cycloadduct **22**, which does not fragment under the experimental reaction conditions, was treated with either Et_3N or the mesoionic compound **3b**, no cleavage of **22** was detected by NMR analysis after 24 h. The results also rule out the E2 and $(E1cB)_{ip}$ mechanisms since the addition of base does not affect reaction rates.

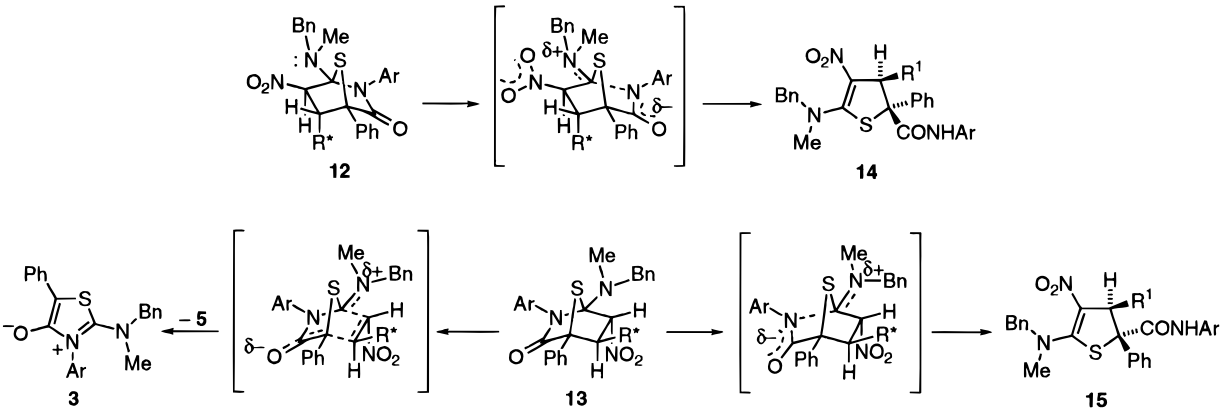
We consider that an intramolecular E1 mechanism (Scheme 12) is the most plausible pathway, which is in full agreement with the experimental observations.

Stereoelectronic effects can be invoked to explain both the opening and cycloreversion of cycloadducts since the lone pair of the methylbenzylamine nitrogen and the leaving group should be arranged in an *anti* disposition. With an *exo* nitro group, the substituents on the nitrogen atom move away, thus favoring the cleavage of the C1−N2 bond as a consequence of the preferential *anti* conformer. With an *endo* nitro group, however, both the heterolysis and the competing retrocycloaddition by C1−C6 cleavage are equally possible, which will be dependent on the nature of nucleofuges at the N2 atom. Furthermore, the *exo* nitro group should be able to stabilize electrostatically the positive charge on the methylbenzylamine nitrogen generated by cleavage of the C1−N2 bond. No such stabilization is possible for the *endo* nitro group. Consequently, one might expect that the cleavage of an *exo* nitro compound should be faster than that of an *endo* nitro compound, leading to the observed products.

Cycloadditions of mesoionics **3a**−**c** with other substrates are under way to elucidate whether these or other possibilities lie on the cleavage pathway.

Conclusions. Thioisomünchnones bearing a dialkylamino substituent at the C2 atom react more rapidly with nitroalkenes than those substituted with aryl groups to afford transient cycloadducts that convert into 4,5-dihydrothiophenes. This 1,3-dipolar cycloaddition appears to be a reversible process as shown by NMR studies at variable temperatures and trapping experiments. The utilization of chiral nitroalkenes provides an excellent

Scheme 12



procedure to obtain diastereoselectively 4,5-dihydrothiophene derivatives. The interesting facial selectivity results from the attack of the mesoionic ring to one face of the chiral nitroalkene. The reactivity, regiochemistry, and diastereoselectivity of these 1,3-thiazolium-4-olate systems are in agreement with PM3 semiempirical calculations. The mechanistic considerations described above suggest that the *N*,*N*-dialkylamino group may participate in cycloadduct opening.

Experimental Section

All mps were determined on a capillary apparatus and are uncorrected. Optical rotations were measured at 18 ± 2 °C. IR spectra were recorded in KBr pellets unless otherwise specified. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were reported in ppm (δ) using Me_4Si as internal standard. Column chromatography was carried out with silica gel Merck 60 (230−400 mesh). Analytical TLC was developed on precoated plates with silica gel Merck 60 GF_{254} of 2 mm thickness. Elemental analyses were performed by the Servicio de Microanálisis, CSIC, Barcelona. Reagents were purchased from commercial suppliers or prepared by literature methods.

Synthesis of Thioureas 1a−c. General Procedure. To a stirred solution of aryl isothiocyanate (30 mmol) in Et_2O (50 mL) at 0 °C (external ice bath) was added dropwise *N*-methylbenzylamine (4.2 mL, 32 mmol). The resulting crystalline thioureas were filtered, washed with cold Et_2O, and used without further purification. The characteristic spectral data for various thioureas are given below.

***N*-Benzyl-*N*-methyl-*N*′-phenylthiourea (1a):** yield 81%; mp 134−136 °C; ^{1}H NMR ($CDCl_3$) δ 7.37−7.20 (m, 11H), 4.99 (s, 2H), 3.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 182.0, 139.5, 135.8, 128.6, 128.2, 127.5, 127.0, 125.5, 56.7, 38.2. Anal. Calcd for $C_{15}H_{16}N_2S$: C, 70.27; H, 6.29; N, 10.93; S, 12.51. Found: C, 70.35; H, 6.30; N, 10.90; S, 12.70.

***N*-Benzyl-*N*′-(4-methoxyphenyl)-*N*-methylthiourea (1b):** yield 99%; mp 141−143 °C; ^{1}H NMR ($CDCl_3$) δ 7.35−6.80 (m, 10H), 5.04 (s, 2H), 3.74 (s, 3H), 3.14 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 182.9, 157.7, 136.2, 132.7, 128.8, 127.8, 127.7, 127.2, 57.0, 55.4, 38.4. Anal. Calcd for $C_{16}H_{18}N_2OS$: C, 67.10; H, 6.34; N, 9.78; S, 11.19. Found: C, 67.09; H, 6.45; N, 9.80; S, 11.16.

***N*-Benzyl-*N*-methyl-*N*′-(4-nitrophenyl)thiourea (1c):** yield 96%; mp 168−169 °C; ^{1}H NMR ($CDCl_3$) δ 8.17−7.26 (m, 10H), 5.09 (s, 2H), 3.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 181.7, 145.6, 143.9, 135.2, 129.3, 128.4, 127.2, 124.4, 123.1, 57.2, 39.6. Anal. Calcd for $C_{15}H_{15}N_3O_2S$: C, 59.78; H, 5.02; N, 13.94; S, 10.64. Found: C, 59.86; H, 5.16; N, 14.01; S, 10.63.

Synthesis of Thioisomüchnones 3a−c. General Preparation. To a stirred suspension of the corresponding thioureas **1a−c** (11.7 mmol) and α-bromophenylacetic acid (2.5 g, 11.7 mmol) in benzene (100 mL) was added dropwise Et_3N (1.6 mL, 11.7 mmol). After 15 h at rt, the reaction mixture was filtered and the solvent was evaporated. The residue was treated with Ac_2O (12 mL) and Et_3N (3 mL). The resulting solid was suspended in 1:1 CH_2Cl_2/Et_2O (100 mL), and the mixture was stirred with $NaHCO_3$ (2.52 g, 30 mmol) and a catalytic amount of 18-crown-6 for 24 h at rt. Addition of CH_2Cl_2 until complete dissolution, filtration, and evaporation gave oily residues that crystallized from Et_2O/hexane.

2-(*N*-Methylbenzylamino)-3,5-diphenyl-1,3-thiazolium-4-olate (3a): yield 52%, mp 147−149 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.75−6.92 (m, 15H), 4.23 (s, 2H), 2.74 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.2, 156.2, 136.6, 135.1, 133.8, 129.2, 128.9, 128.2, 127.5, 127.1, 122.2, 79.8, 57.7, 40.0. This substance is hygroscopic, and satisfactory analytical data (±0.4% for C, H, N) could not be obtained.

3-(4-Methoxyphenyl)-2-(*N*-methylbenzylamino)-5-phenyl-1,3-thiazolium-4-olate (3b): yield 48%; mp 199−201 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.74−6.94 (m, 14H), 4.28 (s, 2H), 3.80 (s, 3H), 2.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.3, 159.9, 156.5, 135.2, 134.0, 129.1, 128.6, 128.3, 127.3, 122.2, 122.1, 114.7, 79.9, 57.6, 55.5, 40.0. Anal. Calcd for $C_{24}H_{22}N_2O_2S$: C, 71.62; H, 5.51; N, 6.96; S, 7.97. Found: C, 71.59; H, 5.51; N, 7.02; S, 7.91.

2-(*N*-methylbenzylamino)-3-(4-nitrophenyl)-5-phenyl-1,3-thiazolium-4-olate (3c): yield 46%; mp 166−168 °C; ^{1}H NMR ($CDCl_3$) δ 8.17−6.91 (m, 14H), 4.12 (s, 2H), 2.64 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.4, 155.5, 147.4, 141.9, 134.8, 133.2, 129.2, 129.0, 128.4, 126.9, 124.3, 122.4, 122.2, 79.8, 58.1, 40.5. Anal. Calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07; S, 7.68. Found: C, 66.24; H, 4.52; N, 10.18; S, 7.70.

Reaction of Mesoionic Compound 3a with β-Nitrostyrene (4). To a solution of **4** (0.20 g, 1.34 mmol) in dry CH_2Cl_2 (10 mL) was added **3a** (0.5 g, 1.34 mmol). After 48 h at rt, the solvent was evaporated to give a 3:1 mixture of dihydrothiophenes **9a** and **10a** (0.65 g, 93% overall). Purification by preparative TLC (benzene−Et_2O, 10:1, three elutions) gave pure samples.

(4*R*,5*R*)- and (4*S*,5*S*)-2-(*N*-Methylbenzylamino)-3-nitro-4,5-diphenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (9a): crystals from $CHCl_3$−Et_2O; mp 248−250 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.66−6.87 (m, 21H), 5.74 (s, 1H), 4.79 (d, J = 15.3 Hz, 1H), 4.60 (d, J = 15.3 Hz, 1H), 3.13 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.5, 166.2, 141.4, 137.0, 136.3, 134.5, 129.5, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 127.9, 126.3, 125.1, 120.7, 120.3, 73.6, 61.9, 56.7, 44.0. Anal. Calcd for $C_{31}H_{27}N_3O_3S$: C, 71.38; H, 5.22; N, 8.06; S, 6.15. Found: C, 71.20; H, 5.16; N, 7.96; S, 6.15.

(4*R*,5*S*)- and (4*S*,5*R*)-2-(*N*-Methylbenzylamino)-3-nitro-4,5-diphenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (10a): crystals from $CHCl_3$−Et_2O; mp 221−223 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.74−7.05 (m, 21H), 5.92 (s, 1H), 4.92 (d, J = 15.8 Hz, 1H), 4.67 (d, J = 15.8 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.1, 161.5, 137.4, 136.9, 135.0, 133.3, 129.2, 129.0, 128.7, 128.5, 128.3, 127.9, 127.8, 127.2, 124.8, 121.7, 119.9, 70.4, 61.6, 58.4, 44.7. Anal. Calcd for $C_{31}H_{27}N_3O_3S$·$CHCl_3$: C, 59.96; H, 4.40; N, 6.55; S, 5.00. Found: C, 60.24; H, 4.58; N, 6.86; S, 4.95.

NMR Monitoring. A solution of **3a** (38 mg, 0.1 mmol) and **4** (15 mg, 0.1 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^{1}H NMR. At that temperature the formation of

(1*S*,4*R*,5*R*,6*R*)- and (1*R*,4*S*,5*S*,6*S*)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-2,4,5-triphenyl-7-thia-2-azabicyclo[2.2.1]-heptane (**7a**), and (1*R*,4*S*,5*R*,6*R*)- and (1*S*,4*R*,5*S*,6*S*)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-2,4,5-triphenyl-7-thia-2-azabicyclo[2.2.1]heptane (**8a**) was detected in 1:3 ratio: ^{1}H NMR ($CDCl_3$) (**7a**) δ 6.19 (d, J = 4.0 Hz, 1H), 4.71 (d, J = 4.0 Hz, 1H), 3.97 (m, 2H), 2.38 (s, 3H); (**8a**) δ 6.17 (d, J = 4.5 Hz, 1H), 4.87 (d, J = 4.5 Hz, 1H), 3.98 (d, 2H), 2.55 (s, 3H).

Reaction of Mesoionic Compound 3b with *β*-Nitrostyrene (4). (4*R*,5*R*)- and (4*S*,5*S*)-5-[(4-Methoxyphenyl)-carbamoyl]-2-(*N*-methylbenzylamino)-3-nitro-4,5-diphenyl-4,5-dihydrothiophene (9b). To a solution of **4** (0.24 g, 1.34 mmol) in dry CH_2Cl_2 (10 mL) was added **3b** (0.5 g, 1.34 mmol). After 48 h at rt, the solvent was evaporated to afford crystals of **9b** (0.67 g, 90%): mp 242−244 °C; ^{1}H NMR ($CDCl_3$) δ 7.72−7.71 (m, 20H), 5.84 (s, 1H), 4.77 (d, J = 15.3 Hz, 1H), 4.57 (d, J = 15.3 Hz, 1H), 3.66 (s, 3H), 3.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.9, 166.2, 156.8, 141.6, 137.3, 134.5, 129.4, 129.3, 129.0, 128.7, 128.6, 128.3, 128.2, 127.9, 126.3, 122.7, 120.5, 113.7, 73.8, 61.9, 56.4, 55.3, 43.9. Anal. Calcd for $C_{32}H_{29}N_3O_4S$: C, 69.67; H, 5.30; N, 7.62; S, 5.81. Found: C, 69.42; H, 5.29; N, 7.55; S, 5.60.

(1*R*,4*S*,5*R*,6*R*)- and (1*S*,4*R*,5*S*,6*S*)-2-(4-Methoxyphenyl)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-4,5-diphenyl-7-thia-2-azabicyclo[2.2.1]heptane (8b). To a solution of **4** (0.47 g, 2.48 mmol) in dry CH_2Cl_2 (20 mL) at −10 °C was added **3b** (1.0 g, 2.48 mmol). After 4 h at that temperature, the solvent was evaporated to dryness. Trituration with ether, filtration, and further washing with ether gave a yellow solid (0.98 g, 67%): mp 221−223 °C; ^{1}H NMR ($CDCl_3$) δ 7.40−6.82 (m, 19H), 6.15 (d, J = 4.4 Hz, 1H), 4.84 (d, J = 4.4 Hz, 1H), 4.01 (d, J = 13.01 Hz, 1H), 3.60 (d, J = 13.01 Hz, 1H), 3.74 (s, 3H), 2.53 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.6, 158.0, 136.0, 135.9, 131.7, 129.1, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 127.7, 127.4, 127.2, 122.6, 113.7, 104.5, 95.9, 68.5, 59.4, 55.3, 55.2, 37.6. Anal. Calcd for $C_{32}H_{29}N_3O_4S$: C, 69.67; H, 5.30; N, 7.62; S, 5.81. Found: C, 69.48; H, 5.41; N, 7.47; S, 5.57.

NMR Monitoring. A solution of **3b** (40 mg, 0.1 mmol) and **4** (15 mg, 0.1 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^{1}H NMR, thus evidencing the formation of **7b** and **8b** in 1:3 ratio. On warming at rt **7b** converted into **9b**, but the transformation of **8b** into **10b** could not be detected. **7b**: ^{1}H NMR ($CDCl_3$) δ 6.14 (d, J = 4.0 Hz, 1H), 4.75 (d, J = 4.0 Hz, 1H), 4.02 (m, 2H), 3.88 (s, 3H), 2.39 (s, 3H).

Thermal Transformation of 8b into 9b. A solution of cycloadduct **8b** (0.5 g, 0.9 mmol) in dry CH_2Cl_2 (5 mL) was kept at rt for 48 h. Solvent evaporation gave **9b** (0.45 g, 90%), having spectroscopic properties coincidental with those of an authentic sample.

Reaction of 8b with Methyl Propiolate. To a solution of **8b** (0.05 g, 0.09 mmol) in dry CH_2Cl_2 (5 mL) was added methyl propiolate (0.01 mL, 0.11 mmol), and the reaction mixture was kept at rt for 10 h. The solvent was evaporated to dryness, and the residue was treated with Et_2O to give crystals of **11** (0.015 g, 38%): mp 170−172 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.09 (s, 1H), 7.73−6.87 (m, 14H), 3.96 (s, 2H), 3.86 (s, 3H), 3.79 (s, 3H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.6, 163.0, 159.2, 157.7, 139.6, 136.1, 131.1, 129.8, 128.8, 128.5, 128.1, 128.0, 127.5, 127.4, 125.9, 114.4, 104.5, 58.9, 55.5, 52.0, 40.0. Anal. Calcd for $C_{28}H_{26}N_2O_4$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.87; H, 5.71; N, 6.15.

Reaction of 8b with 3c. To a solution of **8b** (0.1 g, 0.18 mmol) in dry CH_2Cl_2 (5 mL) was added mesoionic compound **3c** (75 mg, 0.18 mmol), and the reaction mixture was kept at rt for 10 h. The solvent was evaporated, and compounds **9b**, **9c**, and **10c** were separated by flash chromatography (hexane−AcOEt, 3:1) and further crystallized from $CHCl_3$−Et_2O in each case.

Reaction of Mesoionic Compound 3c with *β*-Nitrostyrene (4). To a solution of **4** (0.27 g, 1.8 mmol) in dry CH_2Cl_2 (20 mL) was added **3c** (0.75 g, 1.8 mmol). After 4 h at rt, the solvent was evaporated to afford a mixture of compounds **9c** and **10c** in 1:2 ratio (1.0 g, 98% overall) which were separated by preparative TLC (hexane−AcOEt, 1:1).

(4*R*,5*R*)- and (4*S*,5*S*)-2-(*N*-Methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-4,5-diphenyl-4,5-dihydrothiophene (9c): crystals from $CHCl_3$; mp 244−246 °C dec; ^{1}H NMR (acetone-d_6) δ 8.09−7.18 (m, 20H), 5.83 (s, 1H), 4.90 (d, J = 15.6 Hz, 1H), 4.69 (d, J = 15.6 Hz, 1H), 3.19 (s, 3H); ^{13}C NMR (acetone-d_6) δ 168.0, 165.8, 144.7, 144.4, 142.7, 138.7, 136.4, 130.1, 129.8, 129.7, 129.6, 129.0, 128.9, 128.7, 128.4, 126.9, 125.3, 121.8, 120.4, 75.1, 61.9, 56.1, 44.8. Anal. Calcd for $C_{31}H_{26}N_4O_5S$: C, 65.71; H, 4.62; N, 9.89; S, 5.66. Found: C, 65.81; H, 4.72; N, 9.73; S, 5.47.

(4*R*,5*S*)- and (4*S*,5*R*)-2-(*N*-Methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-4,5-diphenyl-4,5-dihydrothiophene (10c): crystals from $CHCl_3$; mp 238−240 °C dec; ^{1}H NMR (acetone-d_6) δ 8.23−7.03 (m, 20H), 5.83 (s, 1H), 5.04 (d, J = 15.9 Hz, 1H), 4.81 (d, J = 15.9 Hz, 1H), 3.33 (s, 3H); ^{13}C NMR (acetone-d_6) δ 171.7, 162.9, 145.8, 144.3, 138.2, 136.9, 134.4, 129.8, 129.7, 129.2, 129.0, 128.8, 128.6, 128.3, 127.8, 125.5, 122.0, 120.4, 70.8, 61.8, 59.8, 45.3. Anal. Calcd for $C_{31}H_{26}N_4O_5S$: C, 65.71; H, 4.62; N, 9.89; S, 5.66. Found: C, 65.66; H, 4.57; N, 9.78; S, 5.49.

NMR Monitoring. A solution of **3c** (42 mg, 0.1 mmol) and **4** (15 mg, 0.1 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was recorded by ^{1}H NMR. Experiments evidenced the direct transformation of starting materials into 4,5-dihydrothiophenes without detecting the bridged cycloadducts.

Reaction of Mesoionic Compound 3a with Nitroalkene 5. To a solution of **5** (1.16 g, 2.68 mmol) in dry CH_2Cl_2 (20 mL) was added **3a** (1.0 g, 2.7 mmol). After 5 h at rt, the reaction mixture was stirred with silica gel (1.0 g) for an additional period of 5 h. After filtering off, the solvent was evaporated and the residue purified by flash chromatography (hexane−AcOEt, 1:1) to give compounds **14a** and **15a**.

(4*S*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (14a): crystals from Et_2O (0.6 g, 29%); mp 184.5−186 °C; $[\alpha]_D$ −183.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.44−7.08 (m, 16H), 5.93 (d, J = 7.7 Hz, 1H), 5.35 (m, 3H), 4.90 (d, J = 7.7 Hz, 1H), 4.64 (d, J = 15.3 Hz, 1H), 4.39 (d, J = 15.3 Hz, 1H), 4.21 (dd, J = 4.7, 11.7 Hz, 1H), 3.76 (dd, J = 7.9, 11.7 Hz, 1H), 2.92 (s, 3H), 2.34 (s, 3H), 2.24 (s, 3H), 2.05 (s, 3H), 1.97 (s, 3H), 1.24 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.2, 170.2, 170.1, 169.9, 169.5, 168.1, 165.2, 140.1, 136.3, 133.7, 129.5, 128.9, 128.2, 127.7, 126.3, 125.2, 120.3, 115.9, 73.8, 70.1, 67.8, 67.4, 65.9, 62.0, 61.9, 42.3, 20.9, 20.8, 20.5, 20.4, 19.3. Anal. Calcd for $C_{40}H_{43}N_3O_{13}S$: C, 59.62; H, 5.38; N, 5.21; S, 3.98. Found: C, 59.63; H, 5.42; N, 5.21; S, 3.80.

(4*S*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (15a): crystals from Et_2O (0.6 g, 29%); mp 221−223 °C dec; $[\alpha]_D$ −220.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.80−7.06 (m, 16H), 5.19 (dd, J = 7.5, 1.0 Hz, 1H), 5.13 (m, 2H), 5.01 (d, J = 7.5 Hz, 1H), 4.69 (d, J = 15.8 Hz, 1H), 4.58 (d, J = 15.8 Hz, 1H), 4.41 (dd, J = 1.0, 10.0 Hz, 1H), 4.03 (dd, J = 5.0, 11.4 Hz, 1H), 3.70 (dd, J = 7.2, 11.4 Hz, 1H), 3.04 (s, 3H), 2.26 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.9, 170.2, 170.1, 169.8, 169.3, 168.1, 163.6, 137.2, 134.2, 131.8, 129.7, 129.0, 128.9, 128.7, 128.4, 128.2, 127.2, 124.5, 119.7, 117.4, 68.8, 67.4, 67.3, 66.6, 61.7, 61.6, 51.5, 43.6, 20.8, 20.6, 20.4. Anal. Calcd for $C_{40}H_{43}N_3O_{13}S$: C, 59.62; H, 5.38; N, 5.21; S, 3.98. Found: C, 59.56; H, 5.30; N, 5.24; S, 3.83.

NMR Monitoring. A solution of **3a** (22 mg, 0.06 mmol) and **5** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^{1}H NMR. At that temperature the formation of (1*S*,4*R*,5*S*,6*R*)- and (1*R*,4*S*,5*S*,6*R*)-5-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-2,4-diphenyl-7-thia-2-azabicyclo[2.2.1]heptane (**12a** and **13a**) in a 1:1.7 ratio was observed. The reaction mixture was allowed to warm to rt, and thus **12a** was converted into **14a** while **13a** slowly transforms into **15a**: ^{1}H NMR ($CDCl_3$) (**12a**) δ 6.44 (d, J = 3.5 Hz, 1H); (**13a**) δ 6.33 (d, J = 3.3 Hz, 1H).

Reaction of Mesoionic Compound 3b with Nitroalkene 5. To a solution of **5** (0.54 g, 1.24 mmol) in dry CH_2Cl_2 (10 mL) was added **3b** (0.5 g, 1.24 mmol), and the mixture was kept at rt for 5 h. Then, silica gel (0.5 g) was added, and the reaction mixture was stirred for 5 h. After filtration, the

solvent was evaporated, and the crude products were purified by flash chromatography (hexane−AcOEt, 1:1) to give compounds **14b** and **15b**.

(4*S*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-5-[(4-methoxyphenyl)carbamoyl]-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-4,5-dihydrothiophene (14b): precipitate from Et_2O−hexane (0.30 g, 29%); mp 126−128 °C dec; $[\alpha]_D$ −162.6° (*c* 0.38, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.34−6.77 (m, 15H), 5.87 (d, *J* = 7.9 Hz, 1H), 5.31 (m, 3H), 4.82 (d, *J* = 7.9 Hz, 1H), 4.60 (d, *J* = 15.5 Hz, 1H), 4.34 (d, *J* = 15.5 Hz, 1H), 4.16 (dd, *J* = 4.6, 11.6 Hz, 1H), 3.74 (dd, *J* = 7.9, 11.6 Hz, 1H), 3.72 (s, 3H), 2.87 (s, 3H), 2.28 (s, 3H), 2.20 (s, 3H), 2.00 (s, 3H), 1.93 (s, 3H), 1.26 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.2, 170.3, 170.1, 169.9, 169.5, 168.3, 165.0, 157.1, 140.3, 133.8, 129.5, 128.9, 128.2, 127.7, 126.3, 122.1, 116.0, 114.0, 73.7, 70.2, 67.9, 67.6, 66.0, 62.1, 62.0, 55.4, 49.9, 43.2, 20.9, 20.8, 20.6, 19.5. Anal. Calcd for $C_{41}H_{45}N_3O_{14}S$: C, 58.91; H, 5.43; N, 5.03; S, 3.84. Found: C, 58.81; H, 5.53; N, 4.89; S, 3.63.

(4*S*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-5-[(4-methoxyphenyl)carbamoyl]-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-4,5-dihydrothiophene (15b): crystals from Et_2O (0.30 g, 29%); mp 173−175 °C dec; $[\alpha]_D$ −200.4° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.80−6.76 (m, 15H), 5.19 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.12 (m, 2H), 5.01 (d, *J* = 7.5 Hz, 1H), 4.69 (d, *J* = 15.8 Hz, 1H), 4.58 (d, *J* = 15.8 Hz, 1H), 4.41 (dd, *J* = 1.5, 10.0 Hz, 1H), 4.03 (dd, *J* = 5.1, 11.4 Hz, 1H), 3.70 (dd, *J* = 7.2, 11.4 Hz, 1H), 3.76 (s, 3H), 3.04 (s, 3H), 2.26 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.9, 170.2, 170.1, 169.8, 169.3, 168.0, 163.9, 156.5, 134.2, 132.0, 130.3, 129.6, 129.0, 128.8, 128.4, 128.2, 128.1, 121.5, 117.3, 113.8, 68.8, 68.7, 67.5, 67.1, 66.6, 61.7, 61.6, 55.3, 51.5, 43.7, 20.8, 20.6, 20.4. Anal. Calcd for $C_{41}H_{45}N_3O_{14}S$: C, 58.91; H, 5.43; N, 5.03; S, 3.84. Found: C, 59.07; H, 5.60; N, 4.78; S, 3.47.

(1*R*,4*S*,5*S*,6*R*)-5-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-2-(4-methoxyphenyl)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-4-phenyl-7-thia-2-azabicyclo[2.2.1]-heptane (13b). To a solution of **5** (0.32 g, 0.74 mmol) at −10 °C was added **3b** (0.30 g, 0.74 mmol). After 5 h at that temperature, the solvent was evaporated below 25 °C and the resulting residue was dissolved in Et_2O, from which crystals of the title compound were obtained (0.25 g, 40%): mp 153−155 °C (Et_2O−hexane); $[\alpha]_D$ +49.4° (*c* 0.35, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.56−6.80 (m, 14H), 6.29 (d, *J* = 3.4 Hz, 1H), 5.24 (d, *J* = 2.1 Hz, 1H), 5.08 (dd, *J* = 2.1, 9.5 Hz, 1H), 5.00 (m, 2H), 4.15 (dd, *J* = 4.8, 11.8 Hz, 1H), 3.88 (d, *J* = 12.7 Hz, 1H), 3.66 (dd, *J* = 7.2, 11.8 Hz, 1H), 3.47 (d, *J* = 12.7 Hz, 1H), 3.74 (m, 4H), 3.49 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 1.98 (s, 3H), 1.99 (s, 3H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.5, 170.4, 169.7, 169.5, 168.8, 158.0, 135.7, 131.0, 129.5, 129.2, 129.0, 128.6, 128.4, 128.3, 127.7, 127.6, 127.3, 127.1, 105.3, 88.6, 71.1, 67.9, 67.5, 67.2, 66.5, 62.1, 59.5, 55.3, 51.2, 37.3, 21.0, 20.7, 20.5, 20.3, 20.2. Anal. Calcd for $C_{41}H_{45}N_3O_{14}S$: C, 58.91; H, 5.43; N, 5.03; S, 3.84. Found: C, 58.57; H, 5.24; N, 4.78; S, 3.62.

NMR Monitoring. A solution of **3b** (23 mg, 0.06 mol) and **5** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) was monitored by ^1H NMR at different temperatures. At 0 °C the formation of cycloadducts **12b** and **13b** in 1:1.7 ratio was observed. When the reaction was allowed to warm to rt, compound **12b** converted into **14b** whereas **13b** slowly converts into **15b**. **12b**: ^1H NMR ($CDCl_3$) δ 6.40 (d, *J* = 3.6 Hz, 1H).

Transformation of 13b into 15b Catalyzed by Silica Gel. A solution of **13b** (40 mg, 0.05 mmol) in dry CH_2Cl_2 (5 mL) was stirred with silica gel (40 mg) for 24 h. After this period, silica gel was filtered off and washed several times with MeOH. The resulting solution was evaporated to give pure **15b** (40 mg, 100%).

Thermal Transformation of 13b into 14b and 15b. A solution of **13b** (40 mg, 0.05 mmol) in $CDCl_3$ (0.5 mL) was kept at rt and recorded periodically by ^1H NMR. After 30 days, the conversion was complete and compounds **14b** and **15b** were observed in 1:1.4 ratio.

Reaction of Mesoionic Compound 3c with Nitroalkene 5. To a solution of **5** (1.04 g, 2.4 mmol) in dry CH_2Cl_2 (20 mL) was added **3c** (1.0 g, 2.4 mmol). After 4 h at rt, the reaction mixture was evaporated and the residue was several times treated with Et_2O. Compounds **14c** and **15c** were separated by flash chromatography (hexane−AcOEt, 1:1).

(4*S*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-5-phenyl-4,5-dihydrothiophene (14c): precipitate from Et_2O−hexane (0.2 g, 10%); mp 148−150 °C; $[\alpha]_D$ −155° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.21−7.18 (m, 15H), 5.87 (dd, *J* = 7.7, 1.2 Hz, 1H), 5.36 (m, 2H), 5.17 (dd, *J* = 1.2, 9.5 Hz, 1H), 4.89 (d, *J* = 7.7 Hz, 1H), 4.64 (d, *J* = 15.4 Hz, 1H), 4.41 (d, *J* = 15.4 Hz, 1H), 4.20 (dd, *J* = 4.6, 11.7 Hz, 1H), 3.73 (dd, *J* = 8.1, 11.7 Hz, 1H), 2.95 (s, 3H), 2.34 (s, 3H), 2.21 (s, 3H), 2.06 (s, 3H), 1.98 (s, 3H), 1.37 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.2, 170.1, 169.6, 169.4, 167.6, 165.9, 144.0, 142.1, 139.4, 133.5, 129.6, 129.1, 128.8, 128.2, 127.5, 126.2, 124.7, 119.7, 115.5, 73.4, 70.0, 67.8, 67.6, 65.9, 61.9, 61.8, 49.7, 43.3, 20.8, 20.6, 20.4, 20.3, 19.6. Anal. Calcd for $C_{40}H_{42}N_4O_{15}S$: C, 56.47; H, 4.98; N, 6.58; S, 3.77. Found: C, 56.50; H, 4.93; N, 6.44; S, 3.65.

(4*S*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-5-phenyl-4,5-dihydrothiophene (15c): recrystallized from AcOEt−Et_2O (1.26 g, 62%); mp 140−142 °C dec; $[\alpha]_D$ −217° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.14−7.22 (m, 15H), 5.16 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.13 (m, 2H), 4.99 (d, *J* = 7.6 Hz, 1H), 4.69 (d, *J* = 16.0 Hz, 1H), 4.59 (d, *J* = 16.0 Hz, 1H), 4.37 (dd, *J* = 1.2, 10.0 Hz, 1H), 4.03 (dd, *J* = 5.2, 11.6 Hz, 1H), 3.69 (dd, *J* = 7.7, 11.6 Hz, 1H), 3.06 (s, 3H), 2.26 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.0, 170.2, 170.0, 169.8, 169.2, 168.9, 163.9, 143.4, 134.0, 131.2, 130.0, 129.0, 128.4, 128.2, 127.1, 124.6, 119.2, 117.2, 68.8, 68.5, 67.3, 67.2, 66.3, 61.7, 51.4, 43.6, 20.8, 20.7, 20.6, 20.5, 20.4. Anal. Calcd for $C_{40}H_{42}N_4O_{15}S$: C, 56.47; H, 4.98; N, 6.58; S, 3.77. Found: C, 56.14; H, 4.89; N, 6.37; S, 3.57.

NMR Monitoring. A solution of **3c** (24 mg, 0.06 mmol) and **5** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^1H NMR. Initially, the transient cycloadducts were detected as broad signals, but they rapidly evolved to give the 4,5-dihydrothiophenes **14c** and **15c**.

Reaction of Mesoionic Compound 3a with Nitroalkene 6. To a solution of **6** (1.20 g, 2.70 mmol) in dry CH_2Cl_2 (20 mL) was added **3a** (1.0 g, 2.68 mmol), and the reaction mixture was kept at rt for 5 h. Then silica gel (1.0 g) was added, and the stirring was continued for another 5 h. After filtering the solvent was evaporated and compounds **18a** and **19a** were separated by flash chromatography (hexane−AcOEt, 3:2).

(4*R*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (18a): crystals from Et_2O (0.50 g, 23%); mp 107−109 °C; $[\alpha]_D$ +152.2° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.67−7.03 (m, 16H), 5.85 (m, 2H), 5.63 (dd, *J* = 2.0, 5.5 Hz, 1H), 5.21 (s, 1H), 5.03 (m, 1H), 4.72 (d, *J* = 15.3 Hz, 1H), 4.58 (d, *J* = 15.3 Hz, 1H), 4.20 (dd, *J* = 3.4, 12.2 Hz, 1H), 4.05 (dd, *J* = 6.2, 12.2 Hz, 1H), 3.06 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 1.97 (s, 3H), 1.86 (s, 3H), 1.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.9, 170.3, 170.2, 169.6, 169.5, 169.4, 165.8, 140.3, 136.6, 134.0, 129.3, 128.9, 128.8, 128.7, 128.4, 127.6, 125.9, 124.9, 120.1, 114.2, 73.2, 70.9, 69.6, 69.0, 62.1, 60.9, 50.0, 43.0, 21.0, 20.7, 20.4, 20.3. Anal. Calcd for $C_{40}H_{43}N_3O_{13}S$: C, 59.62; H, 5.38; H, 5.21; S, 3.98. Found: C, 59.55; H, 5.48; N, 5.00; S, 3.73.

(4*R*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophene (19a): crystals from Et_2O (0.61 g, 29%); mp 185−187 °C dec; $[\alpha]_D$ +132.8° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.90−7.03 (m, 16H), 5.47 (dd, *J* = 7.0, 2.0 Hz, 1H), 5.38 (dd, *J* = 2.0. 8.0 Hz, 1), 5.30 (d, *J* = 2.5 Hz, 1H), 5.07 (dd, *J* = 2.5, 7.0 Hz, 1H), 4.93 (m, 1H), 4.79 (d, *J* = 15.9 Hz, 1H), 4.68 (d, *J* = 15.9 Hz, 1H), 4.18 (dd, *J* = 3.1, 12.8 Hz, 1H), 3.98 (dd, *J* = 5.0, 12.8 Hz, 1H), 3.18 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H), 1.94 (s, 3H), 1.90 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.5, 170.0, 169.5, 169.3, 168.9, 168.3, 163.6, 137.0, 134.3, 132.7, 129.2, 129.0, 128.9, 128.7,

128.3, 127.9, 126.9, 124.7, 119.9, 116.4, 70.3, 69.5, 68.7, 67.7, 61.7, 61.5, 52.8, 44.2, 20.8, 20.6, 20.5, 20.4. Anal. Calcd for $C_{40}H_{43}N_3O_{13}S$: C, 59.62; H, 5.38; N, 5.21; S, 3.98. Found: C, 59.68; H, 5.23; N, 5.21; S, 3.84.

NMR Monitoring. A solution of **3a** (21 mg, 0.06 mmol) and **6** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was recorded by ^{1}H NMR. At that temperature the formation of (1*R*,4*S*,5*R*,6*S*)- and (1*S*,4*R*,5*R*,6*S*)-5-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-2,4-diphenyl-7-thia-2-azabicyclo[2.2.1]heptane (**16a** and **17a**) in 1:1.2 ratio was observed. When the reaction mixture was allowed to warm to rt, the cycloadduct **16a** converted into **18a** while **17a** slowly transforms into **19a**: ^{1}H NMR ($CDCl_3$) (**16a**) δ 6.11 (d, J = 3.8 Hz, 1H); (**17a**) δ 6.27 (d, J = 3.3 Hz, 1H).

Reaction of Mesoionic Compound 3b with Nitroalkene 6. To a solution of **6** (1.08 g, 2.48 mmol) in dry CH_2Cl_2 (20 mL) was added **3b** (1.0 g, 2.48 mol), and the reaction mixture was kept at rt for 5 h. Then silica gel (1.0 g) was added, and the stirring was continued for other 5 h. After filtering, the solvent was evaporated and compounds **18b** and **19b** separated by flash chromatography (hexane−AcOEt, 1:1).

(4*R*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-5-[(4-methoxyphenyl)carbamoyl]-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-4,5-dihydrothiophene (18b): crystals from Et_2O (0.41 g, 20%); mp 105−107 °C; $[\alpha]_D$ +152.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.59−6.79 (m, 15H), 5.86 (m, 2H), 5.67 (dd, J = 4.7, 2.0 Hz, 1H), 5.18 (s, 1H), 5.07 (m, 1H), 4.72 (d, J = 15.5 Hz, 1H), 4.57 (d, J = 15.5 Hz, 1H), 4.22 (dd, J = 3.6, 12.3 Hz, 1H), 4.10 (dd, J = 6.3, 12.3 Hz, 1H), 3.74 (s, 3H), 3.07 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H), 1.90 (s, 3H), 1.80 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.0, 170.3, 169.6, 169.4, 165.7, 156.8, 140.5, 134.0, 129.6, 129.4, 129.0, 128.7, 128.4, 127.6, 125.9, 122.1, 114.3, 113.9, 73.1, 71.0, 69.7, 69.0, 62.2, 61.0, 55.3, 50.2, 43.0, 21.0, 20.8, 20.6, 20.5, 20.3. Anal. Calcd for $C_{41}H_{45}N_3O_{14}S$: C, 58.91; H, 5.43; N, 5.03; S, 3.84. Found: C, 59.03; H, 5.60; N, 4.94; S, 3.62.

(4*R*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-5-[(4-methoxyphenyl)carbamoyl]-2-(*N*-methylbenzylamino)-3-nitro-5-phenyl-4,5-dihydrothiophene (19b): crystals from Et_2O (0.84 g, 41%); mp 191−193 °C; $[\alpha]_D$ +127.8° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.93−6.74 (m, 15H), 5.47 (dd, J = 6.9, 1.9 Hz, 1H), 5.37 (dd, J = 1.9, 7.8 Hz, 1H), 5.29 (d, J = 2.4 Hz, 1H), 5.07 (dd, J = 2.4, 6.9 Hz, 1H), 4.94 (m, 1H), 4.77 (d, J = 16.0 Hz, 1H), 4.68 (d, J = 16.0 Hz, 1H), 4.17 (dd, J = 2.8, 12.6 Hz, 1H), 3.99 (dd, J = 5.3, 12.6 Hz, 1H), 3.70 (s, 3H), 3.18 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H), 1.90 (s, 3H), 1.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.3, 169.9, 169.4, 169.2, 168.8, 168.3, 163.8, 156.6, 134.3, 132.9, 130.1, 129.0, 128.9, 128.8, 128.2, 127.9, 126.9, 121.8, 113.7, 116.4, 69.4, 70.3, 68.7, 68.7, 67.7, 61.6, 61.5, 52.8, 55.2, 44.2, 20.7, 20.7, 20.5, 20.4. Anal. Calcd for $C_{41}H_{45}N_3O_{14}S$: C, 58.91; H, 5.43; N, 5.03; S, 3.84. Found: C, 58.73; H, 5.40; N, 4.96; S, 3.68.

NMR Monitoring. A solution of **3b** (23 mg, 0.06 mmol) and **6** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^{1}H NMR. At that temperature the formation of (1*R*,4*S*,5*R*,6*S*)- and (1*S*,4*R*,5*R*,6*S*)-5-(1′,2′,3′,4′,5′-penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-2-(4-methoxyphenyl)-1-(*N*-methylbenzylamino)-6-nitro-3-oxo-4-phenyl-7-thia-2-azabicyclo[2.2.1]-heptane (**16b** and **17b**) in 1:1.3 ratio was observed. When the reaction mixture was allowed to warm to rt, the cycloadduct **16b** converted into **18b** while **17b** slowly transforms into **19b**: ^{1}H NMR ($CDCl_3$) (**16b**) δ 6.05 (d, J = 3.8 Hz, 1H); (**17b**) δ 6.25 (d, J = 3.3 Hz, 1H).

Reaction of Mesoionic Compound 3c with Nitroalkene 6. To a solution of **6** (1.04 g, 2.4 mmol) in dry CH_2Cl_2 (20 mL) was added **3c** (1.0 g, 2.4 mmol) and the reaction mixture was kept at rt for 5 h. The solvent was evaporated, and compounds **18c** and **19c** were separated by flash chromatography (hexane−AcOEt, 11:2).

(4*R*,5*S*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-5-phenyl-4,5-dihydrothiophene (18c): precipitated from Et_2O−hexane (0.3 g, 14%); mp 115−117 °C dec; $[\alpha]_D$ +179.8° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.23−7.24 (m, 15H), 5.83 (m, 2H), 5.61 (dd, J = 3.2, 5.1 Hz, 1H), 5.25 (d, J = 1.3 Hz, 1H), 5.04 (m, 1H), 4.75 (d, J = 15.4 Hz, 1H), 4.61 (d, J = 15.4 Hz, 1H), 4.24 (dd, J = 3.6, 12.3 Hz, 1H), 4.09 (dd, J = 6.1, 12.3 Hz, 1H), 3.13 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.1, 170.5, 170.3, 169.6, 169.5, 169.3, 166.5, 143.9, 142.6, 139.6, 133.8, 129.6, 129.0, 128.5, 127.5, 125.8, 124.7, 119.7, 113.9, 73.4, 71.3, 71.0, 69.7, 69.0, 62.2, 60.0, 50.0, 43.3, 21.0, 20.8, 20.6. 20.4, 20.3. Anal. Calcd for $C_{40}H_{42}N_4O_{15}S$: C, 56.47; H, 4.98; N, 6.58; S, 3.77. Found: C, 55.87; H, 5.09; N, 6.24; S, 3.21.

(4*R*,5*R*)-4-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-2-(*N*-methylbenzylamino)-3-nitro-5-[(4-nitrophenyl)carbamoyl]-5-phenyl-4,5-dihydrothiophene (19c): crystals from Et_2O (0.8 g, 40%); mp 140−142 °C dec; $[\alpha]_D$ +155.6° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.13−7.25 (m, 15H), 5.42 (m, 2H), 5.26 (d, J = 2.6 Hz, 1H), 5.04 (dd, J = 2.6, 6.2 Hz, 1H), 4.95 (m, 1H), 4.80 (d, J = 16.1 Hz, 1H), 4.70 (d, J = 16.1 Hz, 1H), 4.17 (dd, J = 2.8, 12.4 Hz, 1H), 4.01 (dd, J = 5.4, 12.4 Hz, 1H), 3.23 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.01 (s, 3H), 1.98 (s, 3H), 1.93 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.0, 169.5, 169.3, 169.1, 168.9, 163.9, 143.6, 143.1, 134.2, 132.0, 129.5, 129.2, 129.0, 128.3, 127.8, 127.0, 124.6, 119.4, 116.2, 70.3, 69.4, 68.8, 67.8, 61.8, 61.5, 52.7, 44.4, 20.8, 20.5. Anal. Calcd for $C_{40}H_{42}N_4O_{15}S$: C, 56.47; H, 4.98; N, 6.58; S, 3.77. Found: C, 56.40; H, 5.09; N, 6.41; S, 3.61.

NMR Monitoring. A solution of **3c** (24 mg, 0.06 mmol) and **6** (25 mg, 0.06 mmol) in $CDCl_3$ (0.5 mL) at 0 °C was monitored by ^{1}H NMR. The intermediate cycloadducts were detected as broad signals that rapidly converted into 4,5-dihydrothiophenes **18c** and **19c**.

Reaction of Mesoionic Compound 20 with *β*-Nitrostyrene (4). (4*R*,5*S*)- and (4*S*,5*R*)-3-Nitro-2,4,5-triphenyl-5-(phenylcarbamoyl)-4,5-dihydrothiophenes (21). To a solution of **4** (0.22 g, 1.5 mmol) in dry toluene (25 mL) was added **20** (0.65 g, 2 mmol), and the resulting suspension was refluxed with stirring for 6 days. The solvent was evaporated until a final volume of 10 mL, crystallizing the title compound as yellow needles (0.3 g, 43%): mp 244−246 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.71 (s, 1H), 7.58−7.07 (m, 20H), 6.06 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 169.6, 150.8, 140.1, 137.4, 134.8, 133.4, 130.7, 130.4, 129.1, 128.6, 128.5, 128.3, 128.0, 127.8, 125.0, 120.0, 71.4, 59.1. Anal. Calcd for $C_{29}H_{22}N_2O_3S$: C, 72.78; H, 4.63; N, 5.85. Found: C, 72.45; H, 4.89; N, 5.63.

Reaction of Mesoionic Compound 20 with Nitroalkene (5). (1*R*,4*R*,5*S*,6*R*)-5-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-6-nitro-3-oxo-1,2,4-triphenyl-7-thia-2-azabicyclo[2.2.1]heptane (22). To a solution of **5** (0.65 g, 1.5 mmol) in dry toluene (25 mL) was added **20** (0.65 g, 2 mmol), and the resulting suspension was refluxed with stirring for 48 h. The solvent was evaporated and the residue chromatographed (hexane−AcOEt, 4:1) to give an oil that was precipitated from Et_2O−hexane (0.5 g, 44%): mp 90−92 °C; $[\alpha]_D$ +67.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (acetone-d_6) δ 7.94−7.06 (m, 15H), 6.68 (d, J = 3.8 Hz, 1H), 5.47 (dd, J = 2.8, 5.9 Hz, 1H), 5.26 (m, 2H), 5.10 (dd, J = 5.9, 8.6 Hz, 1H), 4.15 (dd, J = 4.6, 11.8 Hz, 1H), 3.92 (t, J = 2.8 Hz, 1H), 3.83 (dd, J = 6.9, 11.8 Hz, 1H), 2.07 (s, 3H), 1.97 (s, 3H), 1.96 (s, 3H), 1.92 (s, 3H), 1.86 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.0, 170.3, 170.2, 169.9, 169.4, 169.3, 135.0, 131.1, 130.2, 129.4, 129.2, 129.1, 128.9, 128.7, 128.5, 128.4, 128.2, 91.4, 83.1, 69.9, 68.2, 67.9, 67.1, 64.8, 61.8, 60.2, 20.6, 20.5, 20.3, 20.2. Anal. Calcd for $C_{38}H_{38}N_2O_{13}S$: C, 59.84; H, 5.02; N, 3.67; S, 4.20. Found: C, 60.20; H, 4.96; N, 3.55; S, 3.82.

Reaction of Mesoionic Compound 20 with Nitroalkene (6). (1*R*,4*R*,5*S*,6*R*)-5-(1′,2′,3′,4′,5′-Penta-*O*-acetyl-D-*manno*-pentitol-1-yl)-6-nitro-3-oxo-1,2,4-triphenyl-7-thia-2-azabicyclo[2.2.1]heptane (23). To a solution of **6** (0.65 g, 1.5 mmol) in dry toluene (25 mL) was added **20** (0.65 g, 2 mmol), and the resulting suspension was refluxed with stirring for 24 h. The solvent was evaporated and the residue chromatographed (hexane−AcOEt, 4:1) to give an oil that crystallized from Et_2O (0.68 g, 60%): mp 184−185 °C; $[\alpha]_D$ −20° (*c* 0.5, $CHCl_3$); ^{1}H NMR (acetone-d_6) δ 8.07−7.13 (m, 15H), 6.58 (d, J = 3.8 Hz, 1H), 5.43 (t, J = 4.0 Hz, 1H), 5.39 (dd, J = 1.5, 4.0 Hz, 1), 5.12 (dd, J = 4.1, 6.9 Hz, 1H), 4.80 (m,

1H), 4.23 (dd, J = 3.8, 1.5 Hz, 1H), 4.13 (dd, J = 3.2, 12.3 Hz, 1H), 3.99 (dd, J = 5.9, 12.3 Hz, 1H), 2.14 (s, 3H), 2.01 (s, 3H), 1.97 (s, 3H), 1.95 (s, 3H), 1.9 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.0, 170.4, 170.0, 169.7, 169.4, 169.3, 135.2, 131.1, 130.3, 129.3, 129.0, 128.6, 128.3, 128.2, 91.7, 84.2, 70.9, 68.8, 68.4, 67.9, 64.7, 61.2, 57.0, 20.7, 20.6, 20.5. Anal. Calcd for $C_{38}H_{38}N_2O_{13}S$: C, 59.84; H, 5.02; N, 3.67; S, 4.20. Found: C, 59.86; H, 4.98; N, 3.57; S, 4.15.

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Supporting Information Available: NMR spectra of compounds **3a**, **10a**, **10c**, **14b**, **14c**, **18c**, and **21** and ORTEP drawings and X-ray experimental data for **10a** and **23** (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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