Phthalimidesulfenyl Chloride. 9.[1] A Simple Access to α,α′-Dioxothiones, a New Class of Bis-heterodienes. Synthesis of 1,4-Oxathiin Systems†

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α,α′-Dioxothiophthalimides **4a** and **4b** react with pyridine to generate the α,α′-dioxothiones **5a** and **5b** which undergo chemo- and regiospecific inverse electron demand Diels–Alder reactions with electron-rich alkenes to give 1,4-oxathiin heterocyclic systems. Enol ethers, silyl enol ethers, vinyl sulfides, vinyl amides, substituted styrenes, and electron rich alkynes and allenes can be fruitfully employed as dienophiles. Among the vinyl ethers tested tri-*O*-benzylglucal was successfully used as a dienophile. Ab initio molecular orbital calculations performed on thiones **5a** and **5b** as well as on a selected enol ether are consistent with the experimental results. When thione **5a** was generated in the presence of 2,3-dimethyl-2-butene (**31**) and -(β)-pinene (**33**) a selective "thiophlic ene reaction" was observed leading to the formation of sulfides **32** and **34**. Thione **5b** reacted similarly with **33** to generate the sulfide **35**. Additionally a competition between the dienic versus dienophilic behavior of α,α′-dioxothiones **5a** and **5b** was observed in reactions with 2,3-dimethoxy-1,3-butadiene (**45**) and 2-methoxyfuran (**50**). A preliminary screening of the reactivity of 1,4-oxathiins **7c** and **8b**, used as model substrates, is also outlined.

Introduction

Diverse groups of heterodienes have been described as participants in direct or inverse electron demand Diels–Alder reactions.[2-4] Many examples report the formation of a carbon–carbon bond and a carbon–heteroatom bond or two carbon–heteroatom bonds as key steps for the synthesis of various biologically active compounds.[5] Although α,β-unsaturated thiocarbonyl compounds have found several applications as effective dienes[2,3,6] relatively few examples of bis-heterodienic sulfur substituted species have been reported as useful in Diels–Alder reactions. Among these systems dithiooxalates,[7] α-oxosulfines,[8] and α-oxolsulfenes[9] are noteworthy. However, the chemistry of these species is often characterized by their carbon–sulfur double bond dienophilic or enic reactivity rather than by their dienic behavior.

Several methods for the preparation of α-oxothiones have been published,[10-12] but to the best of our knowledge no example of simple α-oxothiones acting as bis-heterodienes was described before our preliminary report.[13] In this paper we describe our study on the trapping and reactivity of α,α′-dioxothiones **5a,b** with particular emphasis of their use as dienes in the Diels–Alder reaction.

The key starting materials for our effort arose from our recently developed new and general method for simple preparation of precursors of α,α′-dioxothiones. The method exploits the reaction of phthalimidesulfenyl chloride **1**, with easily enolizable carbonyl compounds or with their corresponding silyl enol ethers which produces α-oxothiophthalimides in good to excellent yield.[14]

The phthalimides are precursors of α-oxothiones since the high acidity of the proton linked to the thio-substituted carbon allows easy deprotonation followed by phthalimide anion elimination with formation of the carbon–sulfur double bond. The use of phthalimde

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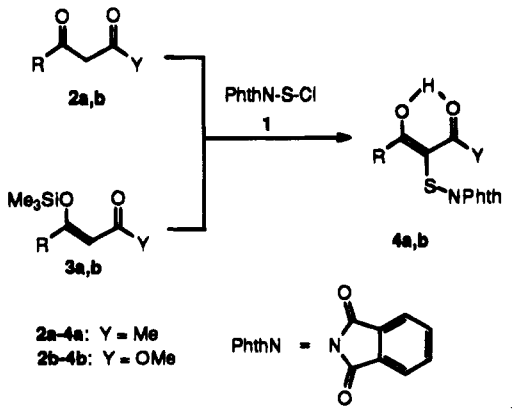
Scheme 1



precursors for the generation of thiones,[11,15] selenones,[16] as well as thionitroso species[17] via base-catalyzed 1,2 elimination is well documented. Our use of carbonyl compounds and sulfenyl chloride **1** as precursors of oxothiones increases the generality of the method and makes available α,α′-dioxothiones, a rarely reported class of difunctionalyzed thiocarbonyl compounds.[11,12]

Results and Discussion

Synthesis of Thione Precursors. Preparation of α,α′-dioxothiophthalimides **4a,b** can be simply accomplished as previously reported[14] by addition of phthalimidesulfenyl chloride to an excess (usually 10 equiv) of acetylacetone (**2a**) or methyl acetoacetate (**2b**) in dichloromethane at room temperature. Alternatively, compounds **4a,b** have been prepared by reaction of silyl derivatives **3a,b** with 1 equiv of **1** in dichloromethane at −18 °C (Scheme 1).

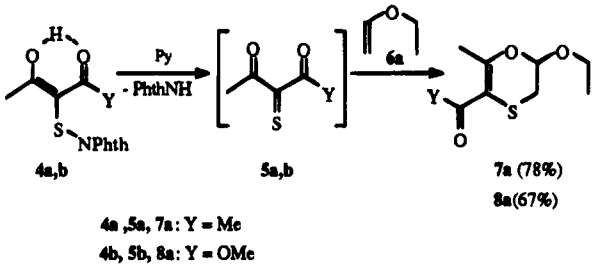
The sulfenamides were purified by recrystallization from chloroform/*n*-hexane and kept at room temperature for periods of more than 1 year without any appreciable decomposition. β-Dicarbonyl derivatives **4a,b**, in $CDCl_3$ solution at 23 °C, are present only in their enolic form as revealed by ^1H NMR spectra which show signals at 17.75 ppm and 13.90 ppm for the enolic proton of **4a** and **4b**, respectively.

Generation and Trapping of Thiones. In our earlier work, treatment of compounds **4a,b** in chloroform at room temperature with an excess of pyridine (3 equiv) had led to the trapping of the transient corresponding thiones **5a,b** with electron-rich dienes.[14] In order to be trapped as electron-deficient or inverse-electron-demand dienes, **5a** and **5b** were now generated in the presence of electron rich alkenes.

Thus, generation of **5a,b** in the presence of 2 equiv of ethyl vinyl ether **6a** afforded compounds **7a** and **8a**, respectively. The formation of the 1,4-oxathiin ring system is rationalized via the cycloaddition of thiones **5a** and **5b** acting as dienes with the dienophile **6a** (Scheme 2).

The formation of cycloadducts **7a** and **8a** as single compounds indicates that the reaction is regiospecific;

Scheme 2



moreover, the formation of **8a** indicates also that the reaction is chemospecific as well for thioketone **5b** since the ketone carbonyl is the exclusive participant to the cycloaddition.

The structures of compounds **7a** and **8a** are supported by their spectroscopic data. ^1H NMR shows for **7a** an ABX system at 5.26 and 2.97−2.77 ppm (J_{AB} = 13.0 Hz), an ABX_3 system at 4.02−3.85, 3.77−3.61, and 1.26 (t, 3H, $J_{AX} = J_{BX}$ = 7.1 Hz), and two isolated A_3 systems at 2.30 and 2.28 ppm as expected for the 1,4-oxathiin system. Moreover, the more diagnostic ^{13}C NMR signals reveal the presence of a ketonic carbonyl carbon at 195.6 ppm and two other quaternary carbons at 158.0 and 105.4 ppm typical of a vinylic group substituted with a conjugated carbonyl and an ether oxygen. The IR spectrum of compound **7a** clearly shows the stretching of an α,β-unsaturated ketonic group at 1673 cm^{-1} and a carbon−carbon double bond stretching (very strong) at 1562 cm^{-1} as expected for an oxygen-substituted and conjugated vinylic residue.

Spectroscopic data of compound **8a** are also in agreement with a 1,4-oxathhiine ring system (see the Experimental Section); moreover, the presence of a signal at 165.5 ppm in the ^{13}C NMR spectrum and a stretching at 1712 cm^{-1} in the IR spectrum indicates that the ester functionality is unchanged in the cycloadduct, thus confirming that only the ketonic group participated in the reaction.

In parallel with experiments, quantum mechanic calculations were carried out. In particular, oxothiones **5a,b** and ethyl vinyl ether were minimized with a geometry optimization ab initio calculation using a 3-21G* basis set implemented via a Spartan program running on a IBM-Risk 6000 workstation. Features of interest revealed by the calculations include the conformational energy minima for thiones **5a,b**. In the case of **5a** the low energetic conformer appears to have the two carbonyl groups oriented with dihedral angles of about 100° with the thiocarbonyl group (Figure 1, A) which is not a favorable conformation for a reactive Diels−Alder diene. Perturbing the molecule so that with one of the O−C−C−S dihedral angles becames 0° creates another minimum only about 1.6 kcal mol^{-1} less stable than A (Figure 1, B). Thus, a reactive geometry for cycloadditions can be easily reached at room temperature. For thione **5b** the more stable conformer shows the ketone carbonyl and thiocarbonyl having a dihedral angle of 160°, an almost "transoid" conformation, while the ester carbonyl and the carbon sulfur double bond have a dihedral angle of 55.3°. Forcing the ketone carbonyl and the thione groups into a "cisoid" conformation produces (Figure 1, B′), a conformer that is about 2.37 kcal mol^{-1} less stable than A′ (Figure 1).

Experiments carried out on thiophthalimide **4c**, prepared by reacting **1** with dimedone (**2c**), showed that the

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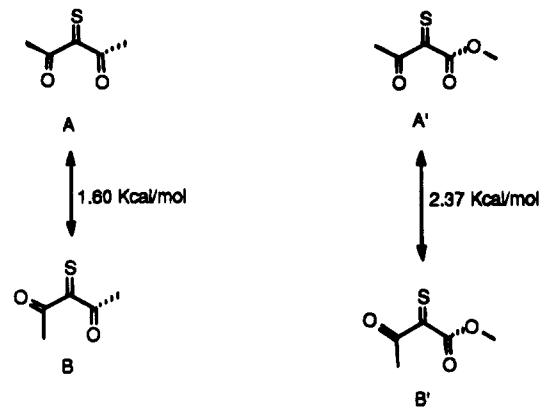


Figure 1. Ab initio calculated absolute minimum and reactive conformer of **5a** and **5b**.

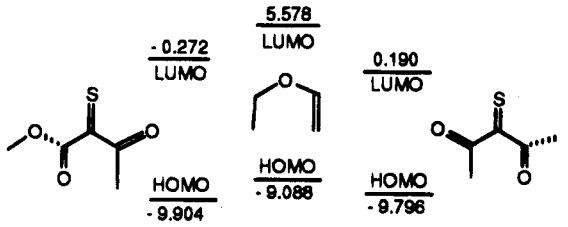
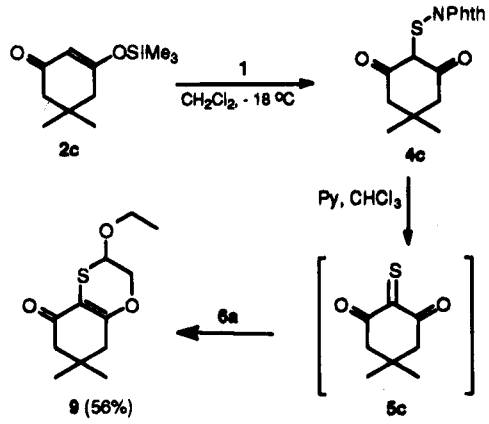


Figure 2. Calculated energies (eV) of orbitals involved in the cycloaddition.

Scheme 3

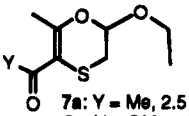
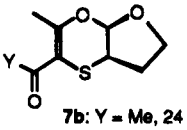
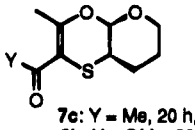
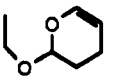
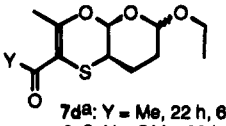
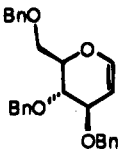
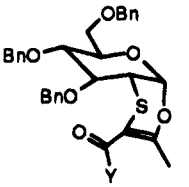
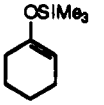
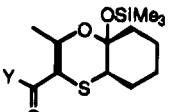
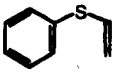
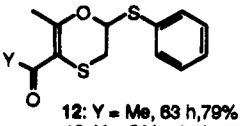
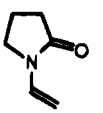
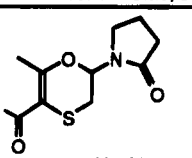


corresponding thione **5c**[11] can be successfully employed as diene in Diels–Alder reactions with ethyl vinyl ether, to give cycloadduct **9**, but there was no appreciable increase of the reaction rate despite the essentially cisoid conformation of diene **5c** due to the three adjacent carbon–heteroatom double bonds exo to the six-membered ring (Scheme 3).

Additional useful data from the molecular orbital calculations were the energies of the molecular orbitals involved in the cycloadditions, *i.e.*, the HOMO and LUMO of both thiones **5a,b**, in their presumed reactive conformations, and ethyl vinyl ether **6a**. As shown in Figure 2 the energetically favored interaction is between the dienophile HOMO and the diene LUMO as expected for an inverse electron demand Diels–Alder reaction.

The program used supplies information regarding the shape of the MO involved in cycloaddition. Thus, by matching the HOMO of **6a** and the LUMO of **5a** and **5b** it appears that the symmetry is optimal for superimposition and that the favored interactions (*i.e.*, the π orbitals with the largest coefficients) are found on the sulfur atom of thiones **5a** and **5b** and the vinylic methylene of **6a**. As a necessary consequence, the orbitals with the smaller coefficients pair the oxygen of the acylthione and the oxygen-substituted carbon of ethyl vinyl ether. Thus, the molecular orbital calculation predicts the preferred formation of the regioisomers which we have actually isolated from the reaction mixture.

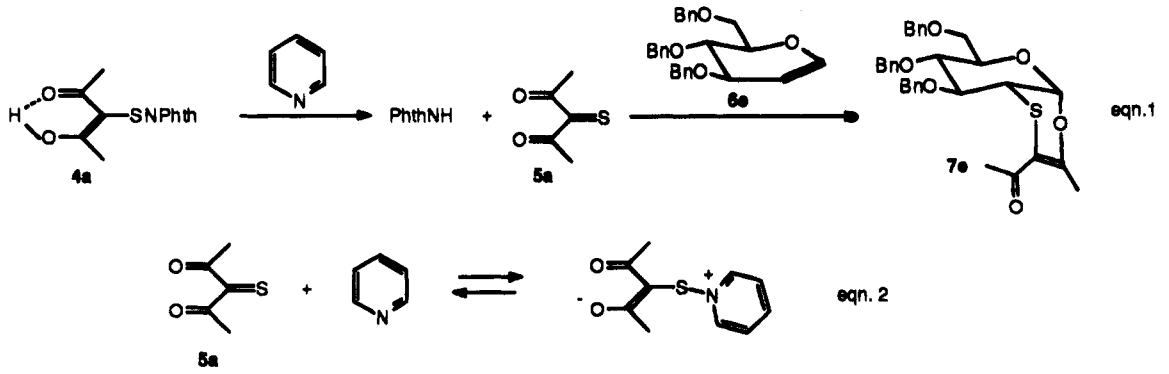
Table 1. Reaction of Thiones 5a,b with Enol Ethers 6a–f, Vinyl Sulfide 10, and Vinyl Pyrrolidone 11

Entry	Dienophile	Product (Reac. time, Isolated yield)
1	 **6a**	 **7a**: Y = Me, 2.5 h, 78% **8a**: Y = OMe, 17 h, 67%
2	 **6b**	 **7b**: Y = Me, 24 h, 85%
3	 **6c**	 **7c**: Y = Me, 20 h, 97% **8b**: Y = OMe, 23 h, 88%
4	 **6d**	 **7d**[a]: Y = Me, 22 h, 67% **8c**[a]: Y = OMe, 39 h, 61%
5	 **6e**	 **7e**[b]: Y = Me, 120 h, 48% **8d**: Y = OMe, 290 h, 40%
6	 **6f**	 **7f**: Y = Me, 40 h, 80% **8e**: Y = OMe, 63 h, 54%
7	 **10**	 **12**: Y = Me, 63 h,79% **13**: Y = OMe, 64 h, 89%
8	 **11**	 **14**: Y = Me, 52 h,75%

[a] As 80:20 mixture of diastereoisomers.[18] [b] 83% yield using 1 equiv of 2,6-lutidine as base (see Experimental Section).

Generality of the Cycloaddition Reaction. To evaluate the generality of this new cycloaddition reaction, we generated thiones **5a,b** in the presence of a variety of different electron rich alkenes; data of cycloadducts **7a-f**, **8a-e**, and **12–14** obtained are reported in Table 1.

Scheme 4



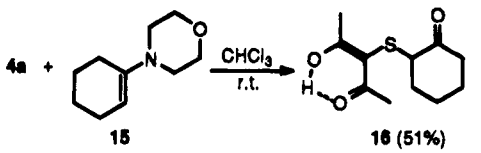
Thus, enol ethers **6a–e** (Table 1, entries 1–5), silyl enol ether **6f** (Table 1, entry 6), vinyl sulfide **10** (Table 1, entry 7), and 2-vinyl pirrolydone **11** (Table 1, entry 8) are good dienophiles for cycloadditions with thiones **5a** and **5b**.

In each case the cycloaddition is regiospecific, that is, the ketone carbonyl of the acylthiones is linked to the heterosubstituted carbon of the dienophile, and in all the reactions of **4b** the chemospecificity of the cycloaddition is maintained with the exclusive participation of the ketone carbonyl.

The products in entries 3–5 (Table 1) reveal ^3J values of the hydrogens linked to ring fusion carbon (C_2) of 4.4 Hz for **7b** and in the range 2.3–3.4 Hz for **7c–e** and **8b–d**. These data, together with the ^3J values of the hydrogens linked to C_3 (in the range 11.3–7.3 Hz), clearly indicate a *cis* fusion of the two cyclic systems as expected for a simultaneous formation of the two new carbon–heteroatom bonds. In entry 4 the cycloadditon leads to the formation of the corresponding cycloadducts **7d** and **8c** as a mixture of diastereoisomers in 80/20 ratio.[18]

Entry 5 (Table 1) requires comment. When thiones **5a,b** are generated via our standard conditions (3 equiv of pyridine) in the presence of tri-*O*-benzylglucal (**6e**) a slow cycloaddition takes place to give the cycloadducts **7e** (48%) and **8d** (40%), respectively, while 45% and 37% of unreacted **6e** was recovered which is equivalent to yields of 87% and 63%. The low conversion of these reactions was first rationalized taking into account the energy of the occupied π orbital acting as the dienophile.[19] The HOMO is completely localized on one of the phenyl rings and not centered on the vinylic system; thus, in this case, the HOMO^{-1} or HOMO^{-2} (approximately −9.5 eV), which have the right symmetry, participate in the cycloaddition. This value, compared to the simpler dihydropyrans (approximately −9.2, −9.3 eV), increases the HOMO–LUMO gap and is expected to reduce the rate of the cycloaddition. Nevertheless, the reaction was easily optimized when the fate of the reactive thione intermediate **5a** was considered. Thus, we postulated the equilibrium of eq 2 in Scheme 4. Although pyridine is required as a catalyst in eq 1 to form **5a**, it is not consumed and remains at its original concentration in the reaction mixture so that it could serve to decrease the concentration of **5a** available for cycloaddition. Hence, when the initial concentration of pyridine was reduced, or 2,6-lutidine was susbstituted for pyridine, the concentration of available **5a** was increased so that a typical cycloaddition on a mmol scale afforded greater than 80% isolated yield of adduct **7e** (Scheme 4).

Scheme 5



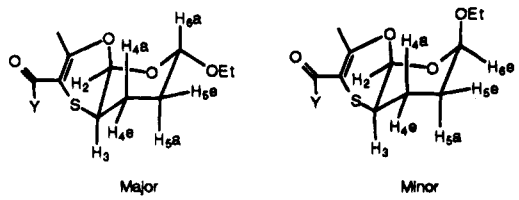
The synthesis of compounds **7e** and **8d**, whose ^3J values ($^3J_{H2-3}$ = 3.4 and 3.0, $^3J_{H3-4}$ = 10.4 and 10.4 Hz respectively) clearly indicate the presence in both cases of a single stereoisomer with the H_2 in equatorial and the H_3 in axial positions (i.e., 100% α anomer), represents an innovative stereocontrolled entry into 2-thiocarbohydrates which is being explored in these laboratories.

Entries 6–8 of Table 1 show that it is possible to use heterosubstituted electron rich alkenes different from enol ethers as dienophiles.

Enamines were also examined as potential dienophiles. When *N*-cyclohexylmorpholine **15** was reacted with **4a** the reaction mixture afforded the triketone **16** (51% yield) which can be viewed as the typical electrophilic sulfenylation product of the enamine[20] (Scheme 5). Compound **16** could be also considered as the ring-opened product of an initial cycloadduct formed since enamine **15** is basic enough to deprotonate **4a**, thus generating thione **5a**.

The generality of this new class of cycloaddition reaction is further demonstrated by the usefulness of electron rich styrenes, 4-methoxystyrene (**17**) or anethole

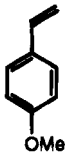
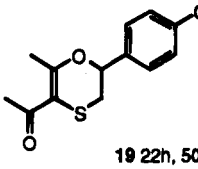
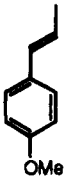
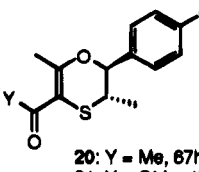
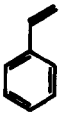
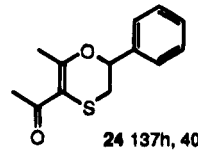
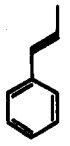
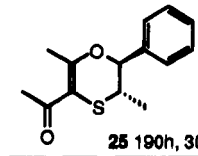
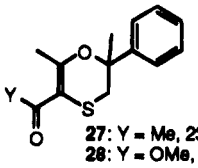
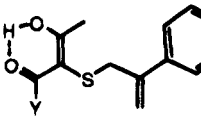
(18) ^{1}H NMR analysis of the two diastereisomeric mixtures **7d** and **8c** allows the determination of the structures of the major and minor stereoisomer as reported below. Indeed, the major isomer of **7d** (Y = Me) shows a doublet (J_{H2-3} = 2.4 Hz) at 5.59 ppm for H_1 and a doublet of doublets (J_{H6-5e} = 2.8; J_{H6-5a} = 7.2 Hz) at 4.96 ppm for H_6. By irradiation at 5.59 ppm it is possible to measure the J values of H_3 which shows a doublet of doublets (J_{H3-4e} = 3.8; J_{H3-4a} = 9.1 Hz) at 3.15 ppm, indicating the "*cis*" junction of the oxathiin ring with the C_2–O bond axial, the C_3–S bond equatorial, and the C_6–O bond (ethoxy group) equatorial. For the minor isomer of **7d** the J values clearly indicate that the oxathiin ring lays in the same position but the C_6 ethoxy group is in the axial position [H_6 doublet of doublets (J_{H6-5e} = 3.1; J_{H6-5a} = 3.3 Hz) at 5.53 ppm] (see Experimental Section). The same considerations allow attribution of an identical structure to the major and minor isomer of **8c** (Y = OMe).



(19) Tri-*O*-benzylglucal **6e** was minimized using an AM1 semiempirical calculation on a Spartan program working on a IBM-Risk work station. Energies (eV) of **6e** orbitals probably involved in the cycloaddition are as follows: HOMO^{-2} (correct symmetry), −9.48547; HOMO^{-1} (correct symmetry), −9.43635; HOMO (uncorrect symmetry) −9.32477.

(20) Kuehne, E. M. *J. Org. Chem.* **1963**, *28*, 2124.

Table 2. Reactions of Thiones 5a,b with Styrenes 17, 18, 22, 23, and 26

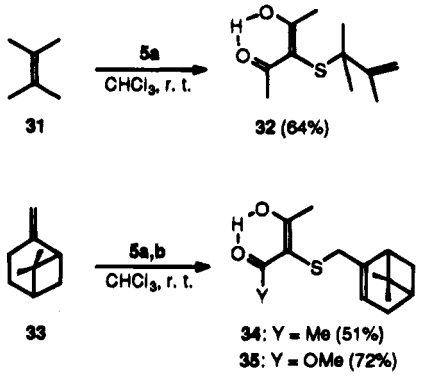
Entry	Dienophile	Product (react. time, isolated yield)
1	 17	 19 22h, 50%
2	 18	 20: Y = Me, 67h, 83% 21: Y = OMe, 47h, 56%
3	 22	 24 137h, 40%
4	 23	 25 190h, 30%
5	 26	 27: Y = Me, 23h, 10% 28: Y = OMe, 63h, 21%  29: Y = Me, 23h, 58% 30a : Y = OMe, 63h, 63%

[a] About 25% of **30** as ketonic tautomer was present in solution.[21]

(**18**), as dienophiles. The reaction remains regiospecific with the oxygen of thiones **5a,b** linked only to the benzylic carbon in cycloadducts **19–21**. The cycloaddition with **5a** was carried out using styrene (**22**) and *β-trans*-methylstyrene (**23**) as dienophiles to give cycloadducts **24** and **25**, albeit in lower yield, with our results summarized on Table 2.

In the case of cycloadducts **20**, **21**, and **25** (Table 2, entries 2 and 4) the stereochemistry of the alkenes is retained in the oxathiin systems as clearly indicated by the ^3J values of the benzylic protons ($^3J_{H2-3}$ = 8.3, 8.3, and 8.1 Hz respectively). This is consistent with the cycloaddition beeing concerted. When thiones **5a,b** were generated in the presence of α-methylstyrene (**26**) (entry 5) the ^{1}H NMR analysis of the crude reaction mixture showed the presence of cycloadducts **27** and **28** in only about 10 and 20% yields, respectively, while the major components were the "thiophilic enic" adducts **29** and **30**. The structure of latter compounds is clearly indicated by their ^{1}H NMR spectra which show two signals at 17.19 and 13.41 ppm for **29** and **30**, respectively, as expected for the presence of a β-dicarbonyl group.[21]

Scheme 6



Ene reactions of thiocarbonyl compounds have been frequently described, but usually a mixture of thiophilic and carbophilic adducts is obtained.[22] The formation of the thiophilic adduct as single compound in the reaction of **5a,b** with **26** indicates that the presence of the two flanking carbonyl groups strongly influences the chemoselectivity of the reaction and is consistent with the published examples of the chemistry of EWG-substituted thiones.[12,23]

The selective formation of the "thiophilic ene" adducts has been also observed when thione **5a** was generated in the presence of 2,3-dimethyl-2-butene (**31**) which leads to the formation of sulfide **32** and in the reaction of **5a** and **5b** with β-pinene **33** which affords sulfides **34** and **35**,[24] respectively (Scheme 6).

Allenes and Acetylenes as Dienophiles. The reaction of **5a** with allene **36** led to the formation of expected cycloadduct **37** (as a 4:1 mixture of diastereoisomers) which was isolated by flash chromatography in 42% yield. These materials showed a high sensitivity to acid hydrolysis; *i.e.*, after storage in $CDCl_3$ solution for 120 h, the adducts were transformed into the α,β-unsaturated aldehyde **38** through formal elimination of ethyl vinyl ether (Scheme 7).

When thione **5a** was generated in the presence of the silyl-substituted allene **39** the α,β-unsaturated thioacylsilane **40** was isolated from the reaction mixture as the sole product in 64% yield. No trace of the corresponding cycloadduct **41** was detected by NMR monitoring of the reaction within minutes following the addition of the pyridine. Our data, however, cannot determine whether **40** arises from an electrophilic attack of the thiocarbonyl sulfur to allene **39** (Scheme 7, path a) or from a very fast decomposition of the intermediate unstable cycloadduct **41** (Scheme 7, path b).

Treatment of sulfenamide **4a** with pyridine in the presence of a large excess of ethoxy acetylene **42** leads to the formation of orthocarbonate **43** in 91% isolated yield (Scheme 8). This result can be rationalized assuming the initial formation of monoadduct **44** which, due to the presence of a dioxygen-substituted double bond, reacts much faster than **42** with the electron poor diene **5a** to give the bicyclic compounds **43** (Scheme 8).

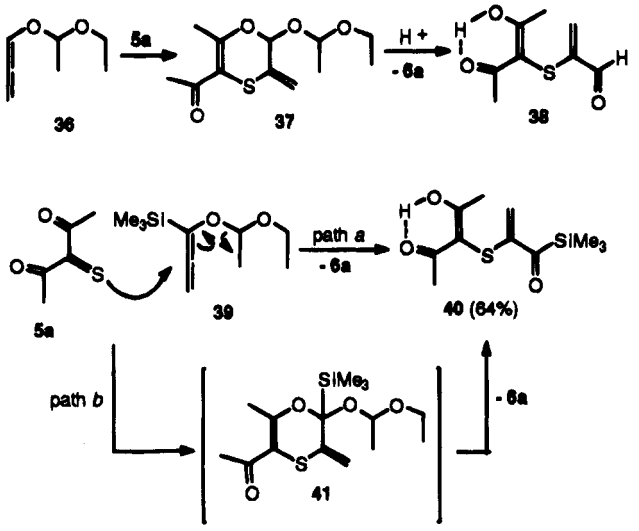
(21) ^{1}H NMR analysis of thiophilic ene adduct **30** showed the presence of the enolic and ketonic forms in a 3:1 ratio in $CDCl_3$ at 23 °C.

(22) (a) Metzner, P. *Synthesis* **1992**, 1185 and references cited therein. (b) Baldwin, J. E.; Lopez, G. C. *Tetrahedron* **1983**, *39*, 1487. (c) Kirby, G. W.; Choi, S. S. S.-M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3225.

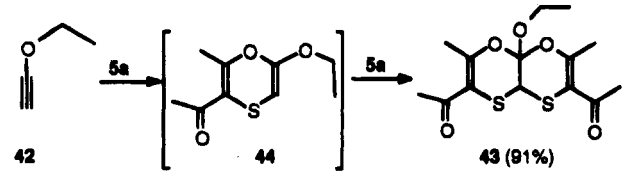
(23) (a) Middleton, W. J. *J. Org. Chem.* **1965**, *30*, 1395. (b) Snider, B. B.; Hrib, N. J.; Fuzesi, L. *J. Am. Chem. Soc.* **1976**, *98*, 7115.

(24) ^{1}H NMR analysis of thiophilic ene adduct **35** showed the presence of the enolic and ketonic form in 4:1 ratio in $CDCl_3$ at 23 °C.

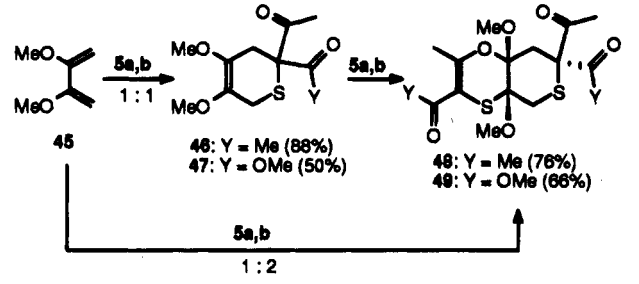
Scheme 7



Scheme 8



Scheme 9

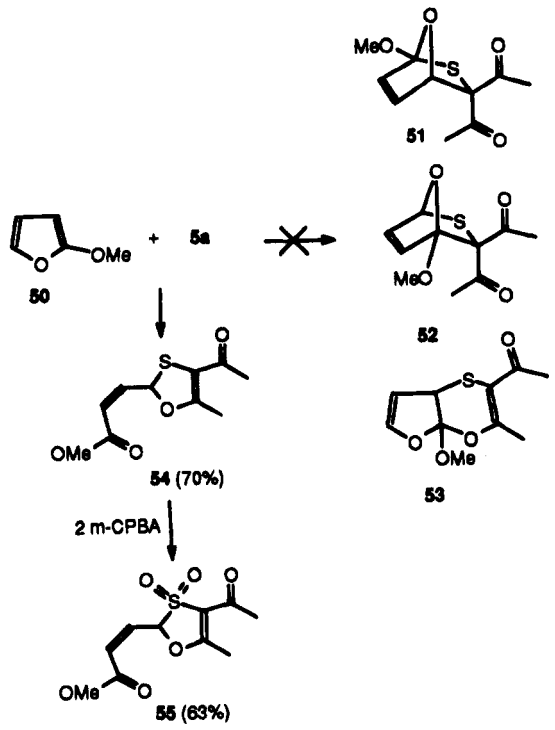


Dienophilic *versus* Dienic Character of α,α′-Dioxothiones. The reactivity of α-oxo- and α,α′-dioxothiocarbonyls as dienophiles in 4 + 2 cycloadditions with electron rich dienes has been extensively studied by us[14] as well as by other authors.[10-12,16,22]

Since thiones **5a,b** have now been shown to have dual reactivity, as both diene and dienophile, we designed a qualitative competition experiment. 2,3-Dimethoxy-1,3-butadiene (**45**) was chosen as substrate since it is a diene and a bis-vinyl ether. In the event, the reaction of **5a,b** with 1 equiv of **45** led to formation of dihydrothiopyrans **46** and **47**, respectively, as single reaction products.[25] These compounds arise from a well-documented cycloaddition of a thiocarbonyl species acting as dienophile with the diene **45**. Hence, the dienophilic character of the thiones predominates in this case (Scheme 9). Interestingly, compounds **46** and **47** possess an electron rich double bond which makes them good dienophiles for a second equivalent of thiones **5a,b** which now can react

(25) No trace of bis-adducts **48** and **49** was detected in the crude mixtures obtained from the reaction of **5a** and **5b** with **45**. Monoadducts **46** and **47** can be purified by flash chromatography but they decompose rapidly in $CDCl_3$ solution so that it has been impossible to record their ^{13}C NMR spectra. ^1H and GC–MS analyses together with their reaction with thiones **5a** and **5b** which gives the stable bicyclic derivatives **48** and **49**, respectively (Scheme 9), were considered sufficient to establish the identity of monoadducts.

Scheme 10



in a subsequent cycloaddition as dienes. Indeed, the reaction of monoadducts **46** and **47** with 1 equiv of **5a** and **5b**, respectively, affords the bicyclic compounds **48** and **49** which can be directly prepared carrying out the reaction of dimethoxybutadiene **45** with thione precursors **4a** or **4b** in a 1:2 stoichiometry (Scheme 9).

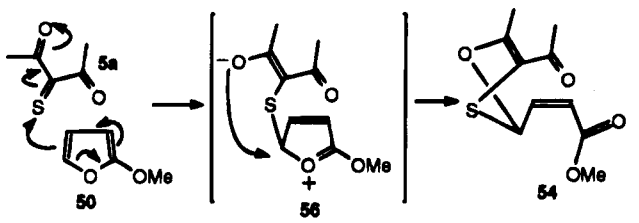
The formation of bicyclic compounds **48** and **49** is worthy of a brief comment. The approach of thione **5a** to **46** and **5b** to **47** could lead to two different regioisomers because of the nonequivalence of the methoxy-substituted vinylic carbons. Moreover, in the reaction of thione **5b** with dihydrothiopyran **47**, the presence of the stereocenter adjacent to the sulfur atom would also lead to the formation of a mixture of two different diastereoisomers for each regioisomer (*i.e.*, four different stereoisomers).

A careful analysis of the crude reaction mixtures showed that compound **48** (isolated in 76% yield) was present as a 95:5 mixture of regioisomers, while **49** was a single compound isolated in 66% yield. This curious selectivity is probably due to secondary orbital interaction since there seems to be no evident steric or electronic feature that explains either the regioselection or the complete stereoselection of the reaction.

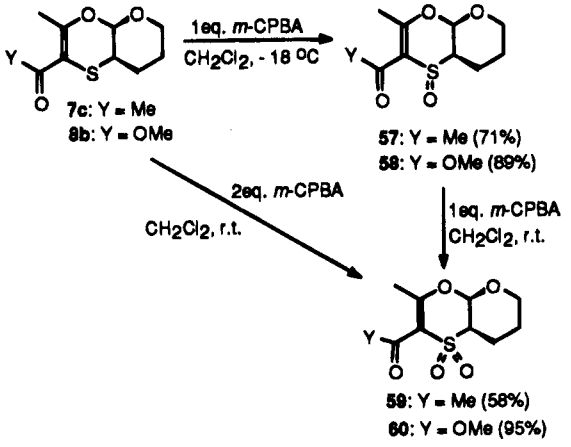
The assignment of the exact structure of the adducts via spectroscopic data was not possible. Suitable crystals of **49** were obtained for X-ray analysis which showed the structure reported in Scheme 9; since the NMR data for the adducts are very similar, we assign the same regiochemistry to **48**. The isomer obtained clearly reveals the two sulfur atoms separated by two carbons with the oxathiin ring *cis* fused with the oxygen in an axial position and the sulfur in an equatorial position. The bridgehead methoxy groups are *anti* to the carbomethoxy residue of the dihydrothiopyran ring.

Another unanticipated result was obtained when thione **5a** was generated in the presence of 2-methoxyfuran **50**. Our expectation was the formation of two bicyclic dihydrothiopyran regioisomers **51** and **52** (*i.e.*, the thione acting as dienophile) and/or the oxathiin **53** (*i.e.*, the thione acting as diene) (Scheme 10).

Scheme 11



Scheme 12



Spectroscopic data of the single compound **54** obtained from the reaction of **5a** and **50** were consistent with none of the structures **51**–**53**. X-ray diffractometric analysis of the sulfone **55** obtained by oxidation of **54** with 2 equiv of *m*-CPBA showed the structure reported in Scheme 10, so the reaction of **5a** with 2-methoxyfuran **50** must have given rise to the oxathiolene **54** (Scheme 10).

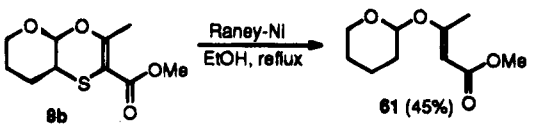
This outcome can be tentatively explained assuming the formation of a sulfur–carbon bond between the thiocarbonyl sulfur of **5a** and C_5 of the furan **50**. Then cleavage of C_5–O bond coupled with attack at C_5 by a carbonyl oxygen of the acylthione in **56** affords the observed product (Scheme 11).

Reactivity of 1,4-Oxathiin Ring Systems. We report a preliminary investigation of the properties of 1,4-oxathiin ring systems obtained through the cycloaddition of **5a,b** with enol ethers. In fact, very few examples of the reactivity of these systems have been reported.[26,27] Adducts **7c** and **8b** were used as model substrates. Oxidation of compounds **7c** and **8b** with 1 equiv of *m*-CPBA leads to the formation of the expected sulfoxides **57** and **58**, respectively. The stereoselectivity of the oxidation is noteworthy since in both cases a single sulfoxide is formed. Thus, in each of the oxathiins one of the faces is favored for the peroxidic oxygen attack (although we have not proven that the face selectivity is identical) (Scheme 12).

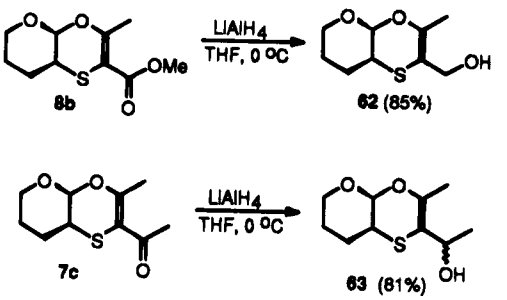
The corresponding sulfones **59** and **60** can be prepared both from the sulfides **7c** and **8b** or from the sulfoxides **57** and **58** using 2 or 1 equiv of oxidizing agent (Scheme 12).

Reductive desulfurization of oxathiin **8b** can be achieved using Raney nickel in refluxing ethanol to give the α,β-unsaturated ester **61** in 45% yield (Scheme 13). Cycloadduct **7c** is much more sensitive to Raney nickel; the same reaction conditions lead to extensive decomposition.

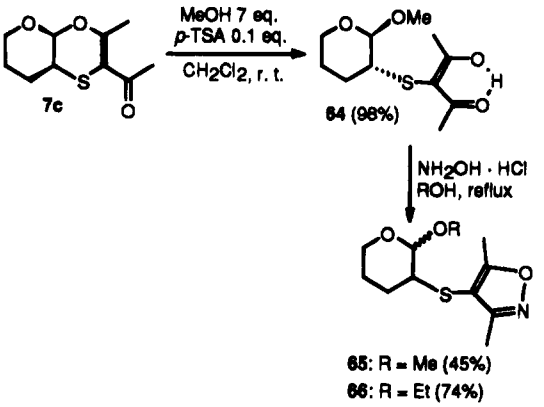
Scheme 13



Scheme 14



Scheme 15



Compounds **7c** and **8b** can be reduced to the corresponding alcohols using $LiAlH_4$ in anhydrous THF at 0 °C. Ester derivative **8b** gives rise to the primary alcohol **62** in 85% yield (Scheme 14), while ketone **7c** leads to the formation of alcohol **63** as a mixture of two diastereoisomers in a 76/24 ratio. In the latter reaction stereoselectivity is not increased by carrying out the reduction at −78 °C. Cycloadduct **7c** is reduced very slowly by sodium borohydride in THF, while the rate of the reduction can be increased using pyridine as solvent. We did not detect the reduction of the endocyclic double bond of the oxathiin systems, even when the reaction was done with excess $LiAlH_4$ at room temperature for extended rection times (Scheme 14).

When oxathiin **7c** was treated with methanol (10 equiv) in CH_2Cl_2 in the presence of 10% of *p*-TSA we observed the ring opening with formation of the methoxy derivative **64** which was isolated in almost quantitative yield (Scheme 15). Complete inversion of configuration was achieved by methanol attack at acetalic carbon as revealed by the ^3J values of the protons linked to C_2 and C_3 (see the Experimetal Section). Compound **64** can be further transformed into the isoxazole **65** by treatment with hydroxylamine in refluxing methanol[28] (Scheme 15). During the transformation we observed isomerization at position 2; thus, we obtained **65** as a 1:1 mixture of *cis* and *trans* isomer. The isomerization is simply explained

(26) (a) Asinger, F.; Saus, A.; Offermanns, H.; Scherberich, P. *Liebigs Ann. Chem.* **1971**, *753*, 151. (b) Corbeil, M. A.; Curcumelli-Rodostamo, M.; Fanning, R. J.; Graham, B. A.; Kulka, M.; Pierce, J. B. *Can. J. Chem.* **1973**, *51*, 2650. (c) Kulka, M. *Can. J. Chem.* **1980**, *58*, 2044.

(27) von Schmeling, B.; Kulka, M. *Science* **1966**, *152*, 659.

(28) Katritzky, A. R.; Ostercamp, D. L.; Yousaf, T. I. *Tetrahedron* **1987**, *43*, 5186 and references cited therein.

as an acid-catalyzed process which occurs under the conditions required for isoxazole ring closure. In fact, when the hydroxylamine reaction was performed in refluxing ethanol a 1:1 mixture of the *cis* and *trans* ethoxy derivative **66** was obtained, thus confirming that a solvolytic process is responsible for the observed epimerization (Scheme 15).

Conclusion

We have shown that α,α′-dioxothiones can act as electron poor dienes in inverse electron demand Diels–Alder reactions with a variety of dienophiles including enol ethers, silyl enol ethers, vinyl sulfides, vinyl amides, styrenes, activated allenes, and acetylenes. The cycloaddition reaction was regio- and chemospecific in every case, and a remarkable stereoselectivity was achieved for selected dienophiles.

Ab initio molecular orbital calculations showed an orbital array in perfect agreement with the experimental data obtained for both the electron demand and for the regiochemistry of the cycloaddition. These new reactions offer the possibility of facile preparation of 1,4-oxathiin systems which are unexplored in their chemistry and possible biological activity. Furthermore, this method offers a new approach to 2-thiocarbohydrates derivatives. A comparison between the dienic and the dienophilic character as well as the enic aspect of the reactivity of such polyfunctionalized thiones has been also described.

Further aspects of the reactivity of α,α′-dioxothiones as well as of the 1,4-oxathiin systems are currently under investigation in our laboratories.

Experimental Section

^1H and ^{13}C NMR spectra were recorded (when not specified) in $CDCl_3$ at 200 and 50 MHz, respectively, using residual $CHCl_3$ at 7.26 ppm for ^1H and central peak of $CDCl_3$ at 77 ppm for ^{13}C as reference lines. Mass spectra and GC–MS analyses were obtained using a gas chromatograph, equipped with a OV101 30 m capillary column, interfaced on a mass spectrometer. Melting points are uncorrected. $CHCl_3$, CH_2Cl_2, and THF were dried following standard procedures, and all commercial reagents were used without further purification as obtained from freshly opened containers. Phthalimidesulfenyl chloride (**1**)[29] and thiophthalimides **4a–c**[14] were prepared as reported elsewhere.

General Procedure for the Trapping of Thiones 5a and 5b as Dienes. All the cycloadditions were performed in dry $CHCl_3$ at rt by adding 3 equiv of freshly distilled pyridine to a mixture of the sulfenamide and the dienophile in a 1:2 ratio. The reactions were monitored by NMR (0.1 mmol scale/$CDCl_3$). The crude reaction mixtures were diluted with CH_2Cl_2 (30 mL), washed with saturated NH_4Cl (2 × 30 mL) and water (2 × 30 mL), and dried over anhydrous Na_2SO_4. Flash chromatography on silica gel (ethyl acetate–petroleum ether) was used to purify the crude products (solids were recrystallized when necessary). Physical and spectroscopic data of compounds **7a–f**, **8a–e**, **9**, **12–14**, **19–21**, **24**, **25**, **27–30**, **32**, **34**, **35**, **38**, **40**, **43**, **46–49**, and **54** obtained using this general procedure are as follows.

1-(6-Ethoxy-5,6-dihydro-2-methyl-1,4-oxathiin-3-yl)-ethanone (7a): 78% yield; colorless oil; IR 2978, 2928, 1673, 1562, 1246 cm^{-1}; ^1H NMR 1.26 (X_3 part of an ABX_3 system, $J_{AX} = J_{BX} = 7.1$ Hz, 3H), 2.28 (s, 3H), 2.30 (s, 3H), 2.77–2.97 (AB part of an ABX system, $J_{AB} = 13.0$ Hz, 2H), 3.61–3.77 and 3.85–4.02 (AB part of an ABX_3 system, 2H), 5.26 (X part of an ABX system, $J = 2.6$, 4.9 Hz, 1H) δ; ^{13}C NMR 15.0 (q), 28.6 (t), 22.0 (q), 29.7 (q), 64,8 (t), 96.6 (d), 105.4 (s), 158.0 (s), 195.6 (s) δ; MS *m*/*z* (rel int) 202 ($M^{\bullet+}$, 27), 160 (32), 88 (78), 43 (100). Anal. Calcd for $C_9H_{14}O_3S$: C, 53.44; H, 6.98. Found: C, 53.57; H, 7.19.

1-(2-Methyl-4a,5,6,7a-tetrahydrofurano[2,3-*b*][1,4]oxathiin-3-yl)ethanone ((4aα,7aα)-7b): 85% yield; pale yellow oil; IR 2959, 1649, 1244 cm^{-1}; ^1H NMR 1.86–2.06 and 2.22–2.41 (m, 2H), 2.31 (s, 3H), 2.33 (s, 3H), 3.48–3.59 (M part of an AMXY, $J_{AM} = 4.4$ Hz, $J_{MX,\ MY} = 10.6$ and 8.4 Hz, 1H), 3.97–4.24 (m, 2H), 5.50 (A part of an AMXY system, $J_{AM} = 4.4$ Hz, 1H) δ; ^{13}C NMR 22.1 (q), 28.5 (t), 30.0 (q), 39.4 (d), 68.7 (t), 100.3 (d), 103.4 (s), 160.8 (s), 195.8 (s) δ; MS *m*/*z* (rel int) 200 ($M^{\bullet+}$, 40), 158 (5), 88 (30), 70 (100). Anal. Calcd for $C_9H_{12}O_3S$: C, 53.98; H, 6.04. Found: C, 54.12; H, 6.20.

1-(2-Methyl-4a,5,6,8a-tetrahydro-7*H*-pyrano[2,3-*b*][1,4]-oxathiin-3-yl)ethanone ((4aα,8aα)-7c): 97% yield; pale yellow oil; IR 2928, 1670, 1558, 1245 cm^{-1}; ^1H NMR 1.65–2.00 (m, 4H), 2.29 (s, 3H), 2.32 (s, 3H), 3.00–3.12 (m, 1H), 3.60–3.90 (m, 2H), 5.49 (d, $J = 2.7$ Hz, 1H) δ; ^{13}C NMR 21.6 (q), 24.6 and 25.0 (t), 30.1 (q), 35.3 (d), 60.5 (t), 95.2 (d), 102.3 (s), 158.4 (s), 195.8 (s) δ; MS *m*/*z* (rel int) 214 ($M^{\bullet+}$, 7); 153 (2); 84 (100). Anal. Calcd for $C_{10}H_{14}O_3S$: C, 56.05; H, 6.58. Found: C, 55.87; H, 6.82.

1-(7-Ethoxy-2-methyl-4a,5,6,8a-tetrahydro-7*H*-pyrano-[2,3-b][1,4]oxathiin-3-yl)ethanone ((4aα,8aα)-7d): 67% yield, obtained as 79:21 mixture of diasteroisomers.[18] The following data refer to the major isomer; an asterisk indicates common signals: IR* 2931, 1675, 1563, 1247 cm^{-1}; ^1H NMR 1.24 (X_3 part of an ABX_3, $J_{AX} = J_{BX} = 7.2$ Hz, 3H)*, 1.55–2.15 (m, 2H)*, 2.30 (s, 3H)*, 2.37 (s, 3H)*, 3.15 (ddd, $J = 2.4$, 3.8, and 9.1 Hz, 1H), 3.40–3.65 and 3.75–4.10 (AB part of an ABX_3 system, 2H)*, 4.96 (dd, $J = 2.80$ and 7.20 Hz, 1H), 5.59 (d, $J = 2.4$ Hz, 1H) δ; ^{13}C NMR 15.1 (q), 21.7 (q), 23.1 and 28.7 (t), 29.9 (q), 35.0 (d), 64.3 (t), 94.0 and 97.2 (d), 103.3 (s), 157.5 (s), 195.7 (s) δ; MS* *m*/*z* (rel int) 258 ($M^{\bullet+}$, 8), 170 (4), 128 (14), 43 (100). Minor isomer: ^1H NMR 3.04–3.13 (m, 1H), 4.81 (dd, $J = 3.1$ and 3.3 Hz, 1H), 5.53 (d, $J = 2.9$ Hz, 1H) δ; ^{13}C NMR 14.8 (q), 21.9 (q), 20.4 and 29.5 (t), 30.0 (q), 35.3 (d), 63.6 (t), 94.7 and 96.8 (d), 102.7 (s), 158.7 (s), 195.7 (s) δ. Anal.* Calcd for $C_{12}H_{18}O_4S$: C, 55.79; H, 7.02. Found: C, 55.73; H, 7.40.

1-*O*,2-*S*-(2-Acetyl-1-methyl-1,2-ethenediyl)-3,4,6-tris-*O*-(phenylmethyl)-2-thio-α-D-glucopyranose (7e): 48% yield, white solid; mp 115–116 °C (*n*-heptane); IR 3090, 2945, 1671, 1552, 1231 cm^{-1}; ^1H NMR 2.31 (s, 6H), 3.23 (dd, $J = 3.4$, 10.4 Hz, 1H), 3.58–4.02 (m, 5H), 4.51–4.94 (m, 6H), 5.63 (d, $J = 3.4$ Hz, 1H), 7.10–7.44 (m, 15H) δ; ^{13}C NMR 21.6 (q), 30.3 (q), 41.5 (d), 67.9, 73.6, 75.3, 76.5 (t), 72.9, 77.6, 78.2, 96.0 (d), 101.8 (s), 127.8, 127.9, 128.0, 128.4, 128.5 (d), 137.6, 137.8 (s), 159.6 (s), 195.3 (s) δ. Anal. Calcd for $C_{32}H_{34}O_6S$: C, 70.31; H, 6.27. Found: C, 70.45; H, 6.42.

Preparation of compound **7e** was optimized as follows: Thiophthalimide **4a** (1.32 g, 4.80 mmol) was dissolved in 10 mL of dry $CHCl_3$ under a N_2 atmosphere with powdered 3A molecular sieves (activated, 0.5 g). To the solution was added tri-*O*-benzyl-D-glucal (**6e**) (1.01 g, 2.4 mmol) followed by dry 2,6-lutidine (0.28 mL, 2.4 mmol) by syringe. The reaction mixture turned brown immediately, and over a 4 d period, it acquired a deep red color. After 4 d the reaction had proceeded almost completely by ^1H NMR analysis. The mixture was washed three times with a saturated solution of NH_4Cl. The organic fraction was dried with anhydrous Na_2SO_4 and concentrated. The resulting crude was put through a flash silica gel column, and the final product **7e** was isolated and concentrated to give 1.10 g (83%); starting material **6e** (0.156 g, 15%) was also obtained from the chromatography.

1-(4a,5,6,7,8,8a-Hexahydro-2-methyl-8a-[(trimethylsilyl)oxy]-1,4-benzooxathiin-3-yl]ethanone ((4aα,8aα)-7f): 80% yield; yellow oil; IR 2950, 1676, 1566, 1248 cm^{-1}; ^1H NMR 0.13 (s, 9H), 1.20–1.90 (m, 6H), 2.27 (s, 3H), 2.30 (s, 3H), 2.80 (dd, $J = 4.2$, 10.6 Hz, 1H) δ; ^{13}C NMR 1.5 (q), 22.1 (q), 23.3, 24.7 and 30.0 (t), 39.0 (t), 43.7 (s), 97.0 (s), 104.0 (s), 155.6 (s), 196.4 (s) δ; MS *m*/*z* (rel int) 300 ($M^{\bullet+}$, 15), 170 (100), 155 (29), 73 (40). Anal. Calcd for $C_{14}H_{24}O_3SSi$: C, 55.96; H, 8.05. Found: C, 55.89; H, 8.42.

Methyl 1-(6-ethoxy-5,6 dihydro-2-methyl-1,4-oxathiin-3-yl)formate (8a): pale yellow oil; IR 2980, 1712, 1594, 1251 cm^{-1}; ^1H NMR 1.25 (t, $J = 7.5$ Hz, 3H), 2.32 (s, 3H), 2.76–2.94 (AB part of an ABX system, $J_{AB} = 13.5$ Hz, 2), 3.64–3.76

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(m, 1H), 3.73 (s, 3H), 3.84–3.96 (m, 1H); 5.24 (X part of an ABX system, J = 4.0 and 2.0 Hz, 1H) δ; ^{13}C NMR (75 MHz, C_6D_6) 15.1 (q), 21.4 (q), 28.8 (t), 51.4 (q), 64.4 (t), 97.1 (d), 97.6 (s), 158.6 (s), 165.5 (s) δ; MS m/z (rel int) 218 ($M^{\bullet+}$, 73), 186 (100). Anal. Calcd for $C_9H_{14}O_4S$: C, 49.52; H, 6.46. Found: C, 49.72; H, 6.64.

Methyl 1-(2-methyl-4a,5,6,8a-tetrahydro-7*H*-pyrano-[2,3-*b*][1,4]oxathiin-3-yl)formate ((4aα,8aα)-8b): 88% yield; colorless oil; IR 2949, 1709, 1597, 1254 cm^{-1}; ^{1}H NMR 1.65–2.60 (m, 4H), 2.38 (s, 3H), 2.99–3.11 (m, 1H), 3.74 (s, 3H), 3.60–3.95 (m, 2H), 5.49 (d, J = 2.6 Hz, 1H) δ; ^{13}C NMR 21.0 (q), 24.9, 25.0 (t), 35.5 (d), 51.9 (q), 60.6 (t), 93.4 (d), 95.2 (s), 165.8 (s) δ; MS m/z (rel int) 230 ($M^{\bullet+}$, 7), 84 (100). Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13. Found: C, 52.29; H, 6.33.

Methyl 1-(7-ethoxy-2-methyl-4a,5,6,8a-tetrahydro-7*H*-pyrano[2,3-*b*][1,4]oxathiin-3-yl)formate ((4aα,8aα)-8c): 61% yield; yellow oil obtained as a 80:20 mixture of diastereoisomers.[18] The following spectroscopic data refer to major isomer, asterisk indicates common signals: IR* 2979, 1711, 1597, 1243 cm^{-1}; ^{1}H NMR 1.23 (t, J = 7.0 Hz, 3H), 1.56–2.18 (m, 4H)*, 2.36 (s, 3H), 3.11 (ddd, J = 9.2, 4.0 and 2.3 Hz), 3.42–3.64 and 3.84–4.04 (m, 2H)*, 4.97 (dd, J = 2.5, 6.9 Hz, 1H), 5.58 (d, J = 2.3 Hz, 1H) δ; ^{13}C NMR 15.2 (q), 21.1 (q), 23.4, 28.8 (t), 35.1 (d), 52.0 (q), 64.3 (t), 94.5 (d)*, 94.6 (s), 97.2 (d), 158.5 (s)*, 165.5 (s)* δ. Minor isomer: ^{1}H NMR 1.24 (t, J = 7.0 Hz, 3H); 2.35 (s, 3H); 3.10–3.16 (m, 1), 4.80 (dd, J = 3.1 and 3.3 Hz, 1H), 5.50 (d, J = 2.8 Hz, 1H) δ; ^{13}C NMR 14.9 (q), 21.3 (q), 21.1, 29.6 (t), 35.5 (d), 51.9 (q), 63.5 (t), 93.2 (s), 94.5 (d)*, 96.9 (d), 158.5 (s)*, 165.5 (s)*δ; MS* m/z (rel int) 274 ($M^{\bullet+}$, 26), 128 (15), 127 (20), 72 (85), 43 (100). Anal. Calcd for $C_{12}H_{18}O_5S$: C, 52.24; H, 6.61. Found: C, 52.34; H, 6.84.

1-*O*,2-*S*-[2-(Carboxymethyl)-1-methyl-1,2-ethenediyl]-3,4,6-tris-*O*-(phenylmethyl)-2-thio-α-D-glucopyranose (8d): 40% yield; white solid; mp 79 °C (*n*-hexane); ^{1}H NMR 2.35 (s, 3H), 3.17 (dd, J = 2.9, 10.40 Hz, 1H), 3.58–4.12 (m, 5H), 3.76 (s, 3H), 4.58–4.87 (m, 6H), 5.60 (d, J = 2.9 Hz, 1H), 7.11–7.43 (m, 15H) δ; ^{13}C NMR 20.8 (q), 41.7 (d), 51.8 (q), 67.8, 73.3, 75.1, 76.1 (t), 72.8, 77.5, 77.9 (d), 93.6 (s), 95.8 (d), 127.5, 127.7, 127.7, 128.1, 128.2, 128.2, 128.2 (d), 137.5, 137.6, 137.8 (s), 160.1 (s), 165.3 (s) δ; MS m/z (rel int) 562 ($M^{\bullet+}$, 1.26), 454 (31), 253 (24), 163 (58), 91 (100). Anal. Calcd for $C_{32}H_{34}O_7S$: C, 68.31; H, 6.10. Found: C, 68.65; H, 6.02.

Methyl 1-(4a,5,6,7,8,8a-Hexahydro-2-methyl-8a-[(trimethylsilyl)oxy]-1,4-benzooxathiin-3-yl)formate ((4aα,-8aα)-8e): 54% yield; pale yellow oil; IR 2941, 1713, 1600, 1251 cm^{-1}; ^{1}H NMR 0.14 (s, 9H), 1.21–2.30 (m, 8H), 2.34 (s, 3H), 2.78 (dd, J = 4.20 and 10.68 Hz, 1H); 3.75 (s, 3H) δ; ^{13}C NMR 1.5 (q), 21.5 (q), 23.3, 24.6, 30.2 (t), 38.8 (t), 43.6 (d), 51.9 (q), 95.2 (s), 97.0 (s), 157.1 (s), 166.1 (s) δ; MS m/z (rel int) 316 ($M^{\bullet+}$, 28), 170 (100). Anal. Calcd for $C_{14}H_{24}O_4SSi$: C, 53.15; H, 7.64. Found: C, 52.94; H, 7.68.

2-Ethoxy-5,6,7,8-tetrahydro-5-oxo-7,7-dimethyl-1,4-benzooxathiine (9): 53% yield; colorless oil; ^{1}H NMR 1.08 (s, 3H), 1.09 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 2.33 (bs, 2H), 2.36 (bs, 2H), 2.91 (AB part of an ABX system, J_{AB} = 12.7 Hz, 2H), 3.65–4.05 (m, 2H), 5.30 (X part of an ABX system, J = 2.5, 4.9 Hz, 1H) δ.

1-(5,6-Dihydro-2-methyl-6-(phenylthio)-1,4-oxathiin-3-yl)ethanone (12): 79% yield; oil; IR 3059, 2922, 1642, 1535, 1242 cm^{-1}; ^{1}H NMR 2.31 (s, 3H), 2.32 (s, 3H), 3.16 (AB part of an ABX system, J_{AB} = 13.2 Hz, 2H), 5.66 (X part of an ABX system, J = 2.6, 5.8 Hz), 7.25–7.55 (m, 5H) δ; ^{13}C NMR 22.4 (q), 29.6 (q), 29.8 (t), 83.0 (d), 105.9 (s), 128.3 (d), 129.1, 132.9 (d), 132.3 (s), 157.8 (s), 195.4 (s) δ; MS m/z (rel int) 266 ($M^{\bullet+}$, 64), 224 (17), 136 (87), 135 (98), 91 (100). Anal. Calcd for $C_{13}H_{14}O_2S_2$: C, 58.62; H, 5.30. Found: C, 58.78; H, 5.52.

Methyl 1-(5,6-Dihydro-2-methyl-6-(phenylthio)-1,4-oxathiin-3-yl)formate (13): 89% yield; yellow oil; IR 3057, 2952, 1713, 1596, 1250 cm^{-1}; ^{1}H NMR 2.37 (s, 3H), 3.01 (AB part of an ABX system, J = 13.2 Hz, 2H), 3.77 (s, 3H), 5.68 (X part of an ABX system, J = 2.7, 5.4 Hz, 1H), 7.30–7.60 (m, 5H) δ; ^{13}C NMR 20.9 (q), 30.0 (t), 52.0 (q), 82.9 (d), 97.1 (s), 128.1 (d), 132.7 (s), 158.8 (s), 165.2 (s) δ; MS m/z (rel int) 282 ($M^{\bullet+}$, 51), 135 (100), 43 (98). Anal. Calcd for $C_{13}H_{14}O_3S_2$: C, 55.23; H, 5.00. Found: C, 55.50; H, 5.12.

1-[5,6-Dihydro-2-methyl-6-*N*-(2′-oxo-2′,3′,4′,5′-tetrahydropyrrolo)-1,4-oxathiin-3-yl]ethanone (14): 75% yield; white solid; mp 104–105 °C; IR 2982, 1692, 1668, 1545, 1415, 1216, 1037 cm^{-1}; ^{1}H NMR 2.05–2.17 (m, 2H), 2.26 (s, 3H), 2.31 (s, 3H), 2.42–2.51 (m, 2H), 2.95 (AB part of an ABX system, J = 12.8 Hz, 2H), 3.35–3.77 (m, 2H), 6.00 (X part of an ABX system, J = 2.6, 8.84 Hz, 1H) δ; ^{13}C NMR 18.0 (t), 21.9 (q), 26.7 (t), 29.8 (q), 31.0 (t), 42.2 (t), 78.8 (d), 105.2 (s), 159.6 (s), 175.5 (s), 195.3 (s) δ; MS m/z (rel int) 241 ($M^{\bullet+}$, 5), 199 (3), 111 (47), 43 (100). Anal. Calcd for $C_{11}H_{15}NO_3S$: C, 54.75; H, 6.27; N, 5.80. Found: C, 54.38; H, 6.36; N, 5.47.

Triketone 16. Compound **16** was obtained when **4a** was reacted with *N*-cyclohexylmorpholine (**15**) in the absence of pyridine. After 20 h at rt, triketone **16** was isolated in 51% yield by flash chromatography (eluent ethyl acetate:petroleum ether = 1:9) as an oil: ^{1}H NMR 1.60–2.20 and 2.21–2.34 (m, 5H), 2.38 (s, 6H), 2.77–2.94 (m, 1H), 3.22 (dd, J = Hz, 1H), 17.23 (s, 1H) δ; MS m/z (rel int) 228 ($M^{\bullet+}$, 9), 98 (75), 69 (100). Anal. Calcd for $C_{11}H_{16}O_3S$: C, 57.87; H, 7.06. Found: C, 58.05; H, 6.95.

1-[5,6-Dihydro-2-methyl-6-(4′-methoxyphenyl)-1,4-oxathiin-3-yl]ethanone (19): 50% yield; oil; IR 3020, 2940, 1675, 1547, 1232 cm^{-1}; ^{1}H NMR 2.34 (s, 6H), 3.01 (AB part of an ABX system, J_{AB} = 13.3 Hz, 2H), 3.82 (s, 3H), 5.11 (X part of an ABX system, J = 7.32, 3.38 Hz, 1H), 6.80–7.26 (m, 4H) δ; ^{13}C NMR 22.6 (q), 29.9 (q), 31.2 (t), 55.4 (q), 77.9 (d), 105.3 (s), 114.1, 127.1 (d), 131.4 (s), 159.6 (s), 160.1 (s), 195.7 (s) δ; MS m/z (rel int) 264 ($M^{\bullet+}$, 24), 221 (7), 134 (98), 91 (100). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.25; H, 6.34.

1-[5,6-Dihydro-2,7-dimethyl-6-(4′-methoxyphenyl)-1,4-oxathiin-3-yl]ethanone (*trans*-20): 83% yield; pale yellow needles; mp 70–72 °C (ethanol). ^{1}H NMR 1.07 (d, J = 6.8 Hz, 3H), 2.32 (s, 3H), 2.34 (s, 3H), 3.12 (dq, J = 8.3, 6.8 Hz, 1H), 3.82 (s, 3H), 4.67 (d, J = 8.3 Hz, 1H), 6.87–6.96 + 7.14–7.22 (m, 4H) δ; ^{13}C NMR 16.8 (q), 22.2 (q), 29.8 (q), 37.2 (d), 55.3 (q), 84.1 (d), 106.3 (s), 114.1, 128.2 (d), 129.83(s), 159.9 (s), 160.1 (s), 195.7 (s) δ; MS m/z (rel int) 278 ($M^{\bullet+}$, 10), 147 (100), 133 (73), 77 (67). Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52. Found: C, 65.00; H, 6.78.

Methyl 1-[5,6-dihydro-2,7-dimethyl-6-(4′-methoxyphenyl)-1,4-oxathiin-3-yl]formate (*trans*-21): 58% yield; glassy solid; IR 3020, 2954, 1707, 1592, 1237 cm^{-1}; ^{1}H NMR 1.05 (d, J = 6.8 Hz, 3H), 2.37 (s, 3H); 3.12 (dq, J = 6.80, 8.3 Hz, 1H), 3.78 (s, 3H), 3.82 (s, 3H); 4.66 (d, J = 8.3 Hz, 1H); 6.90–7.21 (m, 4H) δ; ^{13}C NMR 16.8 (q), 21.4 (q), 37.2 (d), 51.9 (q), 55.3 (q), 84.1 (d), 97.0 (s), 114.1, 128.3 (d), 130.0 (s), 160.0 (s), 161.5 (s), 165.8 (s) δ; MS m/z (rel int) 294 ($M^{\bullet+}$, 22), 263 (11), 149 (30), 147 (100), 43 (98). Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16. Found: C, 62.17; H, 6.50.

1-(5,6-Dihydro-2-methyl-6-phenyl-1,4-oxathiin-3-yl)-ethanone (24): 40% yield; pale yellow oil; IR 3031, 2953, 1671, 1551, 1234 cm^{-1}; ^{1}H NMR 2.36 (s, 3H), 2.37 (s, 3H), 3.03 (AB part of an ABX system, J_{AB} = 13.2 Hz, 2H), 5.16 (X part of an ABX system, J = 2.8, 8.0 Hz, 1H), 7.28–7.48 (m. 5H) δ; ^{13}C NMR 22.5 (q), 29.8 (q), 31.2 (t), 78.1 (d), 105.4 (s), 125.7 (d), 128.6 (d), 139.3 (d), 160.1 (s), 195.9 (s) δ; MS m/z (rel int) 243 ($M^{\bullet+}$, 40), 192 (48), 104 (100), 43 (99). Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.63; H, 5.71.

1-(5,6-Dihydro-2,7-dimethyl-6-phenyl-1,4-oxathiin-3-yl)ethanone (*trans*-25): 30% yield; oil; IR 3040, 2925, 1672, 1555, 1234 cm^{-1}; ^{1}H NMR 1.09 (d, J = 6.8 Hz, 3H), 3.33 (s, 3H), 2.34 (s, 3H), 3.15 (dq, J = 6.8, 8.15 Hz, 1H), 4.72 (d, J = 8.15 Hz, 1H), 7.22–7.47 (m , 5H) δ; ^{13}C NMR 16.8 (q), 22.1 (q), 29.8 (q), 37.3 (d), 84.3 (d), 106.4 (s), 126.9, 128.7 (d), 128.8 (d), 137.8 (s), 160.0 (s), 195.8 (s) δ; MS m/z (rel int) 248 ($M^{\bullet+}$, 50), 117 (100). Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 67.61; H, 7.00.

Generation of Thione 5a in the Presence of α-Methyl Styrene (26). Analysis of the crude reaction mixture obtained while generating thione **5a** in the presence of α-methylstyrene (**26**) showed the presence of two compounds: cycloadduct **27** and ene adduct **29** in a 1:7 ratio. The latter ratio was obtained by integrating the AB system at 3.00 ppm (J = 13.8 Hz) in the crude ^{1}H NMR which was attributed to SCH_2 methylene of **27** in comparison with the doublet at 5.43 ppm (J = 0.4 Hz)

attributed to one of the vinylic protons of **29**. Flash chromatography purification (eluent ethyl acetate:petroleum ether = 1:10) allowed the isolation of **29** in 58% as a colorless oil: IR 3471, 3019, 2961, 1615, 1546, 1223 cm^{-1}; ^1H NMR 2.24 (s, 6H) 3.58 (bs, 2H), 4.97 (d, J = 0.4 Hz, 1H), 5.43 (d, J = 0.4 Hz, 1H), 7.33–7.51 (m, 5H), 17.19 (s, 1H) δ; ^{13}C NMR 24.4 (q), 41.0 (t), 103.5 (s), 115.7 (t), 126.0, 128.5 (d), 128.0 (d), 138.6 (s), 142.6 (s), 198.1 (s) δ; MS m/z (rel int) 248 ($M^{\bullet+}$, 3), 206 (100), 115 (99), 91 (97), 43 (98). Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 67.46; H, 6.49.

Generation of Thione 5b in the Presence of α-Methylstyrene (26). Analysis of the crude reaction mixture showed the presence of **28** and ene adduct **30** in a 1:4 ratio. Flash chromatography purification (eluent ethyl acetate: petroleum ether = 1:10) allowed the isolation of **28** and **30** in 20 and 63% yield, respectively.

1-(5,6-Dihydro-2,6-dimethyl-6-phenyl-1,4-oxathiin-3-yl)Ethanone (28): ^1H NMR 1.68 (s, 3H), 2.49 (s, 3H), 2.99 (AB system J = 14.3 Hz, 2H), 3.61 (s, 3H), 7.28–7.58 (m, 5H) δ.

Ene Adduct 30. In $CDCl_3$ solution compound **30** was present as a ketone/enol mixture in a 1:4 ratio. The following spectroscopic data refer to the enolic form; an asterisk indicates common signals: ^1H NMR 1.96 (s, 3H), 3.61–3.62 (m, 2H)*, 3.65 (s, 3H); 4.95–4.96 and 5.38–5.39 (broad AB system, 2H), 7.28–7.58 (m, 5H)*, 13.41 (s, 1H) δ; ^1H NMR ketonic form 2.27 (s, 3H), 3.80 (s, 3H), 4.15 (s, 1H), 5.27–5.28 and 5.50-5.51 (broad AB system, 2H) δ; MS m/z (rel int) 264 ($M^{\bullet+}$, 2), 222 (21), 105 (62), 77 (59), 43 (100). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.46; H, 6.39.

Ene adduct 32: 64% yield; yellow oil; ^1H NMR 1.33 (s, 6H), 1.89 (m, 3H), 2.35 (s, 6H), 4.65 (bs, 1H), 4.69–4.74 (m, 1H), 17.45 (s, 1H) δ; ^{13}C NMR 20.15 (q), 24.6 (q), 27.0 (q), 53.4 (s), 103.5 (s), 111.8 (t), 148.0 (s), 199.5 (s) δ; MS m/z (rel int) 214 ($M^{\bullet+}$, 8), 132 (28), 83 (100). Anal. Calcd for $C_{11}H_{18}O_2S$: C, 61.65; H, 8.46. Found: C, 61.37; H, 8.52.

Ene adduct 34: 51%; oil; ^1H NMR 0.83 (s, 3H), 1.30 (s, 3H), 1.10 (d, J = 8.2 Hz, 1H), 2.00–2.45 (m, 5H), 2.42 (s, 6H), 3.05–3.25 (m, 2H), 5.35–5.45 (m, 2H), 17.04 (s, 1H) δ; ^{13}C NMR 24.6 (q), 21.2, 26.2 (q), 31.4, 31.7 (t), 38.1 (s), 43.6 (t), 40.3, 45.4 (d), 104.9 (s), 121.2 (d), 143.1 (s), 197.2 (s) δ; MS m/z (rel int) 266 ($M^{\bullet+}$, 5), 248 (13), 223 (13), 135 (18), 91 (100). Anal. Calcd for $C_{15}H_{22}O_2S$: C, 67.63; H, 8.32. Found: C, 67.32; H, 8.43.

Ene Adduct 35. In $CDCl_3$ solution compound **35** was present as a ketone/enol mixture in a 1:4 ratio. The following spectroscopic data refer to the enolic form; an asterisk indicates common signals: ^1H NMR 0.81 (s, 3H)*, 1.04 (d J = 8.0 Hz, 1H), .28 (s, 3H)*, 2.30 (s, 3H), 2.00–2.48 (m, 5H)*, 2.97–3.40 (m, 2H)*, 3.78 (s, 3H), 5.25–5.50 (m, 1H)*, 14.15 (s, 1H) δ; ketonic form 1.10 (dd, J = 8.0 and 2,7 Hz, 1H), 2.34 (s, 3H), 3.83 (s, 3H); MS m/z (rel int) 282 ($M^{\bullet+}$, 4), 166 (17), 134 (25), 119 (33), 91 (94), 43 (100). Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.28; H, 7.53. Found: C, 65.33; H, 7.34.

1-[6-Ethoxy-1′-ethoxy-5,6-dihydro-2-methyl-5-vinylidene-1,4-oxathiin-3-yl]ethanone (37): 42% yield; oil as 79:21 of diastereoisomers. The following spectroscopic data refer to the major isomer; an asterisk indicates coincident signals: ^1H NMR 1.21 (t, J = 7.0 Hz, 3H), 1.37 (d, J = 5.6 Hz, 3H), 2.28 (s, 3H)*, 2.32 (s, 3H)*, 3.80–4.60 (m, 2H)*, 5.07 (q, J = 5.6 Hz, 1H), 5.37 (bs, 2H), 5.66 (bs, 1H) δ; minor 1.20 (t, J = 7.00 Hz, 3H), 1.43 (d, J = 5.4 Hz, 3H), 4.99 (q, J = 5.4 Hz, 1H); 5.31 (bs, 1H), 5.34 (bs, 1H), 5.70 (bs, 1H) δ; MS m/z (rel int) 258 ($M^{\bullet+}$, 1.2), 186 (25), 169 (21), 73 (100). Attempts to further characterize compound **37** were unsuccessful. Unsaturated aldehyde **38** was obtained after oxathiin **37** stood in $CDCl_3$ for 120 h at rt.

Unsaturated aldehyde 38: 63% yield; yellow oil; ^1H NMR 2.29 (s, 6H), 5.82 (d, J = 1.2 Hz, 1H), 6.15 (d, J = 1.2 Hz, 1H), 9.67 (s, 1H), 17.31 (s, 1H) δ; MS m/z (rel int) 186 ($M^{\bullet+}$, 10), 144 (13), 43 (100).

Propenoylsilane (40): 64% yield; yellow-green oil; IR 2957, 1739, 1603, 1222, cm^{-1}; ^1H NMR 0.32 (s, 9H), 2.25 (s, 6H), 5.59 (d, J = 1.7 Hz, 1H), 6.14 (d, J = 1.7 Hz, 1H) δ; MS m/z (rel int) 258 ($M^{\bullet+}$, 0.15), 243 (5), 225 (10), 73 (100). Anal. Calcd for $C_{11}H_{18}O_3SSi$: C, 51.13; H, 7.02. Found: C, 51.41; H, 6.83.

1,4-Bisoxathiin (43): 91% yield; white solid; mp 79–80 °C (n-hexane); ^1H NMR 1.25 (t, J = 7.0 Hz, 3H), 2.31 (s, 6H), 2.32 (s, 6H), 3.96 (q, J = 7.0 Hz, 2H), 4.38 (s, 1H) δ; ^{13}C NMR 15.0 (q), 21.2 (q), 30.0 (q), 38.1 (d), 59.6 (t), 105,1 (s), 105.8 (s), 154.3 (s), 194.6 (s) δ; MS m/z (rel int) 330 ($M^{\bullet+}$, 6), 288 (29), 209 (100). Anal. Calcd $C_{14}H_{18}O_5S_2$: C, 51.31; H, 5.49. Found: C, 51.14; H, 5.13.

5,6-Dihydro-3,4-dimethoxy-6,6-diacetyl-2*H*-thiopyran (46): 88% yield; yellow oil; ^1H NMR 2.28 (s, 6H), 2.78 (bt, J = 2.0 Hz, 2H), 3.03 (bt, J = 2.0 Hz, 2H), 3.59 (s, 3H), 3.69 (s, 3H) δ; MS m/z (rel int) 244 ($M^{\bullet+}$, 9), 171 (50), 43 (100). Due to the instability showed, no further analyses were carried out on derivative **46**, which was directly used to obtain bicyclic derivative **48**.[25]

5,6-Dihydro-3,4-dimethoxy-6-acetyl-6-(carboxymethyl)-2*H*-thiopyran (47): 50% yield; oil; ^1H NMR 2.33 (s, 3H), 2.83 (AB part of an apparent ABX_2 system $J_{AX} = J_{BX}$ = 2.0 Hz, J_{AB} = 16.4 Hz, 2H), 3.07 (X_2 part of an apparent ABX_2 system, t, $J_{AX} = J_{BX}$ = 2.0 Hz, 2H), 3.50 (s, 3H), 3.66 (s, 3H), 3.81 (s, 3H)δ; MS m/z (rel int) 260 ($M^{\bullet+}$, 21), 185 (33), 75 (77), 43 (100). Due to the instability showed, no further analyses were carried out on derivative **47**, which was directly used to obtain bicyclic derivative **49**.[25]

1-(4a,7,8,8a-Tetrahydro-2-methyl-4a,8a-dimethoxy-7,7-diacetyl-5H-thiopyrano[2,3-*c*][1,4]oxathiin-3-yl)ethanone ((4aα, 8aα)-48): 76% yield; glassy solid (72% starting from **4a** and **45**); ^1H NMR of the crude reaction mixture showed the presence of two regioisomers in a 95:5 ratio; the minor component was eliminated by column chromatography (ethyl acetate:diethyl ether:petroleum ether = 1:3:5); IR 1729, 1709, 1650, 1572, 1242 cm^{-1}; ^1H NMR 2.18 (s, 3H), 2.19 (s, 3H), 2.29 (s, 3H), 2.31 (s, 3H), 2.78 (A part of an AB system, J_{AB} = 14.7 Hz, 1H), 3.13 (X part of an XY system , J_{XY} = 14.7 Hz, 1H), 3.21 (Y part of an XY system , J_{XY} = 14.7 Hz, 1H), 3.26 (B part of an AB system, J_{AB} = 14.7 Hz, 1H), 3.38 (s, 3H), 3.46 (s, 3H) δ; ^{13}C NMR 20.4 (q), 26.3, 26.6 (q), 29.6 (q), 32.4 (t), 35.8 (t), 50.0 (q), 52.0 (q), 71.9 (s), 82.9 (s), 97.3 (s), 107.6 (s), 152.2 (s), 194.7 (s), 199.4, 120.1 (s) δ; MS m/z (rel int) 374 ($M^{\bullet+}$, 0.5), 244 (100), 201 (99), 169 (98), 42 (95). Anal. Calcd for $C_{16}H_{22}O_6S_2$: C, 51.32; H, 5.92. Found: C, 51.56; H, 6.08.

Methyl 1-(4a,7,8,8a-tetrahydro-2-methyl-4a,8a-dimethoxy-7-acetyl-7-(carboxymethyl)-5*H*-thiopyrano[2,3-*c*][1,4]-oxathiin-3-yl)formate ((4aα,8aα)-49): 66% yield (60% from **4b** and **45**); white solid; mp 150–152 °C (methanol); ^1H NMR 2.20 (s, 3H), 2.97 (s, 3H), 2.80 (A part of an AB system, J_{AB} = 14.2 Hz, 1H), 3.10 (B part of an AB system, J_{AB} = 14.2 Hz, 1H), 3.12 (X part of an XY system, J_{XY} = 15.0 Hz, 1H), 3.38 (s, 3H), 3.45 (Y part of an XY system, J_{XY} = 15.0 Hz, 1H), 3.47 (s, 3H), 3.70 (s, 3H), 3.82 (s, 3H) δ; ^{13}C NMR 20.0 (q), 25.6 (q), 33.0 (t), 35.1 (t), 49.7, 53.4 (q), 52.1, 52.3 (q), 64.3 (s), 82.3 (s), 164.7 (s), 168.9 (s), 197.0 (s) δ; MS m/z (rel int) 375 (M − 31, 4), 260 (100). Anal. Calcd for $C_{16}H_{22}O_8S_2$: C, 47.28; H, 5.45. Found: C, 46.64; H, 5.70.

Oxathiolene (54): 70%; colorless oil; IR 2954, 1715, 1586, 1225 cm^{-1}; ^1H NMR 2.22 (s, 3H), 2.23 (s, 3H), 3.73 (s, 3H), 5.78 (dd, J = 11.4, 1.4 Hz, 1H), 6.56 (dd, J = 11.4, 7.4 Hz, 1H), 7.23 (dd, J = 7.4, 1.4 Hz, 1H) δ; ^{13}C NMR 15.2 (q), 30.5 (q), 51.8 (q), 82.1 (d), 111.6 (s), 119.0 (d), 145.9 (d), 158.4 (s), 165.6 (s), 191.2 (s) δ; MS m/z (rel int) 228 ($M^{\bullet+}$, 40), 169 (17), 98 (100). Anal. Calcd for $C_{10}H_{12}O_4S$: C, 52.62; H, 5.30. Found: C, 52.46; H, 5.27.

General Procedure for Oxidation to Sulfoxides and Sulfones Using *m*-CPBA. Oxidation to sufoxides was obtained by adding 1 equiv of m-CPBA to a solution of oxathiin in CH_2Cl_2 at −18 °C. The mixture was kept for 1 h at −18 °C, quenched using 10% sodium metabisulfite solution, diluted with CH_2Cl_2, and washed with saturated Na_2CO_3 (3 × 50 mL) and water (2 × 50 mL). Evaporation of the solvent gave the crude sulfoxides which were purified by flash chromatography (eluent CH_2Cl_2:methanol). For the preparation of sulfones 2.2 equiv of m-CPBA was used and the reaction mixture kept at rt for 12 h. The same procedure was used to isolated the sulfones.

Sulfone 55: 63% yield; white solid; mp 87–90 °C; IR 2980, 1722, 1588, 1235 cm^{-1}; ^1H NMR 2.47 (s, 3H), 2.49 (s, 3H), 3.82 (s, 3H), 5.98 (dd, J = 11.3, 7.3 Hz, 1H), 6.35 (dd, J = 11.3, 1.4

Hz, 1H), 6.66 (dd, J = 1.4, 7.3Hz, 1H) δ; ^{13}C NMR 17.9 (q), 29.4 (q), 52.4 (q), 88.1 (d), 117.1 (s), 128.4 (d), 134.6 (d), 165.3 (s), 174.9 (s), 188.3 (s) δ; MS m/z (rel int) 261 ($M^{\bullet+}$, 14), 228 (12), 137 (42), 67 (100). Anal. Calcd for $C_{10}H_{12}O_6S$: C, 46.15; H, 4.65. Found: C, 46.53; H, 4.27.

1-(2-Methyl-*S*-oxo-4a,5,6,8a-tetrahydro-7*H*-pyrano[2,3-*b*][1,4]oxathiin-3-yl)ethanone (4aα,8aα)-57): 71% yield; pale yellow solid; IR 2924, 1674, 1534, 1261, 1026 cm^{-1}; ^{1}H NMR 1.00–1.26 (m, 2H), 1.69–2.01 (m, 2H), 2.49 (s, 3H), 2.55 (s, 3H), 3.24 (ddd, J = 2.8, 3.7, 13.6 Hz, 1H), 3.89–4.04 (m, 2H), 5.79 (d, J = 2.8 Hz, 1H) δ; ^{13}C NMR 17.7, 23.8 (t), 22.8 (q), 29.4 (q), 51.6 (d), 61.5 (t), 90.9 (d), 114.2 (s), 171.0 (s), 194.3 (s) δ; MS m/z (rel int) 128 (M − 102, 10), 84 (38), 43 (100). Anal. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13. Found: C, 51.69; H, 6.59.

Methyl 1-(2-methyl-*S*-oxo-4a,5,6,8a-tetrahydro-7*H*-pyrano[2,3-*b*][1,4]oxathiin-3-yl)formate ((4aα,8aα)-58): 89% yield; pale yellow solid; IR 2950, 1629, 1559, 1257, 1042 cm^{-1}; ^{1}H NMR 1.06–1.29 (m, 2H), 1.73–2.05 (m, 2H), 2.53 (s, 3H), 3.17 (ddd, J = 2.6, 3.6, 13.6 Hz, 1H), 3.84 (s, 3H), 3.87–3.96 (m, 2H), 5.83 (d, J = 2.6 Hz, 1C) δ; ^{13}C NMR 17.6, 23.9 (t), 21.9 (q), 51.8 (d), 52.4 (q) 61.5 (t), 91.3 (d), 106.3 (s), 164.9 (s), 171.6 (s) δ; MS m/z (rel int) 247 ($M^{\bullet+}$, 30), 163 (37), 84 (100). Anal. Calcd for $C_{10}H_{14}O_5S$: C, 48.77; H, 5.73. Found: C, 49.17; H, 5.98.

1-(2-Methyl-*S*,*S*-dioxo-4a,5,6,8a-tetrahydro-7*H*-pyrano-[2,3-*b*][1,4]oxathiin-3-yl)ethanone ((4aα,8aα)-59): 58%; pale yellow solid; IR 2926, 1682, 1545, 1429, 1254, 845 cm^{-1}; ^{1}H NMR 1.51–1.90 (m, 2H), 2.20–2.32 (m, 2H), 2.56 (s, 3H), 3.24 (ddd, J = 2.6, 4.6, 12.8 Hz, 1H), 3.36 (s, 3H), 3.86–3.92 (m, 2H), 5.57 (d, J = 2.6 Hz, 1H) δ; ^{13}C NMR 19.01 (t), 21.5 (q), 23.1 (t), 31.8 (q), 57.2 (d), 61.2 (t), 96.1 (d), 115.9 (s), 168.3 (s), 191.5 (s) δ; MS m/z (rel int) 246 ($M^{\bullet+}$, 1,6), 100 (100), 84 (97), 43 (72). Anal. Calcd for $C_{10}H_{14}O_5S$: C, 48.76; H, 5.70. Found: C, 48.37; H, 5.65.

Methyl 1-(2-methyl-*S*,*S*-dioxo-4a,5,6,8a-tetrahydro-7*H*-pyrano[2,3-*b*][1,4]oxathiin-3-yl)formate ((4aα,8aα)-60): 95% yield; pale yellow solid; mp 143–144 °C; ^{1}H NMR 1.50–1.91 (m, 2H), 2.18–2.35 (m, 2H), 2.44 (s, 3H), 3.24 (ddd, J = 2.8, 4.2, 13.0 Hz, 1H), 3.72–3.95 (m, 2H), 3.87 (s, 3H), 5.94 (d, J = 2.3 Hz, 1H) δ; ^{13}C NMR 19.54 (t), 21.5 (q), 23.7 (t), 53.2 (q), 58.1 (d), 61.9 (t), 96.9 (d), 109.0 (s), 163.2 (s), 169.7 (s) δ; MS m/z (rel int) 262 ($M^{\bullet+}$, 0.8) 230 (24), 84 (100). Anal. Calcd for $C_{10}H_{14}O_6S$: C, 45.79; H, 5.38. Found: C, 46.00; H, 5.61.

Raney Nickel Reductive Desulfuration of 8b. To a solution of 52 mg (0.23 mmol) of **8b** in 1 mL of dry ethanol was added 300 mg of Raney nickel activated following literature procedure,[30] and the mixture refluxed for 1 h. The crude reaction mixture was filtered over Celite, evaporated to dryness, and chromatographed (eluent ethyl acetate:petroleum ether = 1:5) to give the α,β-unsaturated ester **61** in 45% yield: IR 2976, 1628, 1257 cm^{-1}; ^{1}H NMR 1.50–2.10 (m, 6H), 2.32 (s, 3H), 3.66 (s, 3H), 3.50–3.87 (m, 2H), 5.26–5.32 (m, 1H), 5.36 (bs, 1H) δ; ^{13}C N. M. R.: 18.5 (q), 18.6, 24.9, 29.8 (t), 50.7 (q), 62.3 (t), 94.0 (s), 95.4 (d), 168.5 (s), 169.6 (s) δ; MS m/z (rel int) 200 ($M^{\bullet+}$, 0.13), 85 (98), 67 (100). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.54; H, 8.29.

Reduction of Derivatives 8b and 7c. To a suspension of lithium aluminum hydride in dry THF kept at 0 °C was added a solution of 1 equiv of oxathiin in dry THF, and the reaction mixture maintained at 0 °C for 10 min. Saturated NH_4Cl quenching and evaporation of the solvent afforded the crude alcohols which were purified by column chromatography.

4a,5,6,8a-Tetrahydro-2-methyl-3-(2′-hydroxyethyl)-7*H*-pyrano[2,3-*b*][1,4]oxathiin (62): 85% yield; yellow oil; IR 3408, 2949, 1649, 1225 cm^{-1}; ^{1}H NMR 1.67 (s, 1H, OH), 1.70–1.95 (m, 4H), 1.97 (s, 3H), 3.05–3.14 (m, 1H), 3.62-3.92 (m, 2H), 4.08–4.23 (AB system, J_{AB} = 12.6 Hz, 2H), 5.37 (d, J = 2.6 Hz, 1H) δ; ^{13}C NMR 17.4 (q), 24.9, 25.6 (t), 36.5 (d), 61.0 (t), 62.2 (t), 94.0 (d), 98.1 (s) 144.2 (s) δ; MS m/z (rel int) 202 ($M^{\bullet+}$, 100), 84 (98), 43 (96). Anal. Calcd for $C_9H_{14}O_3S$: C, 53.54; H, 6.97. Found: C, 53.16; H, 6.93.

4a,5,6,8a-Tetrahydro-2-methyl-3-(1′-hydroxyethyl)-7*H*-pyrano[2,3-*b*][1,4]oxathiin (63): 81% overall. 1H NMR analysis showed the formation of two diastereoisomeric alcohols in 74:26 ratio; flash chromatography (eluent ethyl acetate: n-hexane = 1:2) allowed the separation of the alcohols. Major isomer: IR 3438, 2929, 1643, 1436, 1224, 1080; ^{1}H NMR 1.32 (d, J = 6.5 Hz, 3H), 1.63–1.94 (m, 4H), 1.98 (s, 3H), 3.01–3.12 (m, 1H), 3.58–3.96 (m, 2H), 4.62–4.76 (m, 1H), 5.37 (d, J = 2.6 Hz, 1H); ^{13}C NMR 17.5 (q), 22.0 (q), 24.9 (t), 25.1 (t), 35.5 (d), 60.6 (t), 66.2 (d), 94.0 (d), 102.6 (s), 142.7 (s); MS m/z (rel int) 216 ($M^{\bullet+}$, 1), 198 (40), 97(26), 84 (100). Minor isomer: IR 3438, 2927, 1647, 1439, 1225, 1081; ^{1}H NMR 1.34 (d, J = 6.4 Hz, 3H), 1.68–1.88 (m, 4H), 1.92 (s, 3H), 2.98–3.10 (m, 1H), 3.58–3.96 (m, 2H), 4.70–4.85 (m, 1H), 5.38 (d, J = 2.6 Hz, 1H) δ; ^{13}C NMR 17.45 (q), 22.2 (q), 25.0 (t), 25.1 (t), 35.1 (d), 60.6 (t), 67.9 (d), 94.1 (d), 103.2 (s), 141.1 (s); MS m/z (rel int) 216 ($M^{\bullet+}$, 11), 198 (71), 97(10), 84 (100). Anal. Calcd for $C_{10}H_{16}O_3S$: C, 55.53; H, 7.46. Found: C, 55.26; H, 7.33.

2-Methoxy-3-[(2′,4′-dioxopentyl)thio]-2,3,4,5-tetrahydropyran (64). To a solution of 146 mg (0.68 mmol) of **7c** in 6 mL of dry CH_2Cl_2 were added methanol (140 μL) and 11.7 mg (0.07 mmol) of p-toluenesulfonic acid. The reaction mixture was kept at rt for 34 h and then diluted with CH_2Cl_2 (30 mL), washed with saturated Na_2CO_3 (2 × 30 mL) and water (2 × 30 mL), and dried over anhydrous Na_2SO_4. Evaporation of the solvent and column chromatography (eluent ethyl acetate: petroleum ether = 1:4) afforded derivative **64** (98%) as a colorless oil: IR 2940, 1587 cm^{-1}; ^{1}H NMR 1.40–1.80 (m, 2H), 2.00–2.20 (m, 2H), 2.43 (s, 6H), 2.56–2.76 (m, 1H), 3.41 (s, 3H), 3.45–3.85 (m, 2H), 4.30 (d, J = 4.8 Hz, 1H), 17.16 (s, 1H) δ; ^{13}C NMR 23.5, 26.2 (t), 24.7 (q), 48.7 (d), (q), 62.7 (t), 102.6 (d), 103.4 (s), 197.7 (s) δ; MS m/z (rel int) 246 ($M^{\bullet+}$, 2), 214 (51), 115(30), 83 (55), 43 (100). Anal. Calcd for $C_{11}H_{18}O_4S$: C, 53.64; H, 7.36. Found: C, 53.79; H, 7.63.

Isoxazole (65). A solution of 16 mg (0.06 mmol) of pyran **64** and 5 mg (0.07 mmol) of $NH_2OH{\cdot}HCl$ in 3 mL of methanol was refluxed for 3 h. The mixture was allowed to reach room temperature, and 20 mL of CH_2Cl_2 was added. The organic phase was washed with saturated $NaHCO_3$ (2 × 30 mL) and water (2 × 30 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent and flash chromatography (eluent ethyl acetate:petroleum ether = 1:5) afforded isoxazole **65** (45%) as 1:1 mixture of *cis* and *trans* stereoisomers. The following spectroscopic data refer to the mixture of epimers; clearly separated signals have been tentatively attributed: IR 2932, 1585, 1398 cm^{-1}; ^{1}H NMR 1.44–2.13 (m, 4H), 2.29 (s, 3H), 2.45 (s, 3H), 2.68–2.85 (m, 1H), 3.40 (s, 3H, *trans*), 3.41 (s, 3H, *cis*), 3.44–3.96 (m, 2H), 4.25 (d, J = 4.8 Hz, 1H, *trans*) 4.62 (d, J = 3.0 Hz, 1H, *cis*) δ; MS m/z (rel int) 243 ($M^{\bullet+}$, 31), 212 (6), 183 (11), 112 (23), 71 (42), 43 (100). Anal. Calcd for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.04; N, 5.76. Found: C, 54.58; H, 7.15; N, 5.52.

Isoxazole (66). Following exactly the procedure described for the synthesis of **65**, but using absolute ethanol as solvent, derivative **66** was isolated in 74% yield as 1:1 mixture of *cis* and *trans* stereoisomers. The following spectroscopic data refer to the mixture of epimers; clearly separated signals have been tentatively attributed: IR 2929, 1590, 1401 cm^{-1}; ^{1}H NMR 1.19 (t, J = 6.9 Hz, 3H, *trans*), 1.26 (t, J = 6.9 Hz, 3H, *cis*), 1.40–2.15 (m, 4H), 2.28 (s, 3H), 2.44 (s, 3H), 2.69–2.81 (m, 1H), 3.37–3.58 (m, 2H), 3.68–3.95 (m, 2H), 4.35 (d, J = 5.0 Hz, 1H, *trans*), 4.75 (d, J = 3.2 Hz, 1H, *cis*) δ. ^{13}C NMR 10.4, 10.4, 11.6, 11.6, 14.9, 15.0 (q), 23.4, 23.9, 26.1, 26.8 (t), 48.1, 49.9 (d), 59.0, 62.9, 63.1, 63.6 (t), 97.4, 101.3 (d), 105.3, 105.8 (s), 162.4, 162.6 (s), 172.8, 172.9 (s) δ; MS m/z (rel int) 257 ($M^{\bullet+}$, 9), 212 (5), 183 (17), 155 (44), 43 (100). Anal. Calcd for $C_{12}H_{19}NO_3S$: C, 56.01; H, 7.44; N, 5.44. Found: C, 55.86; H, 7.58; N, 5.02.

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Supporting Information Available: ORTEP diagrams for compounds **49** and **55** (2 pages).

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