oxy-Cope [3,3] rearrangement and the other from a fragmentation reaction. Thus the kinetic data could not be used for this compound since there were two competing reactions occurring at the same time. After the rearrangement the sample was separated via HPLC using 6% ethyl acetate/hexane. ^{1}H NMR (C_6D_6) δ 7.36 (apparent dd, 2 H, J = 8.3, 1.5 Hz), 6.95 (m, 3 H), 4.79 (d, 1 H, J = 8.3 Hz), 3.88 (dd, 1 H, J = 8.8, 4.9 Hz), 2.48 (m, 2 H), 2.27 (m, 1 H), 2.16 (ddd, 1 H, J = 14.0, 12.2, 3.9 Hz), 1.85 (ddd, 1 H, J = 13.1, 9.5, 3.9 Hz), 1.52 (m, 2 H), 1.46 (s, 3 H), 0.74 (d, 3 H, J = 5.9 Hz). IR (neat) 3060 (w), 2960 (s), 2930 (s), 2870 (m), 1700 (s), 1580 (w), 1450 (m), 1430 (m), 1090 (m), 730 (m), 680 cm^{-1} (m). MS (70 eV), m/e 260 (M^+), 151, 135, 124 (base), 109, 107, 81, 55. The fragmentation product was not conclusively identified.

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Internal Thioaldehyde Trapping by Enes and Dienes

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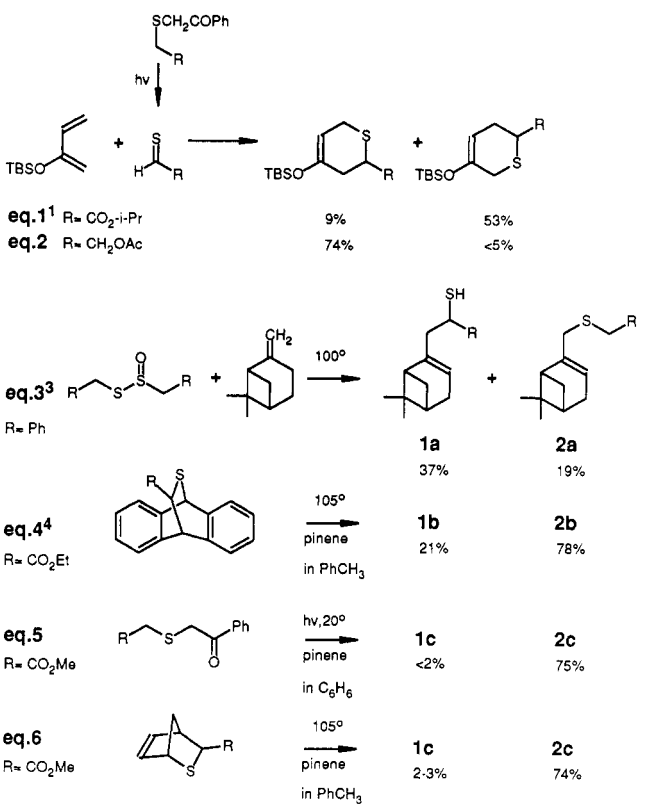
Intermolecular ene insertion of photochemically generated thioaldehyde $MeO_2CCH{=}S$ with β-pinene occurs at room temperature to give the sulfide **2c**. The internal ene insertion of thioaldehyde **6** affords a six-membered carbocycle **9** rather than the seven-membered sulfide **10** which would correspond to the regiochemistry of the intermolecular process (eq 5, 6). Likewise, internal Diels–Alder trapping occurs without a dominant role for the regiochemical preferences seen in intermolecular reactions. Desulfurization of typical internal adducts such as **25,26** or **29,30** affords **31** and **33,34**, respectively.

The synthetic potential of thioaldehydes as reactive carbon bond forming agents has been demonstrated in a variety of intermolecular Diels–Alder reactions.[1,2] There are also some isolated examples of internal Diels–Alder cyclizations, and of intermolecular ene insertions where the thioaldehyde is involved in the generation of carbon bonds.[3,4] We have been interested in the regiochemistry of these processes since the discovery that alkanethials undergo the Diels–Alder reaction with reversed selectivity compared to α-oxo thioaldehydes.[1,5] The typical examples in eq 1 and 2 (Chart I) show that the inherent preferences of electron-deficient thioaldehydes are markedly different from those of the alkanethials, properties that have been attributed to a reversal in LUMO polarization in the C=S group.[5] It was of interest to determine whether the same behavior would be observed in ene insertions as well as in Diels–Alder reactions, and how these preferences would respond to tethering the thioaldehyde and alkene units.

While this work was in progress, two groups reported examples of thermal thioaldehyde generation in the presence of ene substrates. Baldwin and Lopez described the insertion of thiobenzaldehyde into β-pinene (eq 3),[3] while Kirby et al. obtained an ene product from the thermolysis of an anthracene–thioaldehyde adduct (eq 4).[4]

Experiments in our laboratory had failed to detect any ene insertion products from the relatively stable thiopivaldehyde[6] with β-pinene. Likewise, photochemical generation of other alkanethials from phenacyl sulfides gave only decomposition products at room temperature.[1] On the other hand, ene insertion products were formed when the more reactive $CH_3O_2CCH{=}S$ was generated photochemically from the phenacyl sulfide (eq 5). This experiment gave 75% of the allyl sulfide **2c**, but the isomeric mercaptan **1c** was not formed (<2%). For comparison, we

Chart I



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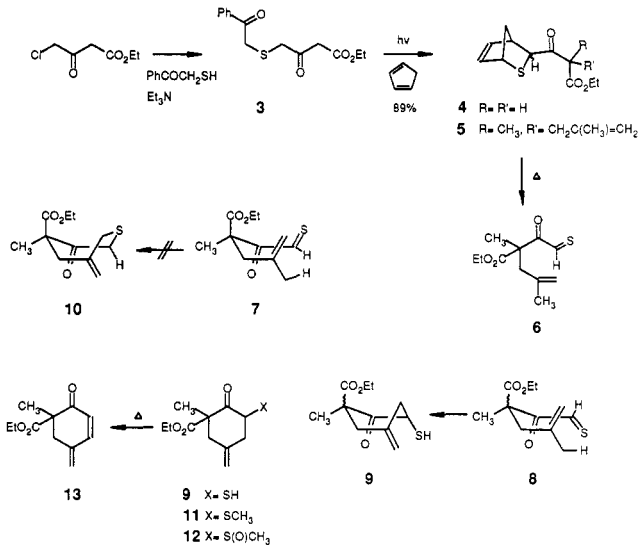

Figure 1.

also examined a thermal route to the same thioaldehyde. Pyrolysis of the readily available thioaldehyde–cyclopentadiene adducts is a convenient source of many thioaldehydes (eq 6),[7] and in the case of $CH_3O_2CCH{=}S$, insertion products were obtained at 105 °C in the presence of β-pinene. In this experiment, the mercaptan **1c** was present in trace amounts (ca. 2%), but **2c** was again the preponderant product (74%). Prolonged heating changed the product ratio only slightly (94:6 **2c**:**1c** after 10 h, toluene reflux). Therefore, it is unlikely that equilibration of the ene insertion products can explain the differences in product ratio between eq 4, 5, and 6. We have also compared the thermolysis of the anthracene adduct of $CH_3O_2CCH{=}S$ with the results of eq 5 and 6 and have observed essentially the same product ratios as reported by Kirby et al. for the ethyl ester.[4] The differences are real, but their origin remains obscure. The increased formation of mercaptan products from the anthracene adduct (eq 4) is apparently due to some other competing mechanism, perhaps involving single-bond cleavage of the thioaldehyde percursor. In any event, the results of eq 5 and 6 are consistent and demonstrate that ene insertion to form sulfide products is strongly favored for the CH_3O_2CCHS reaction. The reversal of ene insertion regiochemistry compared to eq 3 can be attributed to the LUMO polarization differences mentioned earlier.[5] The same regiochemical result and similar yields were observed when methylenecyclohexane was used in place of the β-pinene. However, other alkenes (cyclohexene, 2-methyl-2-butene, 1-methylcyclopentene, methylenenorbornene) gave low yields of insertion products.

Given the preference for the formation of sulfide products, a tethered system was designed where the formation of sulfide vs mercaptan would involve a choice between products having seven-membered vs six-membered rings (Figure 1). The phenacyl sulfide **3** was prepared from the corresponding chloroacetoacetate ester and phenacyl mercaptan,[1] and photolysis in the presence of cyclopentadiene gave the adduct **4** in 89% yield. Conventional alkylation produced the desired ene substrate **5**.

The corresponding thioaldehyde **6** has a choice of several bicyclic transition states. Two of these (**7** and **8**) are relatively free of bond-angle strain, and the previously observed preference for sulfide formation in the intermolecular reaction suggests that **7** might be the favored transition state. However, the thermal reaction at 140 °C favored the mercaptan pathway and gave **9** as a mixture of diastereomers (62% yield). None of the isomeric sulfide product **10** was detected. This observation suggests that the inherent regiochemical preference of the α-oxo thioaldehyde is easily overcome by conformational factors, and the pathway leading to the six-membered ring **9** is favored. However, we cannot rule out the intervention of other mechanisms in this case, such as the single bond cleavage process mentioned earlier. To confirm the structure of **9**, the substance was subjected to a desulfurization procedure. Thus, conversion to the sulfide **11** and sulfoxide **12** followed by thermal elimination[8] at 110 °C afforded the unusual dienone **13** in 52% yield.

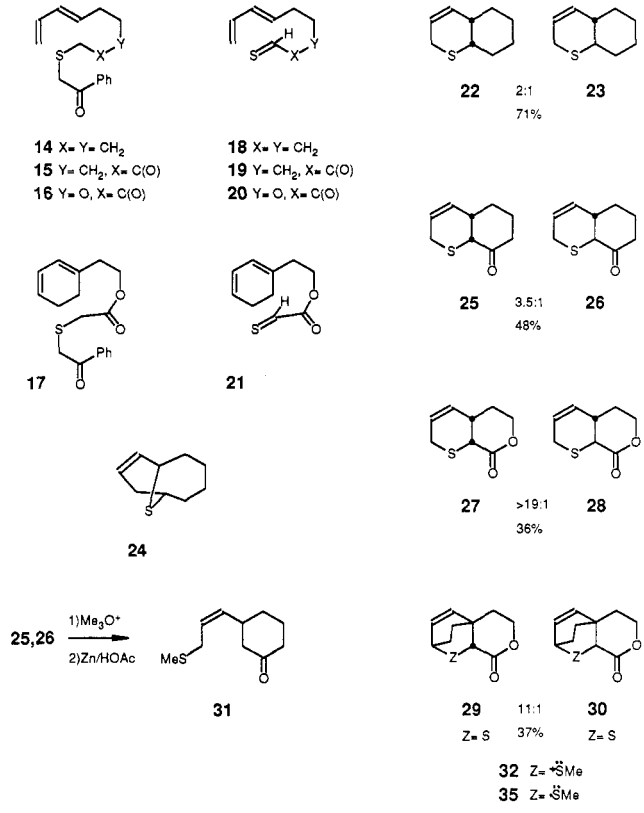

Figure 2.

Investigation of thioaldehydes containing tethered dienyl units suitably placed for (2 + 4) cycloaddition[3] provided further evidence that regiochemical preferences are easily overcome by conformational constraints. Several phenacyl sulfides were prepared from the halides as shown in Figure 2. The corresponding thioaldehydes were generated as usual by photolysis[1] and afforded internal Diels–Alder cycloadducts. Three of the four examples (thioaldehydes **19**–**21**) gave modest yields of adducts, but with regiochemistry that corresponds to the analogous intermolecular reactions (eq 1). In the case of thioaldehyde **18**, the yield is significantly improved even though the regiochemistry is opposite to that seen in the simple (nontethered) system of eq 2. No evidence for the bridged bicyclic adduct **24** which would correspond to the regiochemistry of eq 2 was detected. In all cases, the major products were derived from "endo" transition states, the same result that is seen in the intermolecular analogues.[7]

Two of the internal Diels–Alder adducts were subjected to reductive desulfurization conditions to demonstrate the

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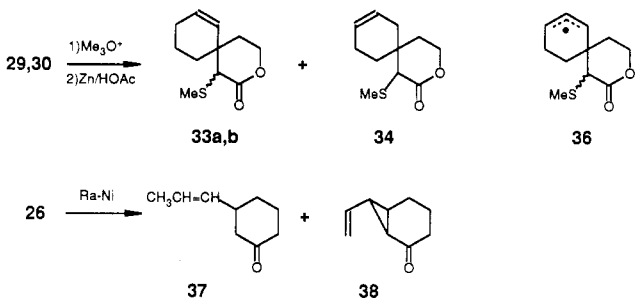

Figure 3.

synthetic potential of this approach. Thus, treatment of **25** + **26** with trimethyloxonium tetrafluoroborate followed by zinc/acetic acid reduction afforded the β-substituted cyclohexanone **31** (60%). When this sequence was applied to the mixture of **29** and **30**, the result proved more surprising (Figure 3). Instead of cleaving the C–S bond α to ketone in the sulfonium salt **32**, the zinc reduction step produced products **33** and **34** from the cleavage of an allylic C–S bond. The structures are clear from the singlets of isolated hydrogens α to sulfur in the NMR spectra of the products and from the coupling patterns of olefinic protons. This unusual cleavage pathway suggests that electron transfer involves empty sulfonium rather than carbonyl orbitals. The resulting sulfur-centered radical **35** is potentially capable of breaking a C–S bond α to the carbonyl group, or the C–S bond next to the carbon–carbon double bond. The latter pathway dominates, probably because geometric constraints place the α C–S bond nearly in the carbonyl plane, and orthogonal to the lactone π-system. According to molecular models, the allylic C–S bond is more nearly aligned with the neighboring olefinic π-orbitals, and cleavage to the allylic radical **36** is the kinetically favored pathway.

As expected, desulfurization of the Diels–Alder adducts with Raney nickel (Ra-Ni) afforded sulfur-free products. This pathway has not been explored in detail, but it is worth noting that Ra-Ni desulfurization can produce cyclopropanes. Thus, **26** gave a ca. 3:2 ratio of **37**:**38** (40–50% combined) in the presence of deactivated Ra-Ni in acetone.

In conclusion, the internal trapping of thioaldehydes by ene insertion or Diels–Alder addition provides access to cyclic structures under mild conditions. A new carbon bond is formed at room temperature by using the photochemical method of thioaldehyde generation, and conventional desulfurization techniques allow the synthesis of carbocyclic or lactonic products.

Experimental Section

Dry reaction solvents were obtained as follows: ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone; chlorocarbons and benzene were distilled from P_2O_5; toluene was distilled from CaH_2. Hexane and workup solvents were flash distilled from bulk sources. Amines were distilled from CaH_2 or BaO.

Chromatography was performed in five media: analytical thin-layer chromatography was performed on precoated Merck EM silica gel 60F-254 plates; column chromatography was done with Davisil 62 60–200-mesh silica gel, and elution solvents were identical with those in the analytical TLC unless otherwise stated; flash chromatography was performed on Merck EM silica gel 60 230–400 mesh; perparative TLC was done on Merck EM silica gel 60 PF-254 plates, 2 mm thick; high-performance liquid chromatography (HPLC) was performed by using an LDC Constametric II pump, Whatman Partisil M9 10/50 column, and Waters Associates differential refractometer detector.

In the following experimental descriptions, photolysis reactions were all performed in an apparatus consisting of a simple 275-W sun lamp under a Pyrex water bath filled with a 6% aqueous $CuSO_4$ solution with a tap-water cooling coil to keep temperatures under 28 °C. The reaction flasks were purged with N_2 prior to starting and were stirred magnetically. The entire apparatus was covered with foil to maximize efficiency.

Thioaldehyde Ene Reaction: Typical Procedure. Synthesis of 2c by Photolysis. Carbomethoxymethyl phenacyl sulfide[1] (1.19 g, 5.30 mmol) was dissolved in 6 mL of dry, distilled benzene, and an equal volume (37.8 mmol) of β-pinene (fractionally distilled) was added. The solution was photolyzed as described above for 7 h, at which time TLC showed completion of the reaction. No TLC spot tested positive for thiol with Aldrithiol-2/acetone. The reaction mixture was evaporated and separated by flash chromatography to afford the product **2c** (949 mg, 3.95 mmol, 75%) as an oil, separated on silica gel 60 F254, 10% ethyl acetate/hexane: R_f 0.46; m/e, exact mass calcd for $C_{13}H_{20}O_2S$ 240.1179, found 240.1183, error = 1.6 ppm; IR ($CDCl_3$, cm^{-1}) 1740 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 5.47–5.40 (1 H, m), 3.71 (3 H, s), 3.21 (1 H, dd, J = 13.4, 1.1 Hz), 3.13 (2 H, s), 3.08 (1 H, dd, J = 13.4, 1.3 Hz), 2.44–2.07 (5 H, m), 1.27 (3 H, s), 1.09 (1 H, d, J = 8.6 Hz), 0.81 (3 H, s).

From Thermolysis of the Cyclopentadiene Adduct. The previously described cyclopentadiene adduct of methyl thioglyoxylate[1] was dissolved in toluene to make a 0.051 M solution. Two flasks were each charged with 2-mL aliquots (0.102 mmol), and one was treated with 15 μL (0.10 mmol) of β-pinene, while to the other was added 1.00 mL (6.31 mmol) of pinene. The flasks were refluxed for 20 h and then cooled. An NMR spectrum of the evaporated crude mixtures showed 78% conversion in the first case and 100% in the second, with the major product in each case being sulfide **2c**, and a very minor amount (<5%) of the two diastereomers of methyl mercapto(2-pinen-10-yl)acetate **1c**. Flash chromatography as above then afforded 11.9 mg (52%) of ene product **2c** from the first reaction and 17.9 mg (74%) from the second.

From Thermolysis of the Anthracene Adduct. The method of Kirby[4] was used to prepare the anthracene cycloadduct of methyl thioglyoxylate. The cycloadduct (43.2 mg) and 100 μL of β-pinene were dissolved in 2 mL of toluene, and the solution was heated to reflux. The NMR spectrum of an evaporated aliquot at 1.5 h showed 80% conversion and products **2c** and **1c** in the ratio 5.5:1. At 4 h, the spectrum of another aliquot showed complete conversion to a product mixture in the ratio 6.5:1. The samples were combined, evaporated, and eluted through a plug of silica gel (hexane, then ether) to afford 36.1 mg of ene products **2c** and **1c**.

Thermal Equilibration of Ene Adduct 2c. Compound **2c** was dissolved in 0.5 mL of toluene-d_8 and heated in an NMR tube at a bath temperature of 120 °C for 10 h. NMR analysis showed the starting material and two new products in the ratio 94:3:3. The spectrum of the new products closely matched literature data[4] for the thiol ene products **1c** and tested positive with Aldrithiol spray on TLC.

Preparation of Sulfide 3. Potassium carbonate (3.38 g, 24.4 mmol) was flame-dried under vacuum and suspended in 25 mL of dry THF. Phenacyl mercaptan[1] (3.31 g, 21.7 mmol) was added, followed by a 10-mL THF solution of ethyl 4-chloroacetoacetate (2.7 mL, 20 mmol, Aldrich). After being stirred overnight, the mixture was poured into water and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and evaporated and the resulting oil separated by flash chromatography to give pure sulfide **3** (5.61 g, 20.0 mmol, 100%) as an oil: silica gel 60 F254, 20% ethyl acetate/hexane, R_f 0.16; m/e, exact mass calcd for $C_{14}H_{16}O_4S$ 280.0765, found 280.0769, error = 1.4 ppm; IR ($CDCl_3$, cm^{-1}) 1740 (C=O),1710 (C=O), 1690 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.94–7.89 (2 H, m), 7.60–7.53 (1 H, m), 7.49–7.41 (2 H, m), 4.16 (2 H, q, J = 7.2 Hz), 3.90 (2 H, s), 3.63 (2 H, s), 3.48 (2 H, s), 1.24 (3 H, t, J = 7.2 Hz).

Photolysis and Trapping of 3. The usual photolysis/trapping procedure was used. Phenacyl sulfide **3** (4.16 g, 14.8 mmol) and 12 mL (146 mmol) of freshly cracked cyclopentadiene gave, after 5.5-h photolysis and flash chromatography, 1.49 g of cycloadduct **4** as a 4.8:1 endo/exo mixture (6.59 mmol, 44%, 89% based on 2.08 g of recovered starting material). The pure endo isomer of **4** was obtained by separation onn HPLC as an oil: silica gel 60 F254, 20% ethyl acetate/hexane, R_f 0.33; m/e, exact mass calcd for $C_{11}H_{14}O_3S$ 226.066, found 226.0662, error = 0.9 ppm; IR

($CDCl_3$, cm^{-1}) 1742 (C=O), 1714 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 6.42 (1 H, dd, J = 5.6, 2.9 Hz), 5.86 (1 H, dd, J = 5.6, 3.0 Hz), 4.49 (1 H, d, J = 3.9 Hz), 4.15 (2 H, q, J = 7.1 Hz), 4.13 (1 H, br s), 3.77 (1 H, br s), 3.45 (1 H, d, J = 16.2 Hz), 3.32 (1 H, d, J = 16.2 Hz), 1.72–1.58 (2 H, m), 1.25 (3 H, t, J = 7.1 Hz).

Preparation and Ene Reaction of 5. A 10-mL DME suspension of NaH (76.4 mg, 3.18 mmol, washed with hexane) was stirred while a 2-mL DME solution of sulfide **4** (749 mg, 3.31 mmol) was added slowly by syringe. The evolution of H_2 was vigorous and immediate. The anionic solution was delivered by cannula to a DME solution of 0.30 mL of methyl iodide (4.82 mmol). After 20 min, the reaction mixture was poured into saturated aqueous NH_4Cl. The organic phase was dried over $MgSO_4$ and evaporated to afford 781 mg of the crude methylated products. They were taken up in DME and alkylated a second time with methallyl iodide (153 mg NaH, followed by addition to 0.70 mL of methallyl chloride/2.13 g of sodium iodide) in the same procedure is detailed above. Workup, filtration through a plug of silica gel (ether), and evaporation afforded 333 mg (1.13 mmol, 35%) of **5** as a mixture of diastereomers, sufficiently pure for the next step.

The sulfides **5** (270 mg, 0.92 mmol) were dissolved in 15 mL of dry, distilled toluene, and the solution was distributed in three aliquots to three 10-mm Pyrex tubes. The solutions were degassed by several freeze–pump–thaw cycles and sealed under vacuum. The tubes were heated to 140 °C for 2 h, then cooled, and opened. The contents were evaporated, and the residue was eluted on a short plug of silica gel with 20% ethyl acetate/hexane. The eluent was evaporated and separated by HPLC to afford two thiol-spray-active bands (61 mg, 0.27 mmol, 29%; and 40 mg, 0.17 mmol, 19%), which were diastereomeric ene products (**9**). The major diastereomer of **9** was an oil, analyzed by HPLC, Partisil M9, 1:1:18 CH_2Cl_2/EtOAc/hexane, flow = 5.00 mL/min, retention time = 11.8 min: m/e, exact mass calcd for $C_{11}H_{16}O_3S$ 228.0816, found 228.0817, error = 0.4 ppm; IR ($CHCl_3$, cm^{-1}) 2590 (SH), 1734 (C=O), 1718 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 4.95 (2 H, br d, J = 1.4 Hz), 4.15 (2 H, qd, J = 7.1, 1.5 Hz), 4.01 (1 H, ddd, J = 13.0, 5.5, 6.4 Hz), 3.04 (1 H, dd, J = 13.9, 2.7 Hz), 2.89 (1 H, ddd, J = 13.4, 6.4, 2.7 Hz), 2.41 (1 H, br t, J = 13.0 Hz), 2.25 (1 H, d, J = 5.5 Hz), 2.20 (1 H, dd, J = 13.9, 1.0 Hz), 1.37 (3 H, s), 1.22 (3 H, t, J = 7.1 Hz). The minor isomer of **9** was an oil, analyzed by HPLC, Partisil M9, 1:1:18 CH_2Cl_2/EtOAc/hexane, flow = 5.00 mL/min, retention time = 14.6 min: formula = $C_{11}H_{16}O_3S$; IR ($CHCl_3$, cm^{-1}) 2590 (SH), 1740 (C=O), 1719 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.02 (2 H, br s), 4.18 (2 H, q, J = 7.1 Hz), 3.88 (1 H, dt, J = 10.3, 6.0 Hz), 3.14 (1 H, br d, J = 14.0 Hz), 2.93 (1 H, dd, J = 14.0, 6.2 Hz), 2.58–2.49 (1 H, m), 2.32 (1 H, br d, J = 14.0 Hz), 2.21 (1 H, d, J = 6.0 Hz), 1.40 (3 H, s), 1.26 (3 H, t, J = 7.1 Hz).

Alkylation of Intramolecular Ene Products. A mixture of thiols **9** (41.6 mg, 182 μmol) was dissolved in 4 mL of THF under N_2 and stirred while triethylamine (39 μL, 280 μmol) and methyl iodide (13 μL, 208 μmol) were added sequentially by syringe. The mixture was stirred for 1 h, poured into water, and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and evaporated and the residue eluted on a short plug of coarse silica gel. The eluent was evaporated and separated by HPLC to afford (in order of elution) minor and major diastereomers of methyl sulfide **11**, ca. 1:2, total weight 37 mg (0.15 mmol, 84%). The major sulfide was an oil, analyzed by HPLC, Partisil M9, 1:1:18 CH_2Cl_2/EtOAc/hexane, flow = 5.00 mL/min, retention time = 15.8 min: m/e, exact mass calcd for $C_{12}H_{18}O_3S$ 242.0972, found 242.0973, error = 0.4 ppm; IR ($CHCl_3$, cm^{-1}) 1739 (C=O), 1703 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.04 (1 H, br s), 4.98 (1 H, br s), 4.19 (1 H, dq, J = 10.8, 7.2 Hz), 3.99 (1 H, dq, J = 10.8, 7.2 Hz), 3.37 (1 H, dd, J = 5.7, 3.2 Hz), 3.21 (1 H, br d, J = 14.0 Hz), 2.87 (1 H, dd, J = 14.3, 5.7 Hz), 2.58 (1 H, dd, J = 14.3, 3.2 Hz), 2.15 (1 H, d, J = 14.0 Hz), 1.98 (3 H, s), 1.36 (3 H, s), 1.22 (3 H, t, J = 7.2 Hz). The minor sulfide was an oil, analyzed by HPLC, Partisil M9, 1:1:18 CH_2Cl_2/EtOAc/hexane, flow = 5.00 mL/min, retention time = 14.0 min: m/e, exact mass calcd for $C_{12}H_{18}O_3S$ 242.0972, found 242.0982, error = 4.2 ppm; IR ($CHCl_3$, cm^{-1}) 1742 (C=O), 1710 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 4.94 (2 H, br s), 4.14 (2 H, q, J = 7.1 Hz), 3.67 (1 H, dd, J = 11.6, 6.1 Hz), 3.02 (1 H, dd, J = 14.0, 2.1 Hz), 2.89 (1 H, ddd, J = 13.8, 6.1, 2.1 Hz), 2.43–2.19 (2 H, m), 2.10 (3 H, s), 1.37 (3 H, s), 1.21 (3 H, t, J = 7.1 Hz).

Oxidation and Elimination of Sulfides 11. A mixture of diastereomeric sulfides of **11** (19.4 mg, 80 μmol) was dissolved in 5 mL of CH_2Cl_2 and cooled to −78 °C under N_2. A CH_2Cl_2 solution of *m*-chloroperoxybenzoic acid (*m*CPBA) (19.8 mg, 80–85%, >92 μmol) was then added dropwise by syringe. After about 10 min, the bath was removed and the mixture allowed to warm to 20 °C and poured into 2 mL of saturated aqueous $NaHSO_3$. The phases were separated, and the organic layer was washed with saturated aqueous Na_2CO_3, dried over $MgSO_4$, and evaporated to afford a mixture of sulfoxides **12**.

The residue (11.9 mg, 46 μmol) was dissolved in a suspension of 10 mg of $CaCO_3$ in 1 mL of toluene under N_2. This mixture was refluxed for 10 h, cooled, filtered, and evaporated. The residue was eluted on an analytical TLC plate to afford 4.6 mg (24 μmol, 52%) of dienone **13** and 2.2 mg of the starting materials. Dienone **13** was an oil: analytical TLC (silica gel F254), 10% EtOAc/hexane, R_f 0.21; m/e, exact mass calcd for $C_{11}H_{14}O_3$ 194.0939, found 194.0948, error = 4.7 ppm; IR ($CHCl_3$, cm^{-1}) 1729 (C=O), 1688 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.03 (1 H, d, J = 9.8 Hz), 5.96 (1 H, d, J = 9.8 Hz), 5.37 (1 H, s), 5.34 (1 H, s), 4.13 (2 H, q, J = 7.1 Hz), 3.22 (1 H, d, J = 14.9 Hz), 2.58 (1 H, d, J = 14.9 Hz), 1.37 (3 H, s), 1.19 (3 H, t, J = 7.1 Hz).

Preparation and Photolysis of Phenacyl Sulfides 14 and 15. (*E*)-4,6-Heptadienol. Ethyl (*E*)-4,6-heptadienoate[9] (20.1 g, 131 mmol) in 40 mL of ether was added over 15 min via cannula to a stirred suspension of lithium aluminum hydride (LAH) (Alfa, 95% reagent, 12.0 g, 300 mmol, 2.3 equiv) in 200 mL of ether at 5 °C. After the addition, the reaction vessel was equipped with a condenser and the mixture was refluxed under nitrogen (static) for 6 h and then recooled to 5 °C. In sequence were added (**carefully**!) (i) 12 mL of H_2O; (ii) 12 mL of 15% aqueous NaOH; (iii) 36 mL of H_2O; (iv) 70 g of anhydrous $MgSO_4$; and then the mixture was filtered through a Celite plug. After rotary evaporation, the residue was taken up in 25 mL of ether and rinsed through a 6 × 4 cm plug of silica gel with an additional 100 mL of ether. Rotary evaporation of the solvent left 14.7 g (100%) of the desired product, homogeneous by TLC (R_f 0.26, 30% EtOAc/hexane): liquid, bp 55–69 °C at 12 mm, short path; m/e, base = 79 amu, exact mass calcd for $C_7H_{12}O$ 112.0885, found 112.0888, error = 2.7 ppm; IR (CCl_4, cm^{-1}) 3620 (OH), 3330 (OH), 1005 (HC=CH); 270-MHz NMR ($CDCl_3$, ppm) 6.30 (1 H, dt, J = 16.5, 10.3 Hz), 6.07 (1 H, dd, J = 15.1, 10.3 Hz), 5.70 (1 H, dt, J = 15.1, 7 Hz), 5.0–9 (1 H, d, J = 16.5 Hz), 4.96 (1 H, d, J = 10.3 Hz), 3.60 (2 H, t, J = 7 Hz), 2.93 (1 H, br s), 2.16 (2 H, q, J = 7 Hz), 1.65 (2 H, p, J = 7 Hz).

1-Iodo-(*E*)-4,6-heptadiene. The alcohol from above (7.30 g, 65.2 mmol) and triethylamine (15.8 g, 21.8 mL, 156 mmol, 2.5 equiv) were combined in 300 mL of ether and cooled to −15 °C under nitrogen (flow). Mesyl chloride (14.9 g, 10.1 mL, 130 mmol, 2.0 equiv) in 20 mL of ether was added via cannula over 5 min with stirring. After 5 min at −15 °C, the mixture was warmed to room temperature and stirred for an additional 15 min and then was poured into a swirled mixture of 500 mL of ice/water and 100 mL of ether. The layers were separated, and the aqueous layer was extracted with 75 mL of ether; the combined ether layers were rinsed with 100 mL of ice-cold water and then with 50 mL of saturated aqueous NaCl and then dried over $MgSO_4$. The crude mesylate was filtered through a 6 × 4 cm plug of silica gel, and after rotary evaporation, the residue was taken up in 500 mL of acetone and sodium iodide (Fisher, 47.0 g, 313 mmol, 4.8 equiv) was added. After the flask was wrapped in aluminum foil, the mixture was stirred under static nitrogen for 20 h at 35 °C. Most of the acetone was removed by rotary evaporation, and the residue was taken up in 200 mL of ether. This solution was rinsed with 100 mL of 0.5 M aqueous $Na_2S_2O_3$ and then with 50 mL of saturated aqueous NaCl, and the organic layer was dried over $MgSO_4$. Filtration through a 6 × 4 cm plug of silica gel (rinsed with ether) gave 11.71 g (81%) of the crude iodide after rotary evaporation. Distillation gave 10.56 g (73%) of the pure iodide (R_f 0.52, 7% EtOAc/hexane): liquid, bp 55–60 °C at 3.5 mm, short path; m/e, exact mass calcd for $C_7H_{11}I$ 221.9905, found 221.9908, error = 1.3 ppm; IR (CCl_4, cm^{-1}) 1005 (HC=CH), 905 (C=CH); 270-MHz NMR ($CDCl_3$, ppm) 6.30 (1 H, dt, J = 16.7, 10.3 Hz),

(9) Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020.

6.11 (1 H, dd, J = 14.9, 10.3 Hz), 5.63 (1 H, dt, J = 14.90, 7 Hz), 5.12 (1 H, d, J = 16.7 Hz), 5.01 (1 H, d, J = 10.3 Hz), 3.19 (2 H, t, J = 7 Hz), 2.20 (2 H, q, J = 7 Hz), 1.92 (2 H, p, J = 7 Hz).

(*E*)-6,8-Nonadienol. 1-Iodo-(*E*)-4,6-heptadiene from above (2.70 g, 12.2 mmol) and magnesium powder (Fisher, 400 mg, 16.5 mmol, 1.35 equiv) were combined in 25 mL of THF, and a small crystal of iodine was added. The mixture was stirred at reflux under nitrogen (flow) for 1 h and then cooled to room temperature. This solution was added via cannula over 5 min to a stirred suspension of cuprous iodide (Alfa, 98% reagent, 348 mg, 1.83 mmol, 0.15 equiv) in 15 mL of THF at −45 °C. The unreacted magnesium metal and magnesium salts which were left behind in the original flask were rinsed with 2 × 5 mL of THF, and these rinsings were also added to the CuI suspension. After the mixture was warmed to −30 °C, ethylene oxide (Matheson, 850 mg, 19.3 mmol, 1.59 equiv), which had been previously condensed at −78 °C into a 5-mL conical flask and diluted with 4 mL of THF, was added dropwise via cannula over 15 min. During this addition, the mixture darkened and turned almost black with the concomitant formation of a very thick precipitate. The reaction mixture was warmed to 3 °C for 20 min and to room temperature for 30 min and then was poured into a stirred mixture of 250 mL of ice-cold 0.5 M aqueous HCl and 70 mL of ether. The aqueous layer was extracted with 2 × 30 mL of ether, and the combined ether layers were rinsed with saturated aqueous NaCl and dried over $MgSO_4$. Filtration through a 3 × 2 cm plug of silica gel and rotary evaporation left 1.51 g of crude product, which was taken up in 3 mL of CH_2Cl_2 and eluted through a 7 × 2 cm column of silica gel with (A) 30 mL of hexane, (B) 35 mL of 5% ether/hexane, (C) 35 mL of 10% ether/hexane, (D) 35 mL of 15% ether/hexane, (E) 30 mL of 25% ether/hexane, and (F) 40 mL of ether to give (A–C) 108 mg of high-R_f materials and (D–F) 1.194 g (70%) of pure (*E*)-6,8-nonadienol: oil; silica gel, 30% EtOAc/hexane, R_f 0.29; m/e, exact mass calcd for $C_9H_{16}O$ 140.1197, found 140.1201, error = 2.8 ppm; IR (CCl_4, cm^{-1}) 3610 (OH), 3330 (OH), 1005 (HC=CH); 270-MHz NMR ($CDCl_3$, ppm) 6.31 (1 H, dt, J = 16.9, 10.3 Hz), 6.05 (1 H, dd, J = 14.9, 10.3 Hz), 5.70 (1 H, dt, J = 14.9, 7 Hz), 5.08 (1 H, d, J = 16.9 Hz), 4.95 (1 H, d, J = 10.3 Hz), 3.62 (2 H, t, J = 7 Hz), 1.94 (1 H, br s), 1.57 (2 H, p, J = 7 Hz), 1.48–1.32 (4 h, m).

1-Iodo-(*E*)-6,8-nonadiene. The procedure was exactly as for the preparation of 1-iodo-(*E*)-4,6-heptadiene (above). The 6,8-nonadienol (728 mg, 5.2 mmol), triethylamine (1.26 mg, 12.5 mmol, 2.4 equiv), and mesyl chloride (1.19 g, 0.80 mL, 10.4 mmol, 2 equiv) reacted to give 1.14 g (100%) of the mesylate, which was treated with sodium iodide (3.14 g, 20.9 mmol, 4 equiv) in acetone to give 1.042 g of the crude iodide. Elution of this material through a 7 × 2 cm column of silica with (A) 125 mL of hexane and (B) 50 mL of ether gave (A) 972 mg (74%) of the pure iodide and (B) 56 mg of more polar materials. 1-Iodo-(*E*)-6,8-nonadiene: oil; silica gel, hexane, R_f 0.50; m/e, exact mass calcd for $C_9H_{15}I$ 250.0217, found 250.022, error = 1.2 ppm; IR (CCl_4, cm^{-1}) 1005 (HC=CH), 900 (C=CH); 270-MHz NMR ($CDCl_3$, ppm) 6.31 (1 H, dt, J = 16.7, 10.3 Hz), 6.05 (1 H, dd, J = 14.9, 10.3 Hz), 5.68 (1 H, dt, J = 14.9, 7 Hz), 5.09 (1 H, d, J = 16.7 Hz), 4.96 (1 H, d, J = 10.3 Hz), 3.18 (2 H, t, J = 7 Hz), 2.09 (2 H, q, J = 7 Hz), 1.83 (2 H, p, J = 7 Hz), 1.46–1.36 (4 H, m).

Phenacyl (*E*)-6,8-Nonadienyl Sulfide (14). The nonadienyl iodide (780 mg, 3.12 mmol), triethylamine (660 mg, 6.54 mmol, 2.05 equiv), and phenacyl mercaptan (484 mg, 3.18 mmol, 1.02 equiv) were combined in 10 mL of THF and heated to 35 °C with stirring under static nitrogen for 70 h. The solvent and excess triethylamine were removed by rotary evaporator, and the residue was rinsed through a 2 × 2 cm plug of silica gel with 50 mL of ether to give 934 mg of crude product after solvent removal. This material was purified by HPLC (M9 column, two injections, 5% EtOAc/hexane) to give the desired product (573 mg, 67%) eluting between 1.7 and 2.9 column volumes. **14**: oil; silica gel, 10% EtOAc/hexane, R_f 0.44; m/e, base = 105 amu, exact mass calcd for $C_{17}H_{22}OS$ 274.1386, found 274.1391, error = 1.8 ppm; IR (CCl_4, cm^{-1}) 1675 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.99–7.43 (5 H, m), 6.29 (1 H, dt, J = 16.9, 10.3 Hz), 6.03 (1 H, dd, J = 14.9, 10.3 Hz), 5.66 (1 H, dt, J = 14.9, 7 Hz), 5.08 (1 H, d, J = 16.9 Hz), 4.95 (1 H, d, J = 10.3 Hz), 3.77 (2 H, s), 2.55 (2 H, t, J = 7 Hz), 2.05 (2 H, q, J = 7 Hz), 1.60 (2 H, p, J = 7 Hz), 1.42–1.32 (4 H, m).

***cis*- and *trans*-5-Thiabicyclo[4.4.0]-2-decene (22 and 23).** The sulfide **14** (573 mg, 2.09 mmol) in 9 mL of 2:1 pentane/ether was added dropwise via syringe pump over 1.5 h to 100 mL of pentane which was stirred and irradiated. Photolysis was continued for another 1.5 h after the addition was complete. The solvent was removed by careful distillation (10 cm glass helices packed column equipped with a short path distillation head) at atmospheric pressure. The pot residue, initially dissolved in 1 mL of CH_2Cl_2 and then diluted with 4 mL of pentane, was eluted through a 7 × 2 cm column of silica gel with (A) 75 mL of 2% ether/hexane and (B) 25 mL of ether to give (after solvent distillation; vide supra) (A) 230 mg (71%) of a 2:1 mixture of **22** and **23** pure by NMR and (B) 254 mg of low-R_f materials. Attempts to separate the products by HPLC (M9 column, pentane) were largely unsuccessful; however, by shaving the front and back edges of the product band (which elutes at 1.3–2.7 column volumes), samples for NMR analysis could be obtained which had very little cross-contamination.

22: oil; silica gel, hexane, R_f 0.38; m/e, base = 154 amu, exact mass calcd for $C_9H_{14}S$ 154.0813, found 154.0816, error = 2 ppm; IR (CCl_4, cm^{-1}) 3015 (C=CH); 270-MHz NMR ($CDCl_3$, ppm) 5.83–5.74 (1 H, m), 5.68–5.60 (1 H, m), 3.21 (1 H, br d, J = 17.6 Hz), 3.13–3.01 (1 H, m), 3.07–3.01 (1 H, m), 2.42 (1 H, br s), 2.88–1.26 (8 H, m).

23: oil; silica gel, hexane, R_f 0.35; m/e, base = 154 amu, exact mass calcd for $C_9H_{14}S$ 154.0813, found 154.0816, error = 2 ppm; IR (CCl_4, cm^{-1}) 3015 (C=CH); 270-MHz NMR ($CDCl_3$, ppm) 5.78–5.70 (1 H, m), 5.52 (1 H, dd, J = 10.7, 1.8 Hz), 3.51 (1 H, ddt, J = 17.6, 4.0, 2.4 Hz), 2.95 (1 H, ddt, J = 17.6, 5.0, 2.2 Hz), 2.50 (1 H, td, J = 10.7, 3.3 Hz), 2.08 (1 H, br t, J = 10.7 Hz), 1.88–1.10 (8 H, m).

1-Chloro-(*E*)-6,8-nonadien-2-one. 1-Iodo-(*E*)-4,6-heptadiene (4.44 g, 20 mmol) and magnesium powder (Fisher, 583 mg, 24 mmol, 1.2 equiv) were combined in 50 mL of THF, and a small crystal of iodine was added. The mixture was stirred at reflux under nitrogen (flow) for 1 h and then cooled to room temperature. This solution was added via cannula over 5 min to a stirred mixture of chloroacetyl chloride (Aldrich, 3.84 g, 34 mol, 1.7 equiv) and approximately 100 mg of CuCl at −78 °C. After rinsing the solids which remained in the original flask with 10 mL of THF and adding this to the reaction mixture, we allowed the mixture to warm to 0 °C over 1 h. Standard aqueous workup gave the crude product, which was purified by elution through an 8 × 2 cm column of silica gel with (A) 30 mL of hexane, (B) 35 mL of 3% ether/hexane, (C) 35 mL of 10% ether/hexane, (D) 60 mL of 20% ether/hexane, and (E) 50 mL of ether to give (B, C) 2.586 g (75%) of the title ketone and (D, E) 257 mg of low-R_f materials. 1-Chloro-(*E*)-6,8-nonadien-2-one: oil; silica gel, 10% EtOAc/hexane, R_f 0.26; m/e, exact mass calcd for $C_9H_{13}OCl$ 172.0652, found 172.0654, error = 1.2 ppm; IR (CCl_4, cm^{-1}) 1715 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 6.30 (1 H, dt, J = 16.9, 10.3 Hz), 6.05 (1 H, dd, J = 14.9, 10.3 Hz), 5.64 (1 H, dt, J = 14.9, 7 Hz), 5.10 (1 H, d, J = 16.9 Hz), 4.98 (1 H, d, J = 10.3 Hz), 4.08 (2 H, s), 2.58 (2 H, t, J = 7 Hz), 2.12 (2 H, q, J = 7 Hz), 1.73 (2 H, p, J = 7 Hz).

Phenacyl 2-Oxo-(*E*)-6,8-nonadienyl Sulfide (15). Phenacyl mercaptan (1.80 g, 11.8 mmol, 1.1 equiv) and triethylamine (1.36 g, 13.5 mmol, 1.25 equiv) were combined in 40 mL of THF and cooled to 5 °C under nitrogen (flow) with stirring. The chloro ketone from the preceeding experiment (1.84 g, 10.5 mmol) in 8 mL of THF was added via syringe with concomitant formation of a precipitate. The mixture was warmed to room temperature for 16 h, diluted with 50 mL of ether, and then filtered through a 4 × 2 cm plug of silica gel. The residue after rotary evaporation was taken up in 10 mL of CH_2Cl_2 and eluted through an 8 × 2 cm column of silica gel with (A) 30 mL of 5% ether/hexane, (B) 35 mL of 10% ether/hexane, (C) 60 mL of 15% ether/hexane, (D) 60 mL of 20% ether/hexane, (E) 35 mL of 30% ether/hexane, (F) 35 mL of 50% ether/hexane, and (G) 35 mL of ether to give (A, B) 577 mg of high-R_f materials, (C–E) 2.726 g (90%) of **15** (R_f 0.21, 15% EtOAc/hexane), which solidified on standing, and (F, G) 160 mg of low-R_f materials. **15**: solid, mp 31–33 °C (crystallized from $CHCl_3$/hexane); IR (CCl_4, cm^{-1}) 1705 (C=O), 1675 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.96–7.44 (5 M, m), 6.30 (1 H, dt, J = 16.9, 10.3 Hz), 6.06 (1 H, dd, J = 14.9, 10.3 Hz), 5.64 (1 H, dt, J = 14.9, 7 Hz), 5.10 (1 H, d, J = 16.9 Hz), 4.98 (1

H, d, J = 10.3 Hz), 3.90 (2 H, s), 3.36 (2 H, s), 2.58 (2 H, t, J = 7 Hz), 2.11 (2 H, q, J = 7 Hz), 1.72 (2 H, p, J = 7 Hz).

***cis*- and *trans*-5-Thiabicyclo[4.4.0]dec-2-en-7-one (25 and 26).** The sulfide **15** (144 mg, 0.50 mmol) in 6 mL of benzene was added dropwise via syringe pump over 1 h to 40 mL of stirred and irradiated benzene. Photolysis was continued for 2 h once the addition was complete. After filtration through a 4 × 2 cm plug of silica gel, the solvent was removed (rotary evaporation) and the crude product was purified by HPLC (M9 column, 10% EtOAc/hexane) to give **25** (31 mg, 37%, 2.5–3.0 column volumes; R_f 0.23, 15% EtOAc/hexane) and **26** (9 mg, 11%, 3.0–3.6 column volumes; R_f 0.21, 15% EtOAc/hexane).

26: solid, mp 85–88 °C (crystallized from $CHCl_3$/hexane); m/e, base = 168 amu, exact mass calcd for $C_9H_{12}OS$ 168.0606, found 168.0608, error = 1.2 ppm; IR (CCl_4, cm^{-1}) 1720 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.87–5.79 (1 H, m), 5.69 (1 H, br d, J = 10.3 Hz), 3.54 (1 H, dd, J = 11.4, 1.3 Hz), 3.50–3.01 (2 H, m), 2.62–2.38 (3 H, m), 2.19–1.46 (4 H, m).

25: solid, mp 60–62 °C (crystallized from $CHCl_3$/hexane); m/e, base = 95 amu, exact mass calcd for $C_9H_{12}OS$ 168.0606, found 168.0608, error = 1.2 ppm; IR (CCl_4, cm^{-1}) 1720 (C=O), 270-MHz NMR ($CDCl_3$, ppm) 5.92–5.84 (1 H, m), 5.62 (1 H, br d, J = 11.0 Hz), 3.57 (1 H, dd, J = 5.7 Hz), 3.31 (1 H, br d, J = 18 Hz), 3.09–2.99 (1 H, m), 3.07 (1 H, br s), 2.61–2.28 (2 H, m), 1.99–1.77 (4 H, m).

Diazabicycloundecene Equilibration of 25 and 26. Seven milligrams of each of the bicycles **25** and **26** was taken up in 0.5 mL of CH_3CN. To each was added diazabicycloundecene (DBU, Aldrich, 9 mg) in 0.5 mL of CH_3CN with stirring under static nitrogen. Both solutions turned purple immediately, but then gradually changed to orange-red. TLC indicated virtually complete equilibration within 5 min; after 30 min, the materials were filtered through 2 × 1 cm plugs of silica gel and analyzed by HPLC (vide supra). Integration of peak areas showed a 1:2.2 ratio of **25** to **26** for each of the products.

Preparation and Photolysis of Phenacyl Sulfide Esters 16 and 17. (Phenacylthio)acetic Acid. Thioglycolic acid (Aldrich, 920 mg, 10.0 mmol) was taken up in 25 mL of THF and cooled to 5 °C with stirring under nitrogen (flow). Triethylamine (2.1 g, 2.9 mL, 20.8 mmol, 2.08 equiv) was added (neat), followed by phenacyl chloride (Aldrich, 1.56 g, 10.1 mmol, 1.01 equiv) in 5 mL of THF, whereupon a thick precipitate developed. The mixture was stirred at 5 °C for 30 min and at room temperature for 1 h and then was poured into a stirred mixture of ice-cold 0.5 M HCl (100 mL) and 50 mL of ether. The aqueous layer was extracted with 2 × 25 mL of ether, and the combined organic layers were rinsed with 25 mL of saturated aqueous NaCl and then dried over $MgSO_4$. Filtration, rotary evaporation, and evacuation gave 2.06 g (98%) of white crystals of the title compound: solid, mp 96–98 °C (crystallized from $CHCl_3$); m/e, base = 105 amu, exact mass calcd for $C_{10}H_{10}O_3S$ 210.0348, found 210.035, error = 1 ppm; IR ($CDCl_3$, cm^{-1}) 3060 (OH), 1710 (C=O), 1675 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 10.72 (1 H, br s), 7.97–7.44 (5 H, m), 4.06 (2 H, s), 3.37 (2 H, s).

General Procedure for Alcohol Esterification. Preparation of Dienyl (Phenacylthio)acetates. Equimolar amounts of the acid from the previous experiment and a dienyl alcohol were combined in 2:1 ether/THF (6 mL/mmol) along with 0.1 equiv of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (Aldrich). Dicyclohexylcarbodiimide (DCC, Aldrich, 1.1 equiv) in 2.1 ether/THF (1 mL/mmol) was added, and the mixture was stirred under nitrogen (static) at room temperature until TLC indicated a complete reaction (8–20 h). During this time a white precipitate (dicyclohexylurea) developed. Filtration through a 4 × 2 cm plug of silica gel followed by rotary evaporation left a residue, which was purified by HPLC or by elution through a 7 × 2 cm column of silica gel with progressively more polar solvents.

(*E*)-3,5-Hexadienyl (Phenacylthio)acetate (16). (*E*)-3,5-Hexadienol was prepared by the method of Martin.[10] Esterification of this alcohol (196 mg, 2 mmol) with (phenacylthio)acetic acid according to the general procedure gave 740 mg of crude product, which was purified by column chromatography, eluting with 30 mL of each of (A) hexane, (B) 10% ether/hexane, (C) 15% ether/hexane, (D) 20% ether/hexane, (E) 30% ether/hexane, and (F) ether. This gave (A, B) 68 mg of high-R_f materials, (C, D) 526 mg (91%) of ester **16**, and (E, F) 31 mg of low-R_f materials.

16: oil; silica gel, 30% EtOAc/hexane, R_f 0.47; IR (CCl_4, cm^{-1}) 1735 (C=O), 1675 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.95–7.47 (5 H, m), 6.29 (1 H, dt, J = 16.7, 10.3 Hz), 6.12 (1 H, dd, J = 14.9, 10.3 Hz), 5.64 (1 H, dt, J = 14.9, 7 Hz), 5.12 (1 H, d, J = 16.7 Hz), 5.01 (1 H, d, J = 10.3 Hz), 4.18 (2 H, t, J = 7 Hz), 4.02 (2 H, s), 3.33 (2 H, s), 2.43 (2 H, q, J = 7 Hz).

***cis*-Bicyclo[4.4.0] Lactone 27.** The ester **16** (368 mg, 1.21 mmol) in 9 mL of THF was added dropwise via syringe pump over 45 min to 100 mL of stirred and irradiated THF. Photolysis was continued for 1.5 h once the addition was complete, and the residue after rotary evaporation was purified by preparative TLC (two plates, 3:1:1 hexane/CH_2Cl_2/ether) to give 78 mg (36%) of the pure cis lactone **27** (R_f 0.12, 2:1:1 hexane/CH_2Cl_2/ether). **27**: solid, mp 84–85 °C (crystallized from $CHCl_3$/hexane); m/e, exact mass calcd for $C_8H_{10}O_2S$ 170.0399, found 170.0402, error = 1.7 ppm; IR ($CHCl_3$, cm^{-1}) 1730 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 6.08–6.01 (1 H, m), 5.71 (1 H, br d, J = 10.8 Hz), 4.35 (2 H, t, J = 6 Hz), 3.81 (1 H, d, J = 5.5 Hz), 3.25 (1 H, br d, J = 18.2 Hz), 3.13–3.03 (2 H, m), 2.22–1.93 (2 H, m).

***trans*-Bicyclo[4.4.0] Lactone 28.** Bicyclic lactone **27** (12 mg, 71 μmol) was dissolved in 1.2 mL of CH_3CN and stirred at room temperature under static nitrogen. DBU (Aldrich, 28 mg, 184 μmol, 2.6 equiv) in 0.3 mL of CH_3CN was added dropwise via syringe, and the solution developed a slight purple tinge after a few minutes. A new higher R_f material was evident by TLC within 10 min; after 2.5 h, the mixture was diluted with 8 mL of ether and filtered through a 3 × 2 cm plug of silica gel. "Preparative" TLC using a 10 × 10 cm analytical plate (two 5-cm developments, 5:2:2 hexane/CH_2Cl_2/ether) gave two zones: (A) 7.1 mg of recovered **27** and 2.4 mg of the trans bicycle, **28** (R_f's 0.15 and 0.19, respectively, 2:1:1 hexane/CH_2Cl_2/ether). **28**: solid, mp 108–109 °C (crystallized from $CHCl_3$/hexane); m/e, exact mass calcd for $C_8H_{10}O_2S$ 170.0399, found 170.0401, error = 1.1 ppm; IR ($CHCl_3$, cm^{-1}) 1735 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.94–5.86 (1 H, m), 5.70 (1 H, br d, J = 10.3 Hz), 4.52–4.32 (2 H, m), 3.63–3.52 (1 H, m), 3.59 (1 H, d, J = 11.8 Hz), 3.17–3.06 (1 H, m), 3.87–2.71 (1 H, m), 2.20–1.68 (2 H, m).

Cyclohexadienyl Ester 17. 1-(2-Hydroxyethyl)-1,3-cyclohexadiene (215 mg, 1.73 mmol) was prepared by the method of Engel et al.[11] and coupled with (phenacylthio)acetic acid (365 mg, 1.73 mmol) according to the general esterification procedure. Filtration through a 4 × 2 cm plug of silica gel (rinsed with 25 mL of 1:1 ether/hexane) gave 566 mg of crude ester, which was purified by HPLC (M9 column, 12% EtOAc/hexane, two injections) to give 440 mg (80%) of the ester **17** eluting between 2.8 and 4.0 column volumes, contaminated with approximately 15% of the nonconjugated 1,4-cyclohexadiene ester. **17**: oil; silica gel, 20% EtOAc/hexane, R_f 0.31; m/e, base = 270.5 amu, exact mass calcd for $C_{18}H_{20}O_3S$ 316.1128, found 216.1134, error = 1.8 ppm; IR (CCl_4, cm^{-1}) 1735 (C=O), 1675 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 7.98–7.45 (5 H, m), 5.87–5.65 (3 H, m), 4.25 (2 H, t, J = 7 Hz), 4.03 (2 H, s), 3.32 (2 H, s), 2.40 (2 H, t, J = 7 Hz), 2.15–2.07 (4 H, m).

Endo and Exo Tricyclic Sulfides 29 and 30. The ester **17** (398 mg, 1.26 mmol) in 10 mL of THF was added dropwise via syringe pump over 1 h to 100 mL of stirred and irradiated THF. Photolysis was continued for 3 h after the addition was complete. The solvent volume was reduced to approximately 10 mL, and hexane was added until the solution became cloudy. This mixture was filtered through a 4 × 2 cm plug of silica gel, and the plug was rinsed with ether. The residue after solvent removal was partially purified by preparative TLC (40% EtOAc/hexane) to give 180 mg of crude product (R_f 0.10–0.20, 30% EtOAc/hexane), which was further purified by HPLC (M9 column, 30% EtOAc/hexane). Products eluted at 5.0–6.2 column volumes (**30**, 8 mg, 3%) and 6.2–7.8 column volumes (**29**, 85.4 mg, 34%).

29: solid, mp 89–91 °C (crystallized from $CHCl_3$/hexane); m/e, exact mass calcd for $C_{10}H_{12}O_2S$ 196.0555, found 196.0558, error = 1.5 ppm; IR (CCl_4, cm^{-1}) 1735 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 6.77 (1 H, dd, j = 8.5, 7 Hz), 6.01 (1 H, d, J = 8.5 Hz),

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4.58–4.52 (2 H, m), 3.91 (1 H, s), 3.56–3.50 (1 H, m), 2.27–1.18 (6 H, m).

30: oil; silica gel, 30% EtOAc/hexane, R_f 0.15; m/e, exact mass calcd for $C_{10}H_{12}O_2S$ 196.0555, found 196.0558, error = 1.5 ppm; IR (CCl_4, cm^{-1}) 1735 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 6.62 (1 H, dd, J = 8.5, 6.6 Hz), 6.08 (1 H, d, J = 8.5 Hz), 4.47 (2 H, dd, J = 7.2, 5.3 Hz), 3.75 (1 H, d, J = 2.2 Hz),3.54–3.47 (1 H, m), 2.40–1.31 (6 H, m).

Desulfurization with Deactivated Raney Nickel. General Procedures. Raney Nickel Deactivation. Raney nickel was deactivated as follows: 6 mL of a well-shaken suspension of Raney nickel in absolute ethanol (containing ca. 600 mg of nickel/mL) was placed in a 10-mL round-bottom flask. After the nickel had settled, the ethanol was removed via pipet and replaced with 6 mL of acetone, and the resulting suspension was stirred at room temperature for 2 h (nickel clings to the stir bar). The acetone was removed via pipet and replaced with 6 mL of fresh acetone. One milliliter of a well-shaken (i.e., homogeneous) suspension of deactivated Raney nickel in acetone thus prepared was appropriate for the desulfurization of 0.05 mmol of a given substrate.

Desulfurizations. The substrate in 1 mL of acetone was added to an appropriate amount (1 mL/0.05 mmol of substrate) of the freshly prepared deactivated Raney nickel suspension in acetone. The mixture was stirred at room temperature and monitored by TLC, which usually indicated complete reaction within 1 h. After the disappearance of starting material, the mixture was diluted with ether (1:1) and filtered (Celite) with ether to rinse the residue.

Desulfurization of 25. The bicyclic ketone **25** (20 mg, 0.12 mmol) was desulfurized according to the general procedure. Purification of the crude product by HPLC (12% EtOAc/hexane) gave three eluates: **37** (1.4–2.0 column volumes, 2.9 mg, 17%, 20% based on recovered **25**), **38** (2.0–2.5 column volumes, 4.2 mg, 26%, 30% based on recovered **25**), and **25** (2.5–3.0 column volumes, 2.6 mg).

37: oil; silica gel, 15% EtOAc/hexane, R_f 0.28; m/e, exact mass calcd for $C_9H_{14}O$ 138.1041, found 138.1045, error = 3 ppm; IR (CCl_4, cm^{-1}) 1705 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.52–5.21 (2 H, m), 2.90–2.75 (1 H, m), 2.57–1.45 (8 H, m), 1.61 (3 H, dd, J = 6.8, 1.6 Hz).

38: oil; silica gel, 15% EtOAc/hexane, R_f 0.14; m/e, exact mass calcd for $C_9H_{12}O$ 136.0885, found 136.0888, error = 2.2 ppm; IR (CCl_4, cm^{-1}) 1685 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.38 (1 H, ddd, J = 16.9, 9.9, 8.1 Hz), 5.15 (1 H, dd, J = 16.9, 1.5 Hz), 4.99 (1 H, dd, J = 9.9, 1.5 Hz), 2.36–1.63 (9 H, m).

General Procedure for Sulfonium Salt Formation and Reduction with Zinc/Acetic Acid. The substrate was dissolved in dimethoxyethane (1 mL/8 mg of substrate) and stirred at room temperature under static nitrogen. Trimethyloxonium tetrafluoroborate (Aldrich, 3 equiv) was added, and the reaction was monitored by TLC; in each case, the substrate had disappeared within 1 h and had been replaced by a baseline spot. Dimethyl sulfide (Aldrich, 1 drop/3 mg of substrate) was added via pipet (quickly removing and replacing the septum/nitrogen inlet), and the mixture was stirred for 5 min. Acetic acid (2 drops/mg of substrate) was added, followed by zinc dust (Fisher, 35 mg/mg of substrate), and the septum was replaced with a caplug. The reaction was monitored by TLC; in each case, the baseline spot disappeared and was replaced by more mobile material(s) within 1 h. The mixture was poured into 50 mL of saturated aqueous $NaHCO_3$/25 mL of saturated aqueous NaCl/25 mL of CH_2Cl_2 and stirred for 10 min. The aqueous layer was extracted with 2 × 20 mL of CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$. Filtration through a 4 × 2 cm plug of silica gel, rotary evaporation, and evacuation gave crude product, which was purified by HPLC (Magnum 9 column, 4:1:1 hexane/CH_2Cl_2/ether).

Sulfide 31. The bicyclic ketone **25** (25 mg, 0.15 mmol) was alkylated and reduced according to the general procedure (vide supra). HPLC purification gave the sulfide **31** (16.5 mg, 60%) eluting at 1.8–2.1 column volumes. **31**: oil; silica gel, 7:1:2 hexane/CH_2Cl_2/ether; m/e, base = 136 amu, exact mass calcd for $C_{10}H_{16}OS$ 184.0918, found 184.0929, error = 6 ppm; IR (CCl_4, cm^{-1}) 1710 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.49–5.37 (2 H, m), 3.12 (2 H, d, J = 6.5 Hz), 2.86–2.74 (1 H, m), 2.40–2.01 (4 H, m), 2.05 (3 H, s), 1.85–1.40 (4 H, m).

Sulfides 33a,b and 34. The tricycles **29** + **30** (16 mg, 82 μmol) were alkylated and reduced according to the general procedure. HPLC purification gave two eluates: **33a** (2.0 mg, 12%, 1.5–1.8 column volumes) and an inseparable mixture of **33b** and **34** (8.9 mg, 51% combined yield, 1.8–2.1 column volumes). **33a**: oil; silica gel, 7:1:2 hexane/CH_2Cl_2/ether, R_f 0.35; m/e, base = 107 amu, exact mass calcd for $C_{11}H_{16}O_2S$ 212.0867, found 212.0878, error = 5.2 ppm; IR (CCl_4 cm^{-1}) 1735 (C=O); 270-MHz NMR ($CDCl_3$, ppm) 5.83 (1 H, dt, J = 9.9, 3.7 Hz), 5.59 (1 H, br d, J = 9.9 Hz), 4.62–4.37 (2 H, m), 3.16 (1 H, d, J = 1.2 Hz), 2.25 (3 H, s), 2.14–1.94 (4 H, m), 2.87–1.61 (4 H, m).

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Synthesis of Azocine Derivatives from Thioaldehyde Diels–Alder Adducts

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Nitrogen-containing phenacyl sulfides **1** or **2** can be readily cleaved to thioaldehydes that are trapped by electron-rich dienes to give the adducts **4**, **5**, **11**, or **17**. The adducts have electrophilic character α to sulfur and can be converted into structures having new C–N bonds at the α-carbon. Thus, **4** leads to lactam **6** by S to N acyl transfer. A similar reaction occurs from **15** to the eight-membered **16**. Internal addition of amine nitrogen to Danishefsky diene adducts **11**, **17**, or **26** affords bicyclic aminals which are converted into azocine derivatives upon desulfurization. Stable structures such as **24**, **25**, and **31** are prepared in this way. The unusual enaminone **20** is not stable and rearranges upon attempted purification to **21**.

Previous reports from this laboratory have detailed the synthesis of 6–13-membered sulfur rings and their conversion into medium ring lactones (eq 1) by acyl transfer.[1,2]

The most difficult rings to prepare in this study were the eight-membered lactones (eq 1, 2). While other ring sizes were readily accessible by S to O acyl transfer (hydroxyalkyl thiolactone to mercaptoalkyl lactone), the two different approaches to eight-membered lactones (Figure 1) resulted in an equilibrium between product and starting material. The least favorable case (eq 1) was further complicated by the competing formation of diolides.[1]

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