(1*R*,2*R*)-2-Acetoxy-9-methyl-9-azabicyclo[4.2.1]nonane methiodide (14) was prepared in the same way as was 4. Pure 14 was isolated by filtration (75% yield): mp 215–217 °C; ^{1}H NMR (D_2O) δ 1.74 (m, 1 H), 1.88 (m, 1 H), 1.9–2.2 (m, 5 H), 2.09 (s, 3 H, CH_3CO), 2.39 (m, 1 H), 2.48 (m, 1 H), 2.60 (m, 1 H), 3.20 (s, 3 H, N-CH_3), 3.28 (s, 3 H, N-CH_3), 3.97 (br s, 1 H, H-6), 4.02 (br s, 1 H, H-1), 5.34 (m, 1 H, H-2). Anal. Calcd for $C_{12}H_{22}INO_2$: C, 42.5; H, 6.5; N, 4.1. Found: C, 42.2; H, 6.5; N, 4.0.

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Supplementary Material Available: IR spectral data for compounds **27**, **31–39**, **41**, and **42** and ^{13}C NMR spectral data for **1**, **3–14**, **27**, **33–39**, **41**, and **42** (4 pages). Ordering information is given on any current masthead page.

Formation of Cyclopentenethiones via Cyclization of β-Thioallyl Cations

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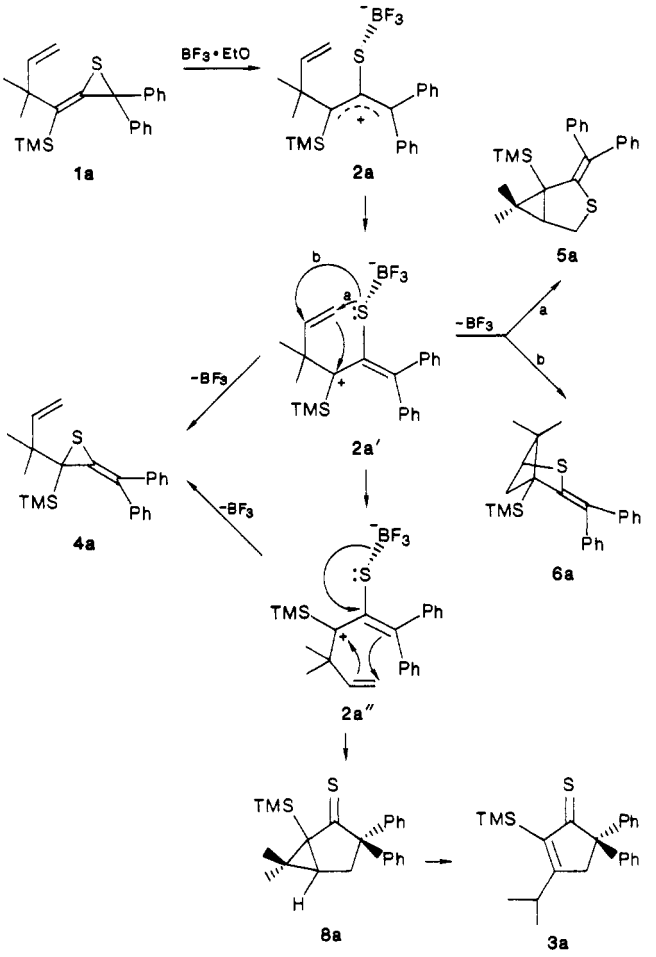
Reaction of 2,2-diaryl-3-[2′,2′-dimethyl-1′-(trimethylsilyl)-3′-butenylidene]thiiranes **1a** and **1b** with BF_3·Et_2O resulted in facile formation of stable cyclopentenethiones **3a** and **3b**, by a new type of cyclization via the initially generated thioallyl cations. The mechanism of this Lewis acid promoted isomerization of allene episulfides **1a** and **1b** is rationalized by taking into account the conformation of the thioallyl cation and the effect of the aromatic substituents. The structure of **3a**, a novel example of a crystalline aliphatic conjugated thione, has been determined by X-ray crystallographic analysis.

In contrast to the wide chemistry associated with oxyallyl ions and their versatile utility in organic synthesis,[2] the nature of sulfur-analogous reactive species, i.e., thioallyl intermediates, has not been fully investigated and its potential synthetic utility is undeveloped.[3]

We have recently described the thermal isomerization reactions of several types of substituted allene episulfides,[4] the substituent effects of which reveal the intrinsic nature of the thioallyl intermediate. The direct observation of the thioallyl cation from protonation of tetramethylallene episulfide with fluorosulfuric acid by low-temperature NMR spectroscopy and its interesting acid-promoted dimerization reactions have been reported.[5] In the case of sterically hindered aryl-substituted allene episulfides, an acid-catalyzed cyclization of the thioallyl intermediate onto the aromatic ring gave benzothiophene or indenethiol derivatives.[4b] However, no definite examples of inter- or intramolecular trapping reactions of the thioallyl cation

Scheme I[a]



[a] TMS = Me_3Si.

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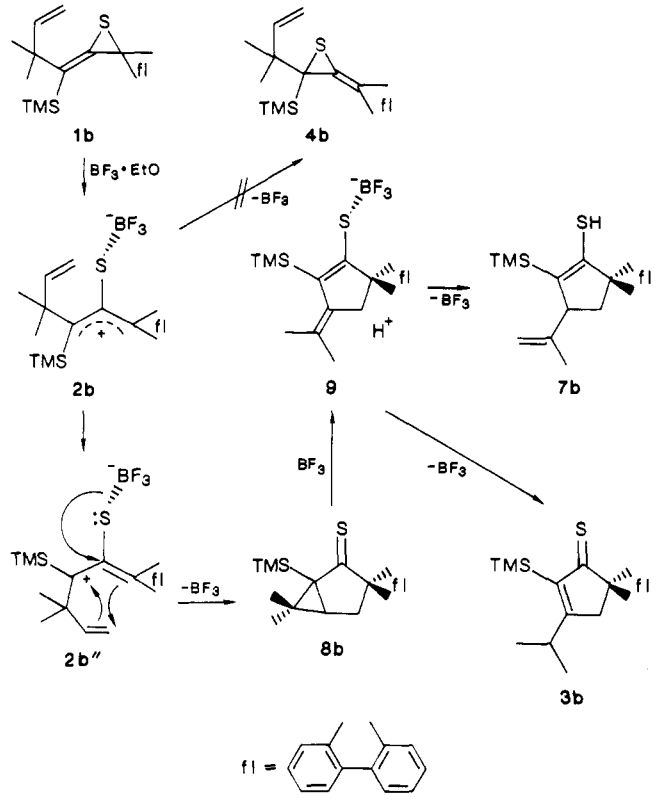
Scheme II



are known in contrast to the facile cycloaddition reactions of oxyallyl ions with a variety of dipolarophiles.[2n] We have investigated a Lewis acid promoted cyclization of allyl-substituted allene episulfides 1[6] and now present a novel and effective intramolecular trapping reaction of the intermediary thioallyl cation resulting in a formation of stable cyclopentenethiones 3.

When allene episulfide **1a** was treated with 0.5 molar equiv of BF_3·Et_2O in chloroform at −5 °C, the color of the solution changed immediately to dark red. Chromatography of the evaporated reaction mixture afforded cyclopentenethione **3a** in 35% yield as stable reddish-purple crystals together with the isomeric allene episulfide **4a** (52%). Lowering the temperature of the reaction of **1a** with BF_3·Et_2O (−20 °C in chloroform) afforded two other types of cyclization products **5a** (10%) and **6a** (15%) besides **3a** (14%) and **4a** (36%) (Scheme I).

This branching of the reaction pathways is attributable to kinetic stabilization of the initially formed thioallyl cation **2a′**, which allows the direct attack of the sulfur atom on the olefinic carbons of the dimethylallyl group (paths a and b) leading to **5a** and **6a**. At higher temperature, cyclization occurs only via the rotated thioallyl cation **2a″** to give **3a** and **4a**. Since **4a** was reluctant to undergo further molecular transformation by the action of BF_3·Et_2O even at room temperature, the cyclization of the thioallyl cation **2a** from once isomerized allene episulfide **4a** is evidently irreversible.

Replacing the two phenyl groups of **1a** by a fluorenyl group (**1b**) resulted in selective formation of thione **3b** and thiol **7b**. These products arose from the thioallyl cation by cyclization at the cationic termini, apparently without any formation of the isomeric allene episulfide **4b** or its other cyclization products (Scheme II). The yields of **3b** and **7b** fluctuated slightly with the reaction conditions as shown in Table I, but in all cases, **3b** was obtained predominantly over **7b**. Considering the similar electronic effects in allene episulfides **1a** and **1b**, the preferential formation of **3b** and **7b** in the latter case might be explained by relief of steric hindrance between the aromatic substituents and the dimethylallyl group in the thioallyl cation **2b″**, which favors the cyclization of **2b″** to **8b** bypassing the allene episulfide **4b**. The formation of cyclopentenethione **3b** and cyclopentenethiol **7b** can be rationalized by isomerization of the strained bicyclic thione **8b**. The oxygen analogue of **8b** has been isolated by Grimaldi in the peracid oxidation of the allyl-substituted allenes via the allene oxide–oxyallyl tautomerization.[2k] Under these Lewis acidic conditions, it is likely that the acid-catalyzed opening of the intermediate **8b** affords **3b** and **7b** as illustrated in Scheme II.

The purple color and characteristic low-field ^{13}C NMR signals of **3a** [λ_{max} = 550 nm (ϵ = 45), δ = 255.7 ppm] and **3b** [λ_{max} = 544 nm (ϵ = 20), δ = 253.5 ppm] are considered to be associated with their conjugated thiocarbonyl unit.[7] The final molecular structure of **3a** was determined by X-ray crystallographical analysis, and an ORTEP view of the

Table I. BF_3•Et_2O Promoted Intramolecular Cyclization Reactions of Allyl-Substituted Allene Episulfides

substrate	solvent	condtns	products (yields,[a] %)
1a	$CHCl_3$	−5 °C, 10 h	**3a** (35), **4a** (52)
	$CHCl_3$	−20 °C, 10 h	**3a** (14), **4a** (36), **5a** (10), **6a** (15)
1b	$CHCl_3$	−20 °C, 10 h	**3b** (68), **7b** (18)
	$CHCl_3$	−5 °C, 10 h	**3b** (53), **7b** (14)
	C_6H_6	rt,[b] 1 h	**3b** (66), **7b** (6)

[a] Isolated yields. [b] Room temperature.

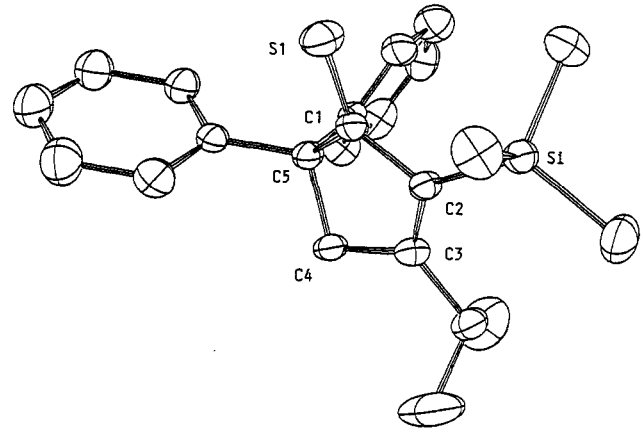
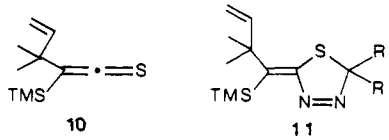


Figure 1. ORTEP drawing of cyclopentenethione **3a**. Selected bond lengths (angstroms) and angles (degrees): S(1)–C(1), 1.632 (4); C(1)–C(2), 1.465 (5); C(2)–C(3), 1.352 (6); C(3)–C(4), 1.506 (6); C(4)–C(5), 1.506 (6); C(1)–C(5), 1.545 (5); ∠S(1)–C(1)–C(2), 127.4 (3); ∠S(1)–C(1)–C(5), 124.1 (3); ∠C(1)–C(2)–C(3), 108.0 (3); ∠C(2)–C(3)–C(4), 112.4 (4); ∠C(3)–C(4)–C(5), 103.1 (3); ∠C(1)–C(5)–C(4), 100.3 (3); ∠C(2)–C(1)–C(5), 108.5 (3).

(6) Episulfides **1a** and **1b** were readily synthesized by the reaction of thioketene 10[10] with the diaryl carbenes generated from the corresponding diazo compounds in good yields. The configuration of the dimethylallyl and trimethylsilyl groups was ascertained by comparison with that of the analogously substituted 2-alkylidene-1,3,4-thiadiazolines 11 as shown below; the latter were the major cycloaddition products in the reactions of the thioketene 10 with dialkyldiazomethanes.



(7) Duus, F. In *Comprehensive Organic Chemistry*; Pergamon Press: Oxford, 1979; Vol. 3, pp 373–377.

structure of **3a** with the atom numbering scheme is shown in Figure 1 along with salient intramolecular material parameters (monoclinic, $P2_1/n$, $R = 0.066$, and $R_w = 0.068$). The structure shows the effective steric protection of the reactive thiocarbonyl group afforded by the two neighboring phenyl groups and the bulky trimethylsilyl group. The structure of **3a** is of great interest as a rare example of a crystalline aliphatic conjugated thione. The C=S bond length is 1.632 (4) Å, which is very close to the known value in diphenylcyclopropenethione (1.634 Å)[8] but slightly shorter than that in 4,4'-dihydroxythiobenzophenone (1.647 Å).[9] Effective conjugation of the coplanar thiocarbonyl and the endocyclic double bond, as shown in Figure 1, is consistent with the longer wavelength absorption maxima of **3a** as compared with those of common aliphatic thiones (λ_{max} = 490–500 nm).[7]

The acid-promoted cyclization of allyl-substituted allene episulfides thus described is of particular note, not only as the first example of trapping of thioallyl cations at the allylic termini but also for the potential utility of the vinylsilane moiety of **3a** and **3b** for further functionalization.

Experimental Section

General. ^1H NMR and ^{13}C NMR spectra were obtained on Bruker AM500 or JEOL FX-90Q spectrometers. Mass spectra were recorded at 20 eV, while high-resolution mass analysis was performed at 70 eV. The purity of all title compounds was judged to be >95% by ^1H NMR and/or ^{13}C NMR determinations. All the experiments were carried out in freshly distilled solvents under a nitrogen or argon atmosphere unless otherwise noted, and $BF_3{\cdot}Et_2O$ was purified by distillation over CaH_2 before use. Melting points were uncorrected.

2-[2',2'-Dimethyl-1'-(trimethylsilyl)-3'-butenylidene]-3,3-diphenylthiirane (1a). To a dichloroethane solution (6 mL) of thioketene **10**[6] (500 mg, 2.53 mmol)[10] was added a solution of diphenyldiazomethane (800 mg, 4.12 mmol) in 2 mL of dichloroethane at room temperature. After being heated at 70 °C for 12 h, the reaction mixture was evaporated, and the residual oil was submitted to column chromatography (SiO_2/hexane) to afford 276 mg (30%) of **1a** as a pale yellow oil. **1a**: ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H), 1.11 (s, 6 H), 4.89 (dd, J = 10, 2 Hz, 1 H), 4.91 (dd, J = 18, 2 Hz, 1 H), 5.85 (dd, J = 18, 10 Hz, 1 H), 7.1–7.5 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 1.2 (q), 28.8 (q), 45.2 (s), 52.1 (s), 111.7 (t), 127.3 (d), 128.1 (d), 128.5 (s), 129.0 (d), 139.4 (s), 141.4 (s), 148.0 (d); UV (cyclohexane) λ_{max} 384 nm (ϵ = 1160); MS, m/z 364 (M^+, 14), 295 (69), 291 (11), 198 (28), 73 (100); exact mass found m/z 364.1686, calcd for $C_{23}H_{28}SiS$ 364.1681.

Spiro[fluorene-9,3'-[2'-[2'',2''-dimethyl-1''-(trimethylsilyl)-3''-butenylidene]thiirane]] (1b). To a chloroform solution (2 mL) of **10** (100 mg, 0.51 mmol) and 9-diazofluorene (110 mg, 0.57 mmol) was added a catalytic amount of copper(I) chloride (ca. 0.5 mg) at room temperature. The mixture was stirred for 12 h until the evolution of nitrogen gas ceased. After filtration of the catalyst and evaporation of the solvent, the residue was subjected to silica gel column chromatography with hexane to give 66 mg (36%) of **1b** as a pale yellow oil. In contrast to the case of **1a**, no **1b** was obtained by the thermal reaction of **10** with 9-diazofluorene. **1b**: ^1H NMR ($CDCl_3$) δ 0.40 (s, 9 H), 0.81 (s, 6 H), 4.60 (d, J = 10 Hz, 1 H), 4.68 (d, J = 18 Hz, 1 H), 5.63 (dd, J = 10, 18 Hz, 2 H), 7.2–7.7 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 1.2 (q), 27.7 (q), 44.8 (s), 48.3 (s), 111.2 (t), 120.3 (d), 122.5 (d), 127.7 (d), 128.3 (d), 129.0 (s), 135.1 (s), 140.6 (s), 145.7 (s), 147.5 (d); UV (cyclohexane) λ_{max} 340 (sh, ϵ = 440) and 288 (ϵ = 1280) nm; MS, m/z 362 (M^+, 11), 330 (11), 293 (14), 73 (100), 69 (37); exact mass found m/z 362.1505, calcd for $C_{23}H_{26}SiS$ 362.1523.

3-Isopropyl-5,5-diphenyl-2-(trimethylsilyl)-2-cyclopentenethione (3a) and 2-(1',1'-Dimethylallyl)-3-(diphenylmethylene)-2-(trimethylsilyl)thiirane (4a). To a solution of **1a** (240 mg, 0.66 mmol) in chloroform (2 mL) was added 40 μL (0.32 mmol) of $BF_3{\cdot}Et_2O$ at −5 °C, and the mixture was stirred for 10 h at this temperature. Condensation under reduced pressure produced a dark brown oil, which was chromatographed on silica gel with hexane to afford cyclopentenethione **3a** (84 mg, 35%) as a reddish-purple oil and allene episulfide **4a** (125 mg, 52%) as a pale yellow oil. **3a** was further purified by slow and careful recrystallization from hexane to give single crystals fit for X-ray structure analysis. **3a**: reddish-purple prisms, mp 95–98 °C; ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H), 1.25 (d, J = 7 Hz, 6 H), 3.38 (sept, J = 7 Hz, 1 H), 3.53 (s, 2 H), 7.0–7.3 (br s, 10 H); ^{13}C NMR ($CDCl_3$) δ 0.9 (q), 21.5 (q), 30.9 (d), 52.8 (t), 71.4 (s), 126.2 (d), 127.8 (d), 128.5 (d), 146.1 (s), 150.0 (s), 191.3 (s), 255.7 (s); UV (cyclohexane) λ_{max} 550 nm (ϵ = 45); MS, m/z 364 (M^+, 79), 349 (28), 321 (65), 291 (24), 259 (21), 73 (100); exact mass found m/z 364.1684, calcd for $C_{23}H_{28}SiS$ 364.1681. **4a**: pale yellow oil; ^1H NMR ($CDCl_3$) δ 0.28 (s, 9 H), 0.95 (s, 3 H), 1.00 (s, 3 H), 4.85 (dd, J = 10, 1 Hz, 1 H), 4.87 (dd, J = 18, 1 Hz, 1 H), 5.6 (dd, J = 10, 18 Hz, 1 H), 7.1–7.7 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 1.2 (q), 24.8 (q), 25.2 (q), 42.9 (s), 51.7 (s), 111.7 (t), 126.9 (d), 127.2 (d), 128.1 (d), 128.2 (d), 129.0 (d), 130.0 (s), 136.4 (s), 140.6 (s), 141.1 (s), 145.6 (d); UV (cyclohexane) λ_{max} 290 (ϵ 14 300) and 380 (70) nm; MS, m/z 364 (M^+, 26), 295 (67), 291 (11), 73 (100); exact mass found m/z 364.1655, calcd for $C_{23}H_{28}SiS$ 364.1681.

1-(Trimethylsilyl)-2-(diphenylmethylene)-6,6-dimethyl-3-thiabicyclo[3.1.0]hexane (5a) and 3-(Diphenylmethylene)-4-(trimethylsilyl)-5,5-dimethyl-2-thiabicyclo[2.1.1]hexane (6a). To a −20 °C chloroform solution (2 mL) of **1a** (280 mg, 0.77 mmol) was added 48 μL (0.39 mmol) of $BF_3{\cdot}Et_2O$, and the mixture was stirred for 12 h at this temperature. After concentration under reduced pressure, the residual oil was subjected to chromatography on silica gel with hexane to give bicyclic sulfides **5a** (28 mg, 10%) and **6a** (42 mg, 15%) along with **3a** (39 mg, 14%) and **4a** (102 mg, 36%). **5a**: colorless oil; ^1H NMR ($CDCl_3$) δ 0.22 (s, 9 H), 1.16 (s, 3 H), 1.16 (s, 3 H), 2.14 (m, 1 H), 2.46 (dd, J = 10, 14 Hz, 1 H), 2.81 (dd, J = 5, 14 Hz, 1 H), 6.9–7.3 (m, 10 H); MS, m/z 364 (M^+, 6), 349 (4), 184 (100), 73 (49); exact mass found m/z 364.1694, calcd for $C_{23}H_{28}SiS$ 364.1681. **6a**: colorless oil; ^1H NMR ($CDCl_3$) δ −0.25 (s, 9 H), 1.23 (s, 3 H), 1.43 (s, 3 H), 2.03 (dd, J = 2, 8 Hz, 1 H), 2.86 (dd, J = 2, 11 Hz, 1 H), 3.16 (dd, J = 8, 11 Hz, 1 H), 7.1–7.3 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 0.8 (q), 18.2 (q), 25.0 (q), 31.7 (t), 31.8 (s), 38.6 (s), 45.7 (d), 126.4 (d), 126.8 (d), 128.0 (d), 128.2 (d), 129.3 (d), 130.0 (d), 132.1 (s), 142.8 (s), 146.1 (s), 147.3 (s); MS, m/z 364 (M^+, 35), 167 (31), 73 (100); exact mass found m/z 364.1644, calcd for $C_{23}H_{28}SiS$ 364.1681.

Spiro[1-isopropyl-3-thioxo-2-(trimethylsilyl)-1-cyclopentene-4,9'-fluorene] (3b) and Spiro[1-isopropenyl-3-mercapto-2-(trimethylsilyl)-2-cyclopentene-4,9'-fluorene] (7b). A typical example of the reaction of **1b** with $BF_3{\cdot}Et_2O$ is as follows. To a chloroform solution (2 mL) of **1b** (240 mg, 0.66 mol) was added 40 μL (0.32 mmol) of $BF_3{\cdot}Et_2O$ at −5 °C, and the mixture was stirred for 12 h at this temperature. After evaporation of the reaction mixture, the residual oil was chromatographed on silica gel with hexane to give thione **3b** (163 mg, 68%) and thiol **7b** (44 mg, 18%) as reddish-purple crystals and a pale yellow oil, respectively. **3b**: reddish-purple crystals, mp 93–95 °C (from hexane); ^1H NMR ($CDCl_3$) δ 0.34 (s, 9 H), 1.30 (d, J = 7 Hz, 6 H), 4.00 (sept, J = 7 Hz, 1 H), 7.0–7.8 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 0.8 (q), 21.5 (q), 31.3 (d), 46.5 (t), 73.7 (s), 120.1 (d), 122.1 (d), 127.7 (d), 127.8 (d), 141.1 (s), 150.4 (s), 151.0 (s), 194.1 (s), 253.5 (s); UV (cyclohexane) λ_{max} 544 nm (ϵ = 20); MS, m/z 362 (M^+, 100), 347 (57), 319 (43), 73 (47); exact mass found m/z 362.1545, calcd for $C_{23}H_{26}SiS$ 362.1525. **7b**: pale yellow oil; ^1H NMR ($CDCl_3$) δ 0.23 (s, 9 H), 1.80 (s, 3 H), 1.82 (s, 1 H), 2.28 (dd, J = 7, 13 Hz, 1 H), 2.60 (dd, J = 13, 9 Hz, 1 H), 3.85 (dd, J = 7, 9 Hz, 1 H), 4.87 (s, 1 H), 4.92 (s, 1 H), 7.2–7.7 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ −0.75 (q), 20.7 (q), 43.7 (t), 57.6 (d), 71.0 (s), 111.6 (t), 119.76 (d), 119.80 (d), 123.1 (d), 124.6 (d), 127.75 (d), 127.85 (d), 127.92 (d), 128.0 (d), 140.1 (s), 140.9 (s), 142.3 (s), 146.5 (s), 149.5 (s), 149.7 (s), 150.8 (s); IR ($CHCl_3$) 2550 cm^{-1} (SH); MS, m/z 362 (M^+, 91), 347 (15), 289 (16), 256 (31), 178 (19), 73 (100); exact mass found m/z 362.1498, calcd for $C_{23}H_{26}SiS$ 362.1525.

Molecular Structure Analysis of 3a. The X-ray crystallographical analysis of thione **3a** was carried out by using an

(8) Reed, L. L.; Schaefer, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 528.
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(10) Schaumann, E.; Grabley, F. F. *Tetrahedron Lett.* **1977**, 4307.

Enraf-Nonius CAD4 diffractometer with graphite-monochromatized Mo Kα radiation (μ = 0.71069 Å). Calculations were performed with the CAD4 structure determination package programs (Enraf-Nonius, Delft, Holland, 1985) and also with UNICS III programs[11] for full-matrix least-squares refinement.

(11) Sakurai, T.; Kobayashi, K. *Rikagaku Kenkyusho Hokoku* **1979**, *55*, 69–77.

Final residuals of R = 0.066 and Rw = 0.068 were obtained, where $w = 1/(0.00651|F_o|^2 - 0.333\ |F_o| + 5.3893)$.

Supplementary Material Available: Complete tables of bond lengths, angles, and thermal parameters for **3a** with a table of its crystallographic parameters, ^{1}H and ^{13}C NMR spectra for **1a,b**, **3a,b**, **4a**, **6a**, and **7b**, and ^{1}H NMR spectrum for **5a** (34 pages). Ordering information is given on any current masthead page.

Trichothecene Synthesis Using Organoiron Complexes: Diastereoselective Total Syntheses of (±)-Trichodiene, (±)-12,13-Epoxytrichothec-9-ene, and (±)-Trichodermol

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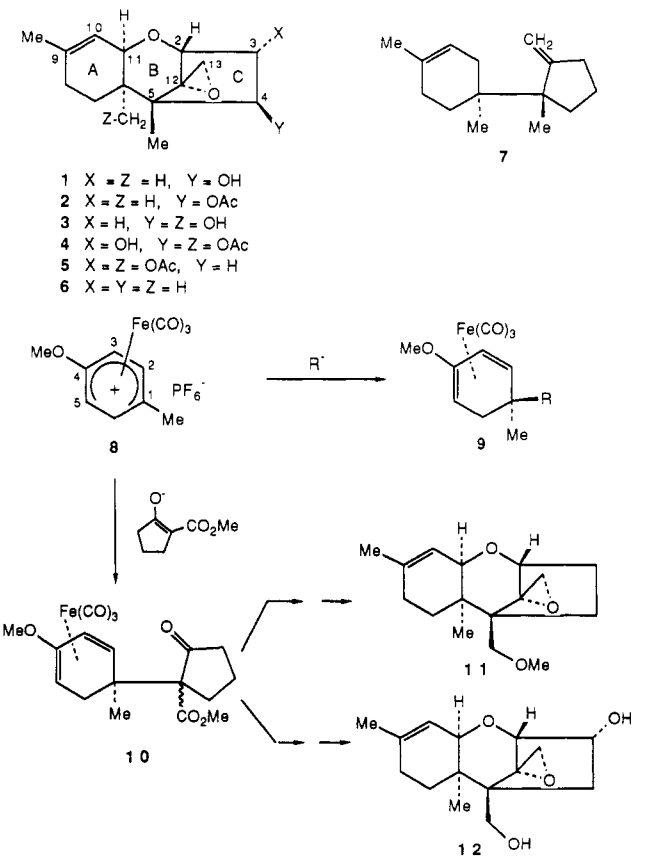
Reactions of tricarbonyl(4-methoxy-1-methylcyclohexadienylium)iron hexafluorophosphate (**8**) with a number of tin enolates are reported. The reaction of **8** with 2-methyl-1-[(tributylstannyl)oxy]cyclopentene and with 3-(dimethylphenylsilyl)-2-methyl-1-[(tributylstannyl)oxy]cyclopentene proceeds regiospecifically by addition to C1 of the dienyl ligand and diastereoselectively to give complexes **23A** and **28A**, respectively, as the major products. Complex **23A** was converted in four steps to (±)-trichodiene and in nine steps to (±)-12,13-epoxytrichothec-9-ene. Complex **28A** was converted in 12 steps to (±)-trichodermol.

Introduction

Previous work in our laboratory has been aimed at the synthesis of various structural analogues of trichothecenes.[1] These compounds are naturally occurring sesquiterpenes that show diverse biological activity[2] and that are of sufficient structural complexity to pose an interesting challenge for total synthesis.[3] Examples are trichodermol (**1**) and its acetate trichodermin (**2**), verrucarol (**3**), anguidine (**4**), and calonectrin (**5**), as well as the biogenetic precursor trichodiene (**7**). Total syntheses of these have already been reported by other groups.[3] Our own work in this area has focused on the use of the cyclohexadienyliron complex **8** as an A-ring precursor for these compounds, based on the observation that stabilized enolate nucleophiles add to **8** exclusively at the methyl-substituted dienyl terminus to give diene complexes of general structure **9**.

A particular example of this reaction is the conversion of **8** to **10**, which is obtained as an equimolar mixture of two diastereomers in greater than 98% yield, one of which has been converted[1] to the trichothecene analogues **11** and **12**. The latter compound has similarities to calonectrin, and the presence of the 3-hydroxy group makes it of potential interest from the point of view of biological activity. However, while complex **8** lends itself very well to the synthesis of analogues via this route, we considered it imperative to demonstrate that this novel chemistry can



be used to construct natural products of predefined structure with high efficiency.

Raphael's group[4] reported the first total synthesis of trichodermin, and while the strategy was elegant in its

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