°C (7 torr), which crystallized in the receiver. Recrystallization from 95% ethanol gave crystals, mp 98–99 °C.

Preparation of Dipropionylmesitylene. In a 250-mL three-necked flask fitted with a condenser protected by a drying tube and a magnetic stirrer was placed 5.0 g (0.04 mol) of mesitylene, 14.8 g (0.16 mol) of propionyl chloride, and 75 mL of carbon disulfide. Aluminum chloride (30 g, 0.22 mol) was added to the stirred mixture and the reaction mixture was heated to reflux for 1 h. Carbon disulfide was removed by distillation and the residue was decomposed with ice water, producing a white solid precipitate. The solid was collected on a filter, dried, and recrystallized from petroleum ether (bp 60–80 °C), giving 8.0 g (83%) of white fluffy crystals: mp 101–102 °C (a mixture with 1,1-dimesitylpropene melted at 77–80 °C); ^{1}H NMR ($CDCl_3$) 1.2 (t, 6 H), 2.05 (s, 3 H), 2.18 (s, 6 H), 2.68 (q, 4 H), 7.25 (s, 1 H); mass spectrum, m/e 232 (M^+), 203, 160, 145, 115, 91, 77, 57, 43.

Acknowledgment. Support for this work by the Robert A. Welch Foundation is gratefully acknowledged.

Registry No. $CH_3C(O)Cl$, 75-36-5; $CH_3CH_2C(O)Cl$, 79-03-8; $AlCl_3$, 7446-70-0; mesitylene, 108-67-8; acetomesitylene, 1667-01-2; propionylmesitylene, 2040-15-5; 1,1-dimesitylpropene, 91190-65-7; 1,1-dimesitylethene, 38575-31-4; dipropionylmesitylene, 6335-36-0.

1,3-Carbonyl Transposition Methodology Employing α-Oxo Ketene Dithioacetals: Application in the Synthesis of Phenols and (±)-Myodesmone

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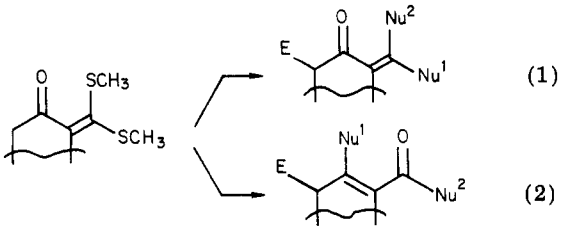
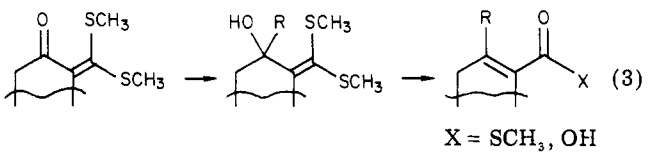
The 1,2-nucleophilic addition of organomagnesium, organolithium, and metal hydride nucleophiles to eight α-oxo ketene dithioacetals and the subsequent aniontropic rearrangement of the resultant allylic alcohols is described. This sequence of reactions represents a 1,3-carbonyl transposition methodology that is utilized in a synthesis of phenols and the furanosesquiterpene (±)-myodesmone (**51**). The aniontropic rearrangement is sensitive to reaction conditions and substrate structure. Tertiary allylic alcohols **15a,d**, **16a**, **17a,c**, **19a,c**, **20a,b**, and **21a,b** are efficiently converted to α,β-unsaturated thiol esters upon treatment with 10% HBF_4 in THF while the secondary allylic alcohols **15b**, **16b**, and **17b** require the addition of HgO or utilization of $HgCl_2$ in acetonitrile for efficient conversion. ^{13}C NMR data for the thiol esters are reported. Utilization of 2 equiv of HgO cleanly transforms allylic alcohols **15a,b**, **17a,b**, and **19a,b** into α,β-unsaturated carboxylic acids **35a,b**, **35c,d**, **36**, and **37**, respectively. Allylic alcohols **15e** and **17d** underwent cyclization to benzenoid aromatic compounds upon attempted aniontropic rearrangement. The methodology establishes the utility of α-oxo ketene dithioacetals as versatile substrates for the sequential regioselective construction of new carbon–carbon bonds.

Introduction

We have been engaged in a systematic investigation of the chemistry of α-oxo ketene dithioacetals[1] aimed at exploiting this rich functionality for the sequential regio- and stereoselective construction of new carbon–carbon bonds (eq 1 and 2). This effort has resulted in the development



of a stereoselective synthesis of α-alkylidene ketones[2] and a 1,3-carbonyl transposition methodology[3] in which the original ketone carbonyl emerges as the carbonyl of a thiol ester or carboxylic acid (eq 3). We now report our extensive examination of this carbonyl transposition sequence, the stereochemical outcome of the process in acyclic substrates, and synthetic applications of the method. The synthesis of the furanosesquiterpene (±)-myodesmone[4] is described and illustrates the powerful synthetic potential of this methodology for sequential regioselective carbon–carbon bond constructions.



Simple and alkylative 1,3-carbonyl transpositions are of considerable synthetic importance as a strategy for introducing new carbon–carbon bonds in a regiospecific manner. Carbon–carbon bond formation occurs during the transposition sequence in an alkylative carbonyl transposition procedure while alkylation of the original and/or transposed carbonyl compound provides additional bond-forming opportunities. Methods for effecting 1,3-carbonyl transpositions[5a] include the Wharton epoxy ke-

(1) β,β-Bis(alkylthio)-α,β-unsaturated ketones have been described in the literature by several convenient and simple descriptive names. These include α-oxo ketene dithioacetals, α-keto ketene mercaptals, α-bis(alkylmercapto)methylene] ketones, and α-(dithiomethylene) ketones.

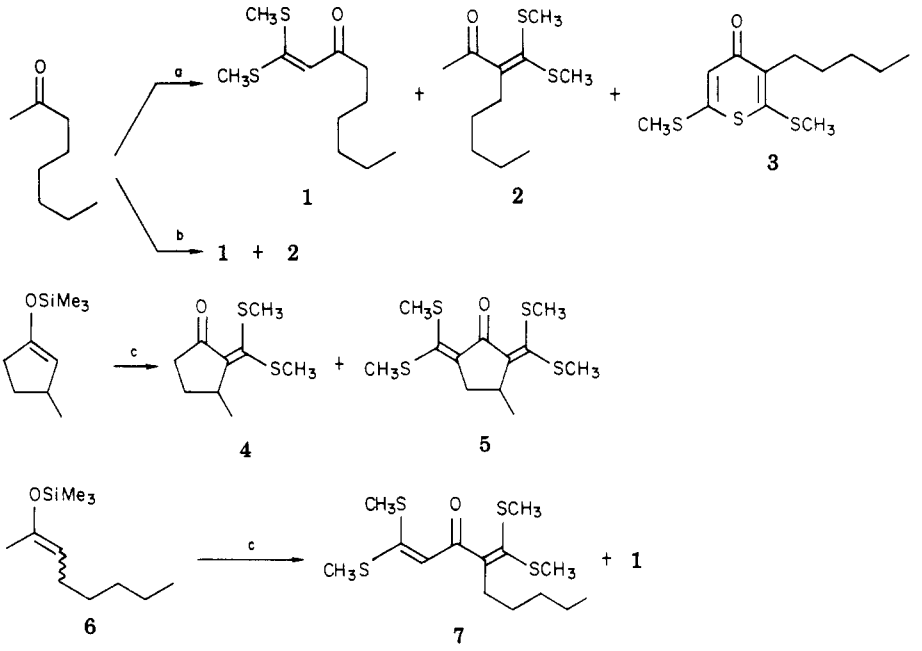
(2) Dieter, R. K.; Silks, L. A. *J. Org. Chem.* **1983**, *48*, 2786.

(3) Dieter, R. K.; Jenkitkasemwong, Y. *Tetrahedron Lett.* **1982**, *23*, 3747.

(4) Blackburne, I. D.; Park, R. J.; Sutherland, M. D. *Aust. J. Chem.* **1971**, *24*, 995.

0022-3263/84/1949-3183$01.50/0

Scheme I[a]



[a] (a) (i) LHMDS, THF, HMPT; (ii) CS_2; (iii) LDA, THF; (iv) CH_3I. (b) Lithium 4,6-di-*tert*-butyl-4-methylphenoxide, THF, CS_2, CH_3I. (c) (i) CH_3Li, THF, HMPT; (ii) CS_2; (iii) LHMDS, THF; (iv) CH_3I.

tone rearrangement,[5b] isoxazole rearrangements,[5c] oxidation of tertiary allylic alcohols,[5d] oxidation and dehydration of β-hydroxy alkylstannanes,[5e] phenylselenenyl chloride addition to allylic alcohols,[5f] and the [2,3] sigmatropic rearrangements of allylic selenoxides,[5g] sulfoxides,[5h,6] and amine oxides.[5i] The α-oxo ketene dithioacetal methodology is closely related to procedures utilizing β-alkoxy[7] and β-(alkylthio)-α,β-unsaturated ketones[8] which are limited to ketone–ketone, ketone–aldehyde, and aldehyde–ketone interconversions. The ketone to thiol ester conversion of the present method provides for additional synthetic flexibility revolving around the thiol ester functionality.

Synthesis of α-Oxo Ketene Dithioacetals. Although many α-oxo ketene dithioacetals are readily prepared from ketone enolates in a one-pot process, the efficiency of these preparations is dependent upon specific enolate structural features and reaction conditions.[9] Several points are noteworthy. First, although lithium 2,6-di-*tert*-butyl-4-methylphenoxide does not add to carbon disulfide, this base effects the transformation under equilibrium conditions and is not effective for carbon acids weaker than saturated ketones.[9b] Use of lithium dialkylamide bases, however, requires the sequential introduction of reagents since they undergo nucleophilic addition to carbon disulfide even in the presence of hexamethylphosphoric triamide (HMPT).[9f] Although carbon disulfide alkylation of thermodynamically or kinetically generated ketone enolate anions provides, in principle, a synthetic route to regiospecifically substituted α-oxo ketene dithioacetals, the strategy is limited by the occurrence of complex equilibria that are difficult to control. Kinetic deprotonation of 2-octanone (Scheme I) with 1.1 equiv of lithium hexamethyldisilazide (LHMDS) in THF followed by sequential addition of carbon disulfide, LDA, and iodomethane afforded ketene dithioacetals **1** (29.2%) and **2** (21.5%) and thiopyranone **3** (21.1%). Thiopyranones have been observed as byproducts in the synthesis of α-oxo ketene dithioacetals and **2** was converted into **3** according to the procedure of Thuillier and Vialle.[9a] Deprotonation of 2-octanone under thermodynamic conditions using 0.9 equiv of lithium hexamethyldisilazide (LHMDS) afforded a substantially different mixture of **1** (22.3%) and **2** (58.5%). Utilization of lithium 2,6-di-*tert*-butyl-4-methylphenoxide according to the procedure of Corey[9b,10] afforded **2** (78%) as the major product and only minor amounts of **1** (4%). Reaction of 2-methylcyclohexanone with the hindered phenoxide and iodomethane gave 2,2-dimethylcyclohexanone as the major product confirming the equilibrium nature of enolate formation under these reaction conditions. However, reaction of 2-methylcyclohexanone with the phenoxide, carbon disulfide, iodomethane combination afforded 2-[bis(methylthio)-methylene]-6-methylcyclohexanone (86%) which could also be prepared by the LDA procedure.[9f]

(5) For a review of carbonyl transpositions see: (a) Nakai, T.; Mimura, T. *J. Synth. Org. Chem., Jpn.* **1977**, *35*, 964. For examples of 1,3-carbonyl transpositions see: (b) Wharton, P. S.; Bohlen, D. H. *J. Org. Chem.* **1961**, *26*, 3615. Wharton, P. S. *Ibid.* **1961**, *26*, 4781. (c) Büchi, G.; Vederas, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 9128. (d) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682. Sundararaman, P.; Herz, W. *Ibid.* **1977**, *42*, 813. Babler, J. H.; Coghlan, M. J. *Synth. Commun.* **1976**, *6*, 469. (e) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836. (f) Liotta, D.; Zima, G.: Saindane, M. *J. Org. Chem.* **1982**, *47*, 1258. Liotta, D.; Zima, G. *Ibid.* **1980**, *45*, 2551. (g) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7154. (h) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147 and references cited therein. (i) Moriwaki, M.; Sawada, S.; Inouye, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 419. Rautenstrauch, V. *Helv. Chim. Acta* **1973**, *56*, 2492.

(6) Trost, B. M.; Stanton, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 4018.

(7) (a) Woods, G. F.; Griswold, P. H., Jr.; Armbrecht, B. H.; Blumenthal, D. I.; Plapinger, R. *Ibid.* **1949**, *71*, 2028. (b) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775. (c) Quesada, M. L.; Schlessinger, R. H. *Synth. Commun.* **1976**, *6*, 555. (d) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 4597.

(8) (a) Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1620. (b) Akiyama, S.; Nakatsuji, S.; Hamamura, T.; Kataoka, M.; Nakagawa, M. *Tetrahedron Lett.* **1979**, 2809. (c) Bernstein, P. R. *Ibid.* **1979**, 1015. (d) Nishio, T.; Omote, Y. *Chem. Lett.* **1979**, 365.

(9) For the preparation of α-oxo ketene dithioacetals see: (a) Thuillier, A.; Vialle, J. *Bull. Soc. Chim. Fr.* **1962**, 2182, 2187. (b) Corey, E. J.; Chen, R. H. K. *Tetrahedron Lett.* **1973**, 3817. (c) Shahak, I.; Sasson, Y. *Ibid.* **1973**, 4207. (d) Augustin, M.; Groth, C. *J. Prakt. Chem.* **1979**, 321, 215. (e) Arjona, O.; Cereceda, J. A.; Quiroga, M. L. *Tetrahedron* **1980**, *36*, 2137. (f) Dieter, R. K. *J. Org. Chem.* **1981**, *46*, 5031.

(10) A modified procedure employing THF instead of diethyl ether was used. The use of diethyl ether has been reported (ref 9e) to afford substantial quantitities of bis(ketene dithioacetals) which were not observed in THF.

The facile occurrence of equilibrium processes caused considerable difficulty in the preparation of α-oxo ketene dithioacetals from regiospecific enolates generated from silyl enol ethers.[11] Although 3-methyl-1-((trimethylsilyl)oxy)-1-cyclopentene was converted to the regiospecifically substituted α-oxo ketene dithioacetal **4** in good yield (75%), significant quantities of the bis[ketene dithioacetal] **5** (12%) were obtained and the procedure could not be extended in a general way to acyclic and 3-alkyl-substituted bicyclic enolate anions. Silyl enol ether **6**, for example, was readily prepared by addition of lithium di-*n*-butylcuprate to methyl vinyl ketone followed by trapping of the regiospecific enolate with chlorotrimethylsilane. Regeneration of the enolate with methyllithium followed by sequential addition of carbon disulfide, LHMDS, and iodomethane afforded **1** (9%) and bis[ketene dithioacetal] **7** (13%) as the only significant products. This is in marked contrast to the direct conversion of 2-octanone to α-oxo ketene dithioacetals. In the cyclic substrates the steric hindrance of the 3-alkyl substituent undoubtedly decreases the rate of enolate–carbon disulfide alkylation and kinetic deprotonation[12] and facilitates uncontrollable equilibrium processes. The formation of bis[ketene dithioacetals] has been observed previously when sodium *tert*-amylate[9a] or lithium 2,6-di-*tert*-butyl-4-methylphenoxide[9e,10] were employed as bases. These results reveal that the reaction of ketone enolates with carbon disulfide is very sensitive to the structure of the ketone and to reaction conditions.

α-Oxo ketene dithioacetals **8–14** were prepared from the appropriate ketone enolate by the sequential addition of carbon disulfide, LDA, or LHMDS as a THF solution containing 1 equiv of HMPT and 2 equiv of iodomethane according to an established procedure.[9f]

The 1,3-Carbonyl Transposition Sequence. The 1,3-carbonyl transposition sequence involves an initial 1,2-nucleophilic addition to the ketone carbonyl of the α-oxo ketene dithioacetal followed by an aniontropic rearrangement[13] of the intermediate α-hydroxy ketene dithioacetal and subsequent loss of methanethiol (eq 3). The 1,2-nucleophilic addition can be effected with a variety of nucleophiles such as organolithium, organomagnesium, and metal hydride reagents (Table I). The electrophilicity of the ketone carbonyl is diminished by conjugation with the ketene dithioacetal functionality and enolization represents the principal side reaction resulting in recovery of starting material. The intermediate allylic alcohols are sufficiently stable to permit chromatographic purification, although prolonged storage results in substantial decomposition. These α-hydroxy ketene dithioacetal intermediates were surprisingly sensitive to the acid-promoted aniontropic rearrangement in view of the relative insensitivity of the γ-hydroxy vinyl sulfides employed in several earlier studies.[8] A range of Brønsted and Lewis acids, and acid/solvent couples were examined. In most instances low yields of the desired unsaturated thiol esters were obtained.[14] Eventually, it was discovered that tetrafluoroboric acid was the most effective acid in promoting the desired rearrangement. The reaction was, however, still extremely sensitive to substrate structure. Tertiary allylic alcohols **15a,d**, **16a**, **17a,c**, **19a,c**, **20a,b**, and **21a,b** (Table I entries 1, 6, 9, 12, 14, 19, 21, 22, 23, 24, and 25, respectively) afforded fair to good yields of the unsaturated thiol esters upon treatment with 10% (v/v) aqueous HBF_4 in THF (1:4) with only traces of the undesired methyl sulfide byproducts being formed. The secondary allylic alcohols **15b**, **16b**, and **17b** (Table I, entries 2, 10, and 13), however, afforded substantial quantities of the unwanted methyl sulfide byproduct under these reaction conditions. The methyl sulfide products presumably arise from methanethiol trapping of stable allylic carbocation intermediates and utilization of sulfur complexing agents provided a solution to this problem. Addition of 0.75 equiv of HgO to the reaction mixture minimized formation of the methyl sulfide byproducts (entries 3 and 11). The α-methylthio ketene dithioacetal **23b** was hydrolyzed to the unsaturated thiol ester **22b** upon treatment with HgO and 10% aqueous HBF_4 in THF and this transformation may account for the efficiency of the hydrolysis conditions. Treatment of α-hydroxy ketene dithioacetal **15b** with $HgCl_2$ in refluxing acetonitrile[6] (Table 1, entry 4) also afforded thiol ester **22b** cleanly in 75% yield and these conditions may prove superior to tetrafluoroboric acid. During this investigation it was discovered that the yield of unsaturated thiol ester was critically dependent upon the quantity of HgO added to the reaction mixture. Utilization of greater than 2.0 equiv afforded good yields of the unsaturated carboxylic acids. In fact, careful control of the reaction conditions permitted isolation of either the unsaturated thiol esters (Table I) or carboxylic acids (Table II) in fair to good yields. Alternatively, the unsaturated thiol esters afford the carboxylic acids in nearly quantitative yield upon alkaline hydrolysis. This methodology provides a very convenient preparative route to cycloalkene-1-carboxylic acids that have previously been prepared with some difficulty.[15]

The acyclic allylic alcohols **19a,c**, **20a,b**, and **21a** underwent aniontropic rearrangement and methanethiol elimination to afford mixtures of double bond geometrical isomers. The ratio of *E*/*Z* geometrical isomers was smaller when the two β-alkyl substituents were of approximately equal steric bulk. As the difference in steric bulk of the two groups increased a stereoselective preference for the isomer with the bulky substituent anti to the thiol ester carbonyl was observed. Addition of methyllithium to α-oxo ketene dithioacetal **13** followed by acid-promoted rearrangement could be induced to proceed with a high degree of stereoselectivity to afford **33a** as an 80:20 *E*/*Z* mixture of geometrical isomers. Similarly, addition of *tert*-butyllithium to **14** afforded, after acid-promoted rearrangement, **34a** in 58% yield as an 85:15 mixture of *E*/*Z* geometrical isomers. The configuration of the double bond in these geometrical isomers was assigned on the basis of the NMR chemical shift of the β-methyl substituent.[16] The *E* isomers (*E*)-**33a** and (*E*)-**34a** where the β-methyl substituent is syn to the carbonyl functionality display absorptions (δ 2.13 and 2.15, respectively) downfield rel-

(11) Dieter, R. K.; Dieter, J. W. *J. Chem. Soc., Chem. Commun.* **1983**, 1378.

(12) Caine, D. In "Carbon–Carbon Bond Formation"; Augustine, R. L., Ed.; Marcel Dekker: New York, 1979; Vol. 1, Chapter 2, p 122.

(13) Braude, E. A. *Q. Rev. Chem. Soc.* **1950**, *4*, 404.

(14) The following reaction conditions converted α-hydroxy ketene dithioacetal **19a** to thiol ester **31a** in the indicated yield: 10% HCl, MeOH (30%); 10% HCl, Et_2O (27%); Amberlyst, Et_2O (25%); silica gel, CH_2Cl_2, trace H_2SO_4 (31%); 10% HCl, acetone (29%). For a review on the hydrolysis of vinyl sulfides and ketene *S*,*S*-acetals see: Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

(15) (a) Harding, K. E.; Tseng, C. *J.* Org. *Chem.* **1978**, *43*, 3974. (b) Trost, B. M.; Whitman, P. *J. J. Am. Chem. Soc.* **1974**, *96*, 7421. (c) McCoy, L. L.; Riecke, E. E. *Ibid.* **1973**, *95*, 7407. (d) Denis, J. N.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1976**, 453. Dinizo, S. E.; Freerksen, R. W.; Pabst, W. E.; Watt, D. S. *J. Am. Chem. Soc.* **1977** *99*, 182. (e) Chan, K. C.; Jewell, R. A.; Nutting, W. H.; Rapoport, H. *J. Org. Chem.* **1968**, *33*, 3382.

(16) A methyl substituent cis to the carbonyl functionality in β-methyl α,β-unsaturated carbonyl compounds resonates downfield in the NMR spectrum relative to the trans methyl substituent. See: (a) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: London, 1969; pp 222–224.

Table I. Nucleophilic Additions to α-Oxo Ketene Dithioacetals and Reactions of the Resultant Allylic Alcohols with Lewis Acids

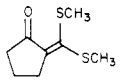
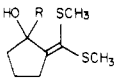
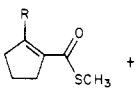
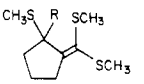
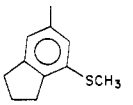
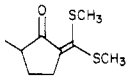
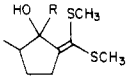
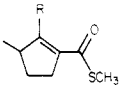
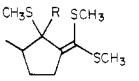
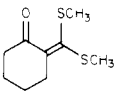
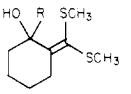
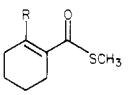
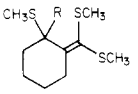
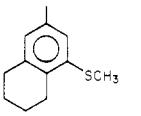
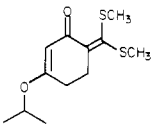
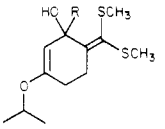
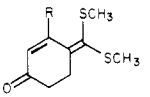
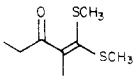
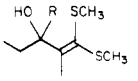
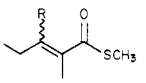
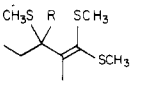
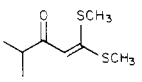
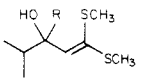
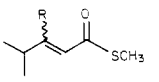
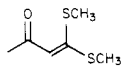
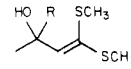
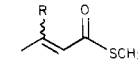
entry	α-oxo ketene dithioacetal	nucleophile R-metal	allylic alcohol, % yield[a]	hydrolysis conditions[b]	products, % yield[a] (E/Z)		
	 8		 15		 22 +  23 + SM		
1		a CH_3Li	69	E	78	<2	
2		b H-metal[c]	98[d]	E	50	47	
3				F	72		
4				G	75		
5		c $H_2C{=}CHLi$	80	E	40		
6		d $Me_3SiCH{=}CHCH_2Li$	89	E	66		11
		e $H_2C{=}C(CH_3)CH_2MgCl$				 24	
7			85	E	20	55	15
8				G		62	
	 9		 16		 25	 26	
9		a CH_3Li	80	E	52	10	
10		b H-metal[c]	98[d]	E	44	35	
11				F	50		
	 10		 17		 27	 28	
12		a CH_3Li	82	E	72	<2	
13		b H-metal[c]	96[d]	E	58	24	
14		c $Me_3SiCH{=}CHCH_2Li$	88	E	78		
		d $H_2C{=}C(CH_3)CH_2MgCl$				 29	
15			92	E		87	
16				G		64	
	 11		 18			 30	
17		a CH_3Li				87	
18		b $(CH_3)_3CO_2CCH_2Li$				75	
	 12		 19		 31	 32	
19		a CH_3Li	76	E	68 (78:22)	<2	
20		b H-metal[c]	96[d]	F	79		
21		c $Me_3SiCH{=}CHCH_2Li$	92	E	40 (42:58)		
	 13		 20			 33	
22		a CH_3Li		E		73 (80:20)	
23		b $Me_3SiCH{=}CHCH_2Li$	99	E		56 (40:60)	

Table I (*Continued*)

entry	α-oxo ketene dithioacetal	nucleophile R-metal	allylic alcohol, % yield[a]	hydrolysis conditions[b]	products, % yield[a] (E/Z)
	 14		 21		 34
24		a $(CH_3)_3CLi$		E	58 (85:15)
25		b $CH_3CH_2CH_2C{\equiv}CLi$		E	52 >(5:95)

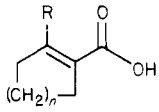
[a] Unless otherwise noted, yields are based upon isolated products purified by chromatography on silica gel. [b] Procedure E: 10% HBF_4, THF, room temperature. ProcedureF: 10% HBF_4, THF, 0.50–0.75 equiv of HgO, room temperature. Procedure G: acetonitrile, $HgCl_2$, 50 °C. [c] $NaBH_4$ was employed. [d] Yields are based upon crude products which were greater than 95% pure.

Table II. Synthesis of α,β-Unsaturated Carboxylic Acids

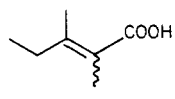
no.	α-oxo ketene dithioacetal	nucleophile	hydrolysis[a] time, days	acid	% yield[b]	ref[c]
1	8	CH_3Li	1	**35a**	51	15a
2		$NaBH_4$	2	**35b**	75	15b
3	10	CH_3Li	1	**35c**	63	15c
4		$NaBH_4$	1	**35d**	75	15d
5	12	CH_3Li	1	**36**	62	
6		$NaBH_4$	2	**37**	69	15e

[a] HgO, THF, H_2O, 10% HBF_4. [b] Yields are based upon isolated products purified by extraction with 10% NaOH. [c] For previous preparation(s) of these acids see the indicated reference(s).

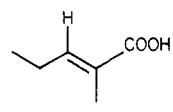
ative to those found in the *Z* isomers (*Z*)-**33a** and (*Z*)-**34a** (δ 1.78 and 1.97, respectively). The chemical shift trends for the isopropyl and *tert*-butyl substituents are, however, reversed with the *Z* isomers (*Z*)-**33a** and (*Z*)-**34a** (δ 1.02 and 0.93, respectively) displaying an upfield absorption relative to the *E* isomers (*E*)-**33a** and (*E*)-**34a** (δ 1.08 and 1.17, respectively). These findings were collaborated by chemical correlation of (*E*)-**33a** with the known methyl ester.[17] Reduction of **12** with $NaBH_4$ afforded allylic alcohol **19b** which could be converted to either α,β-unsaturated thiol ester **31b** or acid **37** as a single stereoisomer in each instance. Acid **37** exhibits NMR chemical shift values (β-CH_2, δ 2.17, β-H, δ 6.90) identical with those reported for the *E* isomer[15e] and the *E* configuration was assigned to thiol ester **31b** by comparison of the β-substituent NMR absorptions (β-CH_2, δ 2.23, β-H, δ 6.60) with those of the acid and methyl ester.[15e] Addition of methyllithium to **12**, however, afforded **31a** and **36** as 78:22 and 56:44 mixtures, respectively, of *E* and *Z* stereoisomers.[18] Addition of 1-lithio-1-pentyne to **14** afforded a



35a, *n* = 1; R = CH_3
b, *n* = 1; R = H
c, *n* = 2; R = CH_3
d, *n* = 2; R = H

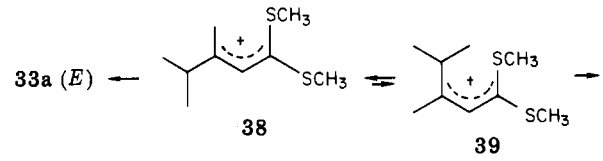


36



37

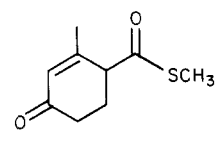
single stereoisomer (**34b**) (β-CH_3 δ 2.01, *Z* configuration) while addition of allyltrimethylsilyl carbanion to **12** and **13** afforded mixtures of *E* and *Z* geometrical isomers in ratios of 42:58 and 40:60, respectively (Table I, entries 25, 21, and 23, respectively). Irradiation of (*Z*)-**34b** (450-watt Hanovia Lamp) afforded a mixture of *E* (β-CH_3, δ 2.21) and *Z* geometrical isomers confirming the original assignment of configuration. The distribution of stereoisomers was shown not to arise from acid-catalyzed equilibration under the rearrangement conditions. Treatment of thiol ester (*E*)-**33a** with 10% aqueous HBF_4 in THF (1:4) did not result in isomerization. These results parallel those reported by Nakagawa[8b] and Trost[6] for the hydrolysis of γ-hydroxy vinyl sulfides. Trost suggests that the observed isomer distributions can be understood in terms of intermediate carbocation stabilities (e.g., **38** and **39**) and this would account for the modest stereoselectivity favoring the isomer having the larger substituent trans to the ester carbonyl.



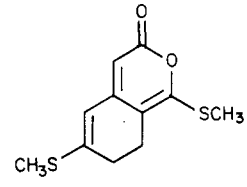
38 **39**

33a (*Z*)

The α-oxo ketene dithioacetal **11** also contains a vinylogous ester moiety which may participate in a 1,3-carbonyl transposition process. Addition of methyllithium or lithium *tert*-butyl acetate to **11** followed by quenching with 10% HCl affords enones **30a** and **30b** in which the ketene dithioacetal functionality remains intact. This is not surprising in view of the greater electron-donating capacity of an oxygen vs. sulfur heteroatom and in fact allylic alcohols **18a,b** did not survive treatment with saturated aqueous NH_4Cl. Dienone **30a** represents a protected form of Hagemann's Ester[19] while **30b** represents the protected form of a 3-alkyl analogue. Dienone **30a** can be hydrolyzed to thiol ester **40** in 69% yield with trifluoroacetic acid.



40



41

Hydrolysis of dienone **30b** under the same conditions, however, afforded the decarboxylation product **40** (8%) and α-pyrone **41** (18%) in poor yields. Structure **41** was assigned by analysis of its spectroscopic properties. The 90-MHz NMR spectrum displays vinyl absorptions at δ 5.66 (s, 1 H) and 5.92 (s, 1 H) and methyl absorptions at δ 2.41 (s, 3 H) and 2.57 (s, 3 H). The ^{13}C NMR spectrum exhibits seven and four absorptions characteristic of sp^2 and sp^3 hybridized carbon atoms, respectively. The

(17) Okano, M.; Lee, K.-H. *J. Org. Chem.* **1981**, *46*, 1138.
(18) The stereoisomers were identified with the aid of the chemical shift values reported for *E* and *Z* methyl 2,3-dimethyl-2-pentenoate: McGreer, D. E.; Wu, W.-S. *Can. J. Chem.* **1967**, *45*, 461.
(19) Begbie, A. L.; Golding, B. T. *J. Chem. Soc., Perkin Trans. 1* **1972**, 602.

downfield absorptions are consistent with an α-pyrone structure[20a] and the methylene carbon absorptions (δ 21.42 and 28.53) are too far upfield for location α to a ketone carbonyl. The absence of a ketone carbonyl was confirmed by the infrared spectrum which displays an absorption at 1725 cm^{-1} consistent with the α-pyrone assignment.[20b] Finally, formation of α-pyrone **41** under the reaction conditions employed parallels a recently reported synthesis of α-pyrones from α-oxo ketene dithioacetals.[21] Dienones **30a,b** and thiol ester **40** should be useful for the synthesis of substituted cyclohexenones or cyclohexanones and for further elaboration into carbocyclic structures.

The bis olefinic alcohols **15e** and **17d** underwent cyclization upon treatment with 10% (v/v) aqueous HBF_4 in THF (1:4) to afford the aromatic compounds **24** and **29**, respectively, in fair to good yields. The cyclization could also be effected with $HgCl_2$ in refluxing acetonitrile. The structure of **29** was initially assigned by an analysis of its spectroscopic properties. The 90-MHz NMR spectrum displays two aromatic absorptions at δ 6.70 (br s, 1 H) and 6.77 (br s, 1 H) and two methyl absorptions at δ 2.23 (s, 3 H) and 2.41 (s, 3 H). The ^{13}C NMR spectrum displays six sp^2-hybridized carbon atoms which give rise to two doublets (δ 122.2 and 126.4) in the single-frequency off-resonance decoupling experiment (SFORD). The presence of six sp^2-hybridized carbon atoms and the disappearance of the disubstituted terminal olefin strongly suggested a cyclization process. The ^{13}C NMR absorptions of **29** are consistent with the calculated[22a] and observed values[22b] for an alkyl-substituted benzene ring containing a methylthio substituent. The structure of **29** was rigorously established by cleavage of the methylthio substituent with ethanethiol and $AlCl_3$ in methylene chloride[23] to afford 6-methyl-1,2,3,4-tetrahydronaphthalene.[24] These results are in contrast to allylic alcohols **15d**, **17c**, **19c**, and **20b** which underwent acid-promoted aniontropic rearrangement and methanethiol elimination to afford unsaturated thiol esters in fair to good yields.

Finally, allylic alcohols **15a**, **16a**, and **20a** could not be successfully dehydrated, under a variety of conditions, to afford olefin-conjugated ketene dithioacetals. The Peterson olefination[25] of α,β-unsaturated enones represents the most efficient route to olefin-conjugated ketene dithioacetals.

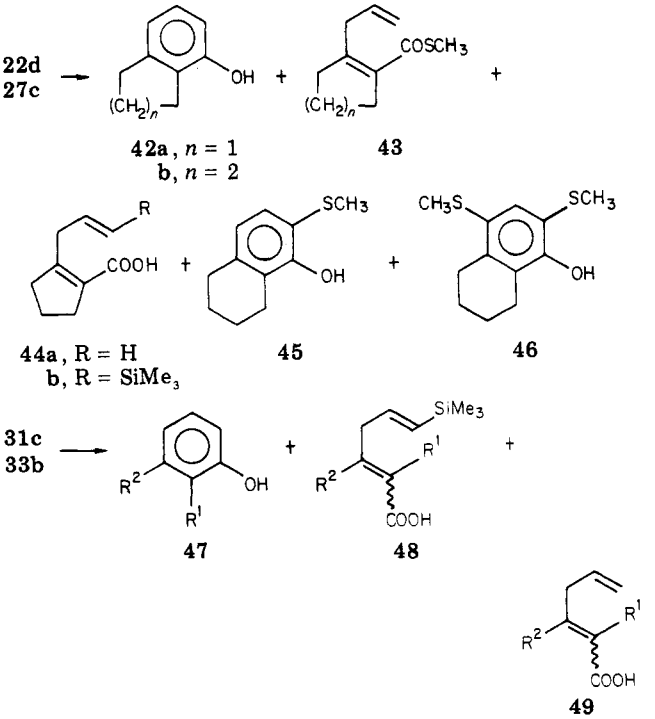
Phenol Synthesis. We have briefly examined the feasibility of utilizing the 1,3-carbonyl transposition methodology in a synthetic route to simple and annulated phenols.[26] The synthetic route involved addition of allyltrimethylsilyl carbanion[27] in a 1,2-fashion to α-oxo ketene dithioacetals **8**, **10**, **12**, and **13** to afford α,β-unsaturated thiol esters **22d**, **27c**, **31c**, and **33b** (Table I, entries 6, 14, 21, 23), respectively, in fair to good yields.

Table III. Phenol Synthesis

no.	thiol ester	equiv of salt[a]	solvent	products, % yield[b]
1	**22d**	1.0	CH_2Cl_2	**42a** (17), **43a** (11)
2		1.0	CH_3CN	**43a** (17), **44a** (9), **44b** (15), **22d** (12)
3	**27c**	1.0	CH_2Cl_2	**42b** (56)
4		2.0		**42b** (24), **45** (33), **46** (13), **27c** (1)
5		1.0	CH_3CN	**42b** (60), **43b** (22), **27c** (3)
6		1.0[c]		**42b** (35), **43b** (12), **27c** (43)
7	**33b**	1.0	CH_3CN	**47b** (14), **48b** (13), **49b** (18)
8		1.0	CH_2Cl_2	**47b** (30)
9	**31c**	1.0	CH_3CN	**47a** (37), **48a** (27), **49a** (28)

[a] Dimethyl(methylthio)sulfonium fluoroborate. [b] Yields are based upon isolated products purified by chromatography on silica gel. [c] 1 equiv of pyridine was added to the reaction mixture.

These α,β-unsaturated thiol esters contain a vinylsilane moiety which was anticipated to undergo an intramolecular acylation[28] upon treatment with Lewis acids. An examination of several acid–solvent systems proved completely unsuccessful and was consistent with a reported attempt to employ vinyl sulfides in a similar manner.[29] Eventually, it was discovered that dimethyl (methylthio)sulfonium fluoroborate[30] effected cyclization of **27c** to phenol **42b** in 56% yield. The reaction, however, proved to be extremely sensitive to substrate structure and reaction conditions. The principle byproducts arose from desilylation of the vinylsilane and/or ester hydrolysis and these products increased as the polarity of the solvent increased (Table III, entries 3–6). Utilization of 2 equiv of the sulfonium salt in CH_2Cl_2 afforded phenols **45** and **46** in 33% and 13%



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(22) (a) Levy, G. C.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists"; Wiley-Interscience: New York, 1972; Chapter 4, pp 80–81. (b) Bzhezovskii, V. M.; Kalabin, G. A.; Aliev, I. A.; Donskikh, V. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1981**, 1525; *Chem. Abstr.* **1981**, *95*, 149421g.

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(24) Ando, T.; Yamawaki, J.; Saito, Y.; Takai, Y.; Yamataka, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2348.

(25) (a) Seebach, D.; Kolb, M.; Gröbel, B.-T. *Chem. Ber.* **1973**, *106*, 2277. (b) Carey, F. A.; Court, A. S. *J. Org. Chem.* **1972**, *37*, 1926.

(26) For alternative routes to phenols see: (a) Tius, M. A.; Thurkauf, A.; Truesdell, J. W. *Tetrahedron Lett.* **1982**, *23*, 2823. (b) Takaki, K.; Okada, M.; Yamada, M.; Negoro, K. *J. Chem. Soc., Chem. Commun.* **1980**, 1183. (c) Chan, T. H.; Brownbridge, P. *Ibid.* **1979**, 578.

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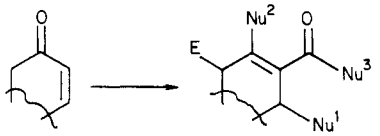
(29) Tius, M. A.; Ali, S. *J. Org. Chem.* **1982**, *47*, 3163.

(30) (a) Smallcombe, S. H.; Caserio, M. C. *J. Am. Chem. Soc.* **1971**, *93*, 5826. (b) Trost, B. M.; Murayama, E. *Ibid.* **1981**, *103*, 6529.

yield, respectively, from **27c** (Table III, entry 4). Treatment of phenol **42b** with dimethyl(methylthio)sulfonium fluoroborate in CH_2Cl_2 afford **45** (47%), **46** (6.4%), and 5-hydroxy-8-(methylthio)-1,2,3,4-tetrahydronaphthalene (3.9%) confirming the structure and probable origin of these byproducts. Thiol ester **22d** and the acyclic analogues **31c** and **33b** afforded only poor yields of the desired phenols (Table III, entries 1–2, 7–9). Attempted utilization of pyridine to minimize the desilylation products resulted in lower yields of products with no discernable effect on the distribution of products (Table III, entry 6).

Synthesis of (±)-Myodesmone. The preparation of regiospecifically substituted α-oxo ketene dithioacetals[11] and the known acylation of organocuprates[31] by unsaturated thiol esters extends considerably the synthetic potential of the 1,3-carbonyl transposition methodology for sequential regioselective carbon–carbon bond constructions (eq 4).



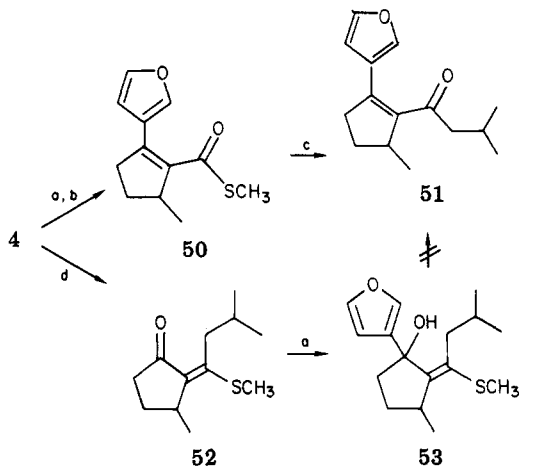
(4)

This potential has been realized in a short and efficient synthesis of the toxic furanosesquiterpene myodesmone recently isolated from *Myoporum deserti* and *Myoporum acuminatum* (Scheme II).[4] Addition of 3-lithiofuran[32] to **4** followed by acid-promoted rearrangement afforded thiol ester **50** in 71% yield. Reaction of **50** with lithium diisobutylcuprate in diethyl ether afforded (±)-myodesmone (**51**) in 53% yield. An alternative route involving vinylogous thiol ester **52** was also examined. Reaction of **4** with lithium isobutyl(phenylthio)cuprate afforded **52** in 54% yield. Reaction of **52** with 3-lithiofuran afforded alcohol **53** in 89% yield. Conditions for the conversion of **53** to (±)-myodesmone were not found. These results indicate that the sequence of carbon–carbon bond constructions must be carefully considered since the 1,3-carbonyl transposition sequence is sensitive to the reaction conditions and substrate structure. This synthetic route to (±)-myodesmone involves the synthesis of a regiospecifically substituted α-oxo ketene dithioacetal, utilization of the 1,3-carbonyl transposition methodology, and exploitation of the product unsaturated thiol ester for additional carbon–carbon bond constructions and illustrates the synthetic potential of this methodology for sequential regioselective carbon–carbon bond constructions.

Conclusion

In summary, the α-oxo ketene dithioacetal functionality has been exploited as a versatile substrate for 1,3-carbonyl transpositions. Three very effective procedures have been developed for conversion of the intermediate α-hydroxy ketene dithioacetals into α,β-unsaturated thiol esters while a procedure[33] for the conversion of α-hydroxy ketene dithioacetals into methyl enoates has recently been reported. The methodology can be exploited for the homologation of a ketone to a β-alkyl-substituted α,β-unsaturated ester, thiol ester, or acid and is formally equivalent to the organocopper substitution reaction with enol phosphates of β-keto esters developed by Weiler.[34] The α-oxo ketene dithioacetal methodology may provide advantages in the use of a wider range of nucleophiles.[21] The α,β-unsaturated thiol esters have been utilized in a rather limited synthesis of phenols and a very efficient synthesis of (±)-myodesmone. The phenol study does, however, indicate that this methodology has some potential for the synthesis of simple and annulated aromatic compounds.

Scheme II[a]



[a] (a) 3-Lithiofuran, Et_2O, −78 °C. (b) 10% aqueous HBF_4, 80:20 THF-H_2O, room temperature, 16 h. (c) *i*-Bu_2CuLi, Et_2O, −40 °C. (d) (PhSCu-*i*-Bu)Li, THF, −78 °C.

Experimental Section

Proton NMR spectra were recorded on either a Varian EM-360L or JEOL-FX90Q instrument. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane as internal standard. Unless otherwise noted the carbon NMR (^{13}C NMR) spectra were recorded at 22.5 MHz as $CDCl_3$ solutions. The ^{13}C NMR chemical shifts are in parts per million downfield from tetramethylsilane and are referenced with respect to internal $CDCl_3$. Infrared spectra were recorded on a Perkin-Elmer 710B grating spectrophotomer as CCl_4 solutions unless otherwise noted. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analysis were determined by Atlantic Microlab Inc., Atlanta, GA.

Hexamethyldisilazane was distilled and stored over 3-Å molecular sieves. Diisopropylamine was distilled over CaH_2 and stored over KOH. Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone prior to use.

1,1-Bis(methylthio)-3-oxo-1-nonene (1). LHMDS (5.2 mmol) was generated at −5 to 0 °C in 5.0 mL of THF under nitrogen. The solution was cooled to −78 °C and 0.89 mL (5.1 mmol) of hexamethylphosphoric triamide (HMPT) was added. A solution of 2-octanone (641 mg, 5.0 mmol) in 2.0 mL of THF was added dropwise via cannula over 5 min. The solution was stirred at −78 °C for 0.5 h, 395.5 mg (0.31 mL, 5.2 mmol) of carbon disulfide was added, the temperature was allowed to rise to −40 °C, and the solution was stirred at this temperature for 2 h. The solution was cooled to −78 °C, 1 equiv of LDA (amine, 525 mg, 5.2 mmol, *n*-BuLi, 2.45 M, 2.12 mL) in 5.0 mL of THF was added via a double-tipped needle, and the solution was allowed to stir for 0.5 h. Methyl iodide (1.47g, 10.4 mmol) was added at −78 °C and the solution slowly warmed to room temperature and stirred overnight. The solution was diluted with saturated NH_4Cl and extracted with ether. The ether extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo to afford 1537.1 mg of crude material. Purification by MPLC (petroleum ether/2% ethyl acetate, v/v, followed by 5% and 10% ethyl acetate) afforded three fractions. Fraction A (R_f 0.68, petroleum ether/5% ethyl acetate) afforded 250 mg (21.5%) of pure 3-[bis(methylthio)methylene]-2-octanone (**2**): IR 2920 (vs), 2855 (m), 1688 (vs), 1420 (s), 1345 (s), 1242 (s), 1120 (s), 905 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.90 (br t, J = 5.0 Hz, 3 H), 1.07–1.67 (m, 6 H), 2.07–2.73 (m, 2 H), 2.27 (s, 3 H), 2.33 (s, 6 H).

Fraction B (R_f 0.33, petroleum ether/5% ethyl acetate) afforded 338 mg (29%) of pure **1**: IR 2920 (vs), 2850 (s), 1695 (s), 1480

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(vs), 1430 (s), 1138 (m), 1183 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.90 (br t, J = 5.0 Hz, 3 H), 1.00–1.87 (m, 8 H), 2.17–2.63 (m, 2 H), 2.47 (s, 6 H), 5.97 (br s, 1 H).

Fraction C (R_f 0.05, petroleum ether/5% ethyl acetate) afforded 289 mg (21%) of pure 2,6-bis(methylthio)-3-pentyl-4*H*-thiopyran-4-one (**3**): IR 2920 (s), 1595 (vs), 1550 (m), 1510 (m), 1430 (s), 1340 (s), 1318 (s), 1085 (m), 911 (m) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.89 (br t, J = 5.5 Hz, 3 H), 1.12–1.65 (m, 6 H), 2.55 (s, 3 H), 2.56 (s, 3 H), 2.60–2.91 (br t, J = 7.0 Hz, 2 H), 6.79 (br s, 1 H); ^{13}C NMR δ 13.8, 16.2, 16.9, 22.3, 27.3, 28.2, 31.7, 124.2, 140.4, 145.5, 151.9, 177.2.

General Procedure A. Addition of Methyllithium to α-Oxo Ketene Dithioacetals. A solution containing 20 mL of dry THF and 4.0 mmol of α-oxo ketene dithioacetal was cooled under nitrogen to −78 °C, and 3.9 mL (1.55 M in ether, 6.0 mmol) of methyllithium was added. The solution immediately turned pale yellow and was left to stir for 1.5 h while the temperature was slowly raised to −10 °C. The reaction was quenched with saturated aqueous ammonium chloride solution and extracted twice with ether. The combined ether extract was washed with brine and dried over magnesium sulfate. Removal of solvent in vacuo gave crude material. Purification by column chromatography (silica gel, petroleum ether/5% ethyl acetate, v/v) afforded pure α-hydroxy ketene dithioacetal. The following α-hydroxy ketene dithioacetals were prepared by the above procedure.

2-[Bis(methylthio)methylene]-1-methylcyclopentanol (15a). Purification by column chromatography afforded pure **15a** in 69% yield: IR 3475 (m), 2960 (s), 2915 (s), 2865 (m), 1430 (m), 1360 (m), 1350 (m), 1300 (s), 1190 (s), 1165 (s), 1115 (m), 990 (s), 925 (m), 870 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.40 (s, 3 H), 1.46–2.82 (m, 6 H), 2.23 (s, 3 H), 2.57 (s, 3 H), 3.27–3.70 (v br s, 1 H).

2-[Bis(methylthio)methylene]-1-methylcyclohexanol (17a). Purification by column chromatography afforded pure **17a** in 82% yield: IR 3430 (m), 2925 (s), 1620 (w), 1460 (m), 1440 (m), 1360 (m), 1175 (m), 1140 (m), 1120 (m), 1010 (m), 970 (m), 935 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.39 (s, 3 H), 1.47–2.14 (m, 7 H), 2.25 (s, 3 H), 2.36 (s, 3 H), 3.41 (br d, J = 15 Hz, 1 H), 5.19 (s, 1 H).

1,1-Bis(methylthio)-2,3-dimethyl-1-penten-3-ol (19a). Purification by column chromatography afforded pure **19a** in 76% yield: IR (neat) 3425 (m), 2970 (s), 2920 (s), 1430 (m), 1370 (m), 1160 (m), 1000 (m), 920 (m), 880 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.87 (t, J = 6.6 Hz, 3 H), 1.32 (s, 3 H), 1.68 (q, J = 6.6 Hz, 2 H), 2.07 (s, 3 H), 2.26 (s, 3 H), 2.35 (s, 3 H), 4.94 (s, 1 H).

4-[Bis(methylthio)methylene]-3-methyl-2-cyclohexenone (30a). General procedure A was employed and afforded after workup with 2 N HCl dienone **30a**. Purification by MPLC (silica gel, petroleum ether/20% ethyl acetate, v/v) afforded pure **30a** in 87% yield: IR 3300 (w), 2910 (s), 1655 (vs), 1570 (s), 1430 (s), 1365 (m), 1340 (s), 1250 (m), 1210 (s), 1165 (s), 900 (m), 870 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 2.36 (s, 3 H), 2.41 (s, 3 H), 2.44 (s, 3 H), 2.38 (t, J = 6.6 Hz, 2 H), 3.15 (t, J = 6.6 Hz, 2 H), 5.80 (br s, 1 H); ^{13}C NMR δ 17.9, 18.0, 22.8, 35.3, 38.3, 129.5, 138.8, 140.7, 157.4, 198.6.

Anal. Calcd for $C_{10}H_{14}OS_2$: C, 56.01; H, 6.59. Found: C, 55.90; H, 6.64.

1,1-Dimethylethyl 6-[Bis(methylthio)methylene]-3-oxocyclohexene-1-acetate (30b). A solution of LDA (1.11 mmol) was generated at 0 °C in 10 mL of THF and cooled to −78 °C, whereupon 119.1 mg (1.03 mmol) of *tert*-butyl acetate was added dropwise and the solution was stirred at −78 °C for 0.5 h. A solution of 204.6 mg (0.79 mmol) of 6-[bis(methylthio)-methylene]-3-isopropoxy-2-cyclohexenone (**11**) in 5.0 mL of THF was added to the reaction mixture at −70 °C via a cannula and the solution was allowed to stir for 2 h while the temperature was slowly raised to −10 °C. The reaction was quenched with saturated NH_4Cl and extracted with ether. The ether extracts were washed with saturated NH_4Cl and brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude product. Purification by MPLC (silica gel, petroleum ether/15% ethyl acetate, v/v) afforded 186.8 mg (75%) of pure dienone **30b**: IR 3320 (w), 2980 (s), 2920 (s), 1730 (vs), 1670 (vs), 1580 (m), 1415 (m), 1395 (m), 1365 (s), 1315 (m), 1255 (s), 1210 (s), 1145 (vs), 955 (m), 910 (s), 880 (m), 845 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.43 (s, 9 H), 2.37 (s, 3 H), 2.40 (s, 3 H), 2.38 (t, J = 7.0 Hz, 2 H), 3.17 (t, J = 7.0 Hz, 2 H), 3.81 (s, 2 H), 5.78 (s, 1 H); ^{13}C NMR δ 17.7, 28.0, 35.6, 38.4, 42.4, 81.1, 131.0, 137.8, 140.0, 153.2, 169.0, 198.4.

2-[Bis(methylthio)methylene]-1-vinylcyclopentanol (15c). A solution containing 10 mL of dry THF and 213 mg (1.13 mmol) of 2-[bis(methylthio)methylene]cyclopentanone (**8**) was cooled under nitrogen to −60 °C and 3.2 mL (0.49 M in THF, 1.59 mmol) of vinyllithium was added. The solution changed from a greenish yellow to dark brown while the temperature was allowed to rise to −45 °C over 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with ether. The ether extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated in vacuo to afford 260.9 mg of crude material. Purification by MPLC (silica gel, petroleum ether/5% ethyl acetate, v/v) afforded 195.7 mg (80%) of pure **15c**: IR 3470 (m), 2960 (s), 1420 (m), 1340 (m), 1305 (m), 1150 (m), 1060 (s), 925 (s), 875 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.10–2.10 (m, 4 H), 2.24 (s, 3 H), 2.29 (s, 3 H), 2.40–2.80 (m, 2 H), 4.02 (s, 1 H), 4.90 (dd, J = 17.0 Hz, J = 1.0 Hz, 1 H), 4.97 (dd, J = 10.0 Hz, J = 1.0 Hz, 1 H), 5.70–6.18 (m, 1 H).

General Procedure B. $NaBH_4$ Reduction of α-Oxo Ketene Dithioacetals. The α-oxo ketene dithioacetal (1.19 mmol) was dissolved in 4.0 mL of CH_3OH and cooled to 0 °C under a nitrogen atmosphere. Sodium borohydride was added as a solid and the ice bath removed after 10 min whereupon the solution changed from a bright yellow to a pale yellow color. The solution was stirred for 3 h at room temperature, poured into water, and extracted with ether. The ether extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude material (>95% pure) that was used directly without further purification.

2-[Bis(methylthio)methylene]cyclopentanol (15b). General procedure B afforded **15b** in 98% yield: IR 3430 (m), 2960 (s), 2920 (s), 1420 (s), 1300 (m), 1220 (m), 1180 (m), 1050 (m), 1025 (m), 975 (s), 880 (m), cm^{-1}; NMR (60 MHz, CCl_4) δ 1.44–2.14 (m, 4 H), 2.28 (s, 3 H), 2.30 (s, 3 H), 2.36–2.77 (m, 3 H), 4.74 (br s, 1 H).

2-[Bis(methylthio)methylene]cyclohexanol (17b). General procedure B afforded **17b** in 96% yield: IR 3360 (m), 2920 (s), 1430 (m), 1245 (m), 1140 (m), 1085 (m), 985 (s), 890 (m), 850 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.00–2.20 (m, 6 H), 2.27 (s, 6 H), 2.58 (s, 1 H), 2.88–3.34 (m, 2 H), 5.31 (br s, 1 H).

1,1-Bis(methylthio)-2-methyl-1-penten-3-ol (19b). General procedure B afforded **19b** in 96% yield: IR (neat) 3380 (s), 2970 (s), 2920 (s), 1440 (s), 1370 (s), 1320 (m), 1250 (m), 1225 (m), 1090 (s), 1010 (s), 980 (s), 890 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.87 (t, J = 7.2 Hz, 3 H), 1.10–1.74 (m, 2 H), 1.95 (s, 3 H), 2.21 (s, 3 H), 2.25 (s, 3 H), 2.34 (br s, 1 H), 4.99 (t, J = 6.6 Hz, 1 H).

General Procedure C. Addition of Methallylmagnesium Chloride to α-Oxo Ketene Dithioacetals. A solution of α-oxo ketene dithioacetal (3.0 mmol) in 10 mL of THF was added dropwise to a solution of methallylmagnesium chloride in THF (12.0 mL of 0.50 M THF solution, 6.0 mmol) at room temperature under nitrogen. The reaction was stirred at room temperature for 8–10 h. 30 mL of saturated aqueous NH_4Cl was added to quench the reaction. The resultant mixture was poured into an additional 30 mL of saturated aqueous NH_4Cl and extracted with 4 30-mL portions of ether. The combined organic phase was washed with 3 25-mL portions of water, dried over $MgSO_4$, and concentrated in vacuo.

The resulting crude yellow oil was used in subsequent acid hydrolysis reactions without further purification.

2-[Bis(methylthio)methylene]-1-(2-methyl-2-propenyl)-cyclopentanol (15e). General procedure C afforded crude **15e** in 85% yield: IR (neat) 3470 (br, m), 1640 (m), 890 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.37–2.07 (m, 6 H), 1.83 (s, 3 H), 2.07–2.87 (m, 2 H), 2.23 (s, 3 H), 2.30 (s, 3 H), 3.73 (br s, 1 H), 4.67 (br s, 1 H), 4.80 (br s, 1 H).

2-[Bis(methylthio)methylene]-1-(2-methyl-2-propenyl)-cyclohexanol (17d). General procedure C afforded crude **17d** in 92% yield: IR (neat) 3410 (br, m), 1650 (m), 890 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.33–2.13 (m, 8 H), 1.80 (s, 3 H), 2.13–2.67 (m, 2 H), 2.27 (s, 3 H), 2.37 (s, 3 H), 3.50–3.70 (br s, 1 H), 4.72 (br s, 1 H), 4.87 (br s, 1 H).

General Procedure D. Addition of (Lithioallyl)trimethylsilane to α-Oxo Ketene Dithioacetals. *sec*-Butyllithium (4.1 mL of a 1.11 M cyclohexane solution, 4.5 mmol) was added

dropwise to a solution of allyltrimethylsilane (0.57 g, 0.79 mL, 5.0 mmol) in 10 mL of THF at −78 °C under nitrogen. Tetramethylethylenediamine (0.52 g, 0.68 mL, 4.5 mmol) was added immediately afterwards. After stirring at −78 °C for 1 h, the reaction mixture was slowly warmed to −40 °C over 1 h and cooled to −78 °C, whereupon a solution of α-oxo ketene dithioacetal (3.0 mmol) in 5 mL of THF was added dropwise. Stirring was continued at −78 °C for an additional 0.5 h and then the solution was warmed to 0 °C over 2 h and then diluted with 30 mL of saturated NH_4Cl. The saturated aqueous NH_4Cl solution was extracted with 4 30-mL portions of ether and the combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude yellow oils which were used without further purification.

2-[Bis(methylthio)methylene]-1-[3-(trimethylsilyl)-2-propenyl]cyclohexanol (17c). General procedure D afforded **17c** in 88% yield: IR (neat) 3400 (br, m), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.17–2.00 (m, 8 H), 2.00–2.93 (m, 2 H), 2.18 (s, 3 H), 2.30 (s, 3 H), 3.55 (br d, J = 2.0 Hz, 1 H), 5.37–6.00 (m, 2 H).

2-[Bis(methylthio)methylene]-1-[3-(trimethylsilyl)-2-propenyl]cyclopentanol (15d). General procedure D afforded **15d** in 89% yield: IR (neat) 3460 (br, m), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.38–2.97 (m, 8 H), 2.20 (s, 3 H), 2.27 (s, 3 H), 3.73 (br s, 1 H), 5.70–6.08 (m, 2 H).

1,1-Bis(methylthio)-3-ethyl-2-methyl-6-(trimethylsilyl)-1,5-hexadien-3-ol (19c). General procedure D afforded **19c** in 92% yield: IR (neat) 3400 (br, m), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 0.83 (t, J = 7.0 Hz, 3 H), 1.53–2.15 (m, 2 H), 2.00 (s, 3 H), 2.15–2.63 (m, 2 H), 2.27 (s, 3 H), 2.35 (s, 3 H), 3.67 (br t, J = 6.0 Hz, 1 H), 5.73–6.27 (m, 2 H).

1,1-Bis(methylthio)-3-(1-methylethyl)-6-(trimethylsilyl)-1,5-hexadien-3-ol (20b). General procedure D afforded **20b** in 99% yield: IR (neat) 3440 (br, m), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 0.93 (d, J = 7.0 Hz, 3 H), 1.10 (d, J = 7.0 Hz, 3 H), 2.00–2.60 (m, 3 H), 2.28 (s, 3 H), 2.40 (s, 3 H), 3.63 (t, J = 7.0 Hz, 1 H), 5.73–6.45 (m, 3 H).

Hydrolysis of α-Hydroxy Ketene Dithioacetals to α,β-Unsaturated Thiol Esters. Procedure E. To a solution containing the α-hydroxy ketene dithioacetal (1.16 mmol), 16.0 mL of THF, and 4.0 mL of H_2O was added 4.0 mL of 10% aqueous HBF_4 at room temperature. The reaction mixture was stirred at room temperature for 2–24 h and then extracted 3 times with ether. The ether layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated in vacuo to afford a pale yellow liquid which was purified by either thin-layer chromatography (TLC) or medium-pressure liquid chromatography (MPLC).

Procedure F. To a solution containing the α-hydroxy ketene dithioacetal (0.6 mmol), 9.0 mL of THF, and 2.0 mL of H_2O was added 64.4 mg (0.3 mmol) of powdered red HgO and 2.1 mL of 10% aqueous HBF_4. The suspension of powdered red HgO turned clear in about 8 min. After stirring for 1 h, a second portion (32.2 mg, 0.15 mmol) of HgO was added. The reaction was monitored by TLC and was complete after 5 h. The reaction mixture was diluted with H_2O and extracted with ether. The ether extracts were washed with a 10% aqueous KI solution, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude material which was purified by TLC.

Procedure G. To a solution of alcohol **15b** (189.9 mg, 1.0 mmol) in 10.0 mL of acetonitrile and 2.0 mL H_2O was added $HgCl_2$ (285 mg, 1.05 mmol). The solution was heated at 60–70 °C for 20 h, cooled to room temperature and the precipitate was filtered and washed with CH_2Cl_2. The filtrate was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated in vacuo to afford 149 mg of crude material. Purification by TLC (silica gel, 1000 μ, petroleum ether/2% ethyl acetate, v/v, 2×) afforded 107.1 mg (75.4%) of pure thiol ester **22b**.

***S*-Methyl 2-Methylcyclopentene-1-thioate (22a).** Procedure E afforded **22a** in 78% yield after purification by TLC (petroleum ether/5% ethyl acetate, v/v, R_f 0.61): IR 3270 (w), 2930 (s), 1660 (vs), 1625 (vs), 1435 (s), 1375 (m), 1300 (m), 1240 (m), 1170 (vs), 1085 (m), 1015 (m), 945 (s), 855 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.86 (t, J = 7.8 Hz, 2 H), 2.11 (br s, 3 H), 2.28 (s, 3 H), 2.38–3.00 (m, 4 H); ^{13}C NMR δ 10.9 (q), 16.3 (q), 21.5 (t), 32.9 (t), 40.5 (t), 133.2 (s), 153.2 (s), 189.3 (s).

Anal. Calcd for $C_8H_{12}OS$: C, 61.48; H, 7.75. Found: C, 61.29; H, 7.79.

***S*-Methyl Cyclopentene-1-thioate (22b).** Procedure E afforded **22b** in 50% yield after purification by TLC (petroleum ether, 3×, R_f 0.57): IR 3250 (w), 2970 (s), 2930 (s), 1665 (vs), 1155 (s), 960 (m), 925 (m), 895 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.95 (t, J = 7.8 Hz, 2 H), 2.31 (s, 3 H), 2.14–2.84 (m, 4 H), 6.68 (br s, 1 H); ^{13}C NMR δ 11.2 (q), 22.9 (t), 31.2 (t), 33.3 (t), 141.5 (d), 144.0 (s), 189.3 (s).

Anal. Calcd for $C_7H_{10}OS$: C, 59.10; H, 7.09. Found: C, 59.05; H, 7.12.

1-[Bis(methylthio)methylene]-2-(methylthio)cyclopentane (**23b**) was also obtained in 47% yield (R_f 0.73): IR 2960 (s), 2910 (s), 1420 (s), 1310 (w), 885 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.63–2.00 (m, 4 H), 2.10 (s, 3 H), 2.27 (s, 6 H), 2.35–2.75 (m, 2 H), 4.13 (br s, 1 H); ^{13}C NMR δ 15.0, 16.4, 17.4, 23.2, 32.4, 32.7, 51.0, 126.6, 152.2.

Anal. Calcd for $C_9H_{16}S_3$: C, 49.04; H, 7.32. Found C, 49.18; H, 7.34.

***S*-Methyl 2-Vinylcyclopentene-1-thioate (22c).** Procedure E afforded **22c** in 40% yield after purification by TLC (petroleum ether/5% ethyl acetate, v/v, R_f 0.69): IR 3275 (w), 3090 (w), 2930 (s), 2485 (m), 1650 (vs), 1570 (s), 1435 (m), 1305 (m), 1165 (vs), 1040 (vs), 1025 (vs), 1000 (m), 920 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.89 (t, J = 7.2 Hz, 2 H), 2.32 (s, 3 H), 2.45–3.02 (m, 4 H), an ABC pattern [5.35 (d, J = 11.5 Hz, 1 H), 5.40 (d, J = 16.8 Hz, 1 H), 7.51 (dd, J = 16.8 Hz, J = 11.5 Hz, 1 H)]; ^{13}C NMR δ 11.4 (q), 21.6 (t), 33.5 (t), 33.8 (t), 121.6 (t), 131.9 (d), 135.3 (s), 149.4 (s), 189.8 (s).

***S*-Methyl 2-[3-(Trimethylsilyl)-2-propenyl]cyclopentene-1-thioate (22d).** General procedure E (3.00 mmol scale) afforded 456 mg (66%) of **22d** after purification by MPLC (petroleum ether/3–10% ethyl acetate gradient): IR (neat) 1660 (s), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.83–2.17 (m, 2 H), 2.33 (s, 3 H), 2.43–3.00 (m, 4 H), 3.43 (d, J = 5.0 Hz, 2 H), 5.80–6.07 (m, 2 H); ^{13}C NMR δ 1.2 (q), 11.3 (q), 21.9 (t), 33.4 (t), 37.9 (t), 38.1 (t), 132.5 (d), 133.9 (s), 142.0 (d), 154.3 (s), 189.2 (s).

Anal. Calcd for $C_{13}H_{22}OSSi$: C, 61.36; H, 8.71. Found: C, 61.28; H, 8.75.

***S*-Methyl 3-Methylcyclopentene-1-thioate (25b).** Procedure E afforded **25b** in 44% yield after purification by TLC (petroleum ether, 3×, R_f 0.61): IR 2950 (m), 2925 (s), 2850 (m), 1660 (vs), 1615 (s), 1460 (m), 1310 (m), 1255 (m), 1230 (m), 1165 (s), 955 (m), 910 (m), 870 (m) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.14 (d, J = 7.0 Hz, 3 H), 1.27–2.20 (m, 2 H), 2.30 (s, 3 H), 2.40–3.27 (m, 3 H), 6.60 (d, J = 2.0 Hz, 1 H); ^{13}C NMR δ 11.0, 19.5, 30.7, 31.6, 40.7, 142.5, 146.3, 189.2.

Anal. Calcd for $C_8H_{12}OS$: C, 61.48; H, 7.75. Found: C, 61.58; H, 7.75.

1-[Bis(methylthio)methylene]-3-methyl-2-(methylthio)cyclopentane **26b** was also obtained in 35% yield as a mixture of *E* and *Z* diastereomers (R_f 0.77): *trans*-3-methyl-2-(methylthio) NMR (60 MHz, CCl_4) [δ 0.94 (J = 7.0 Hz, 3 H), 3.72 (s, 1 H)]; *cis*-3-methyl-2-(methylthio) [δ 1.13 (d, J = 7.0 Hz, 3 H), 4.05 (d, J = 5.0 Hz, 1 H)]; ^{13}C NMR δ 14.8, 16.7, 17.6, 19.9, 30.5, 30.8, 39.7, 57.3, 127.6, 151.8.

Anal. Calcd for $C_{10}H_{18}S_3$: C, 51.23; H, 7.74. Found: C, 51.30; H, 7.77.

***S*-Methyl 2,3-Dimethylcyclopentene-1-thioate (25a).** Procedure E afforded **25a** in 52% yield after purification by TLC (petroleum ether/3% ether, v/v, R_f 0.64): IR 3420 (w), 3280 (w), 2980 (s), 2930 (s), 1655 (vs), 1635 (vs), 1450 (m), 1430 (m), 1370 (m), 1310 (m), 1240 (m), 1165 (vs), 1085 (s), 935 (s), 900 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.09 (d, J = 6.6 Hz, 3 H), 1.20–1.94 (m, 2 H), 2.05 (br s, 3 H), 2.27 (s, 3 H), 2.36–2.93 (m, 3 H); ^{13}C NMR δ 11.2, 14.7, 18.1, 30.8, 31.2, 46.0, 133.0, 157.0, 190.2.

Anal. Calcd for $C_9H_{14}OS$: C, 63.46; H, 8.29. Found: C, 63.37; H, 8.35.

***S*-Methyl Cyclohexene-1-thioate (27b).** Procedure E afforded **27b** in 58% yield after purification by TLC (petroleum ether/5% ether, v/v, 2×, R_f 0.54): IR 3300 (w), 3050 (w), 2960 (s), 1670 (vs), 1455 (m), 1440 (m), 1185 (s), 1175 (s), 1160 (s), 975 (m), 880 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.40–1.94 (m, 4 H), 1.94–2.50 (m, 4 H), 2.27 (s, 3 H), 6.86 (br s, 1 H); ^{13}C NMR δ 11.2, 21.6, 22.0, 24.0, 25.8, 137.8, 138.3, 193.4.

Anal. Calcd for $C_8H_{12}OS$: C, 61.48; H, 7.75. Found: C, 61.51; H, 7.75.

1-[Bis(methylthio)methylene]-2-(methylthio)cyclohexane **28b** was also obtained in 24% yield (R_f 0.72): IR 2940 (s), 2870 (m), 1440 (m), 870 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.00–2.09 (m, 6 H), 1.94 (s, 3 H), 2.23 (s, 6 H), 2.30–2.76 (m, 1 H) 3.19 (br d, J = 13.2 Hz, 1 H), 4.73 (br s, 1 H); ^{13}C NMR 14.4, 17.4, 21.5, 27.6, 28.9, 32.5, 47.4, 127.2, 149.0.

Anal. Calcd for $C_{10}H_{18}S_3$: C, 51.23; H, 7.74. Found: C, 51.26; H, 7.79.

***S*-Methyl 2-Methylcyclohexene-1-thioate (27a).** Procedure E afforded **27a** in 72% yield after purification by TLC (petroleum ether/5% ether, v/v, R_f 0.71): IR 3300 (w), 2930 (s), 1660 (vs), 1440 (s), 1425 (s), 1380 (m), 1280 (m), 1215 (s), 1145 (vs), 1065 (s), 920 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.38–1.79 (m, 4 H), 1.90 (br s, 3 H), 1.98–2.60 (m, 4 H), 2.28 (s, 3 H); ^{13}C NMR δ 11.6, 21.7, 22.0, 22.3, 26.7, 33.0, 131.4, 141.4, 195.8.

Anal. Calcd for $C_9H_{14}OS$: C, 63.46; H, 8.29. Found: C, 63.42; H, 8.33.

***S*-Methyl 2-[3-(Trimethylsilyl)-2-propenyl]cyclohexene-1-thioate (27c).** General procedure E (3.00 mmol scale) afforded 585 mg (78%) of **27c** after purification by MPLC (petroleum ether/3–8% ethyl acetate gradient): IR (neat) 1665 (s), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.42–1.80 (m, 4 H), 2.00–2.30 (m, 4 H), 2.35 (s, 3 H), 3.08 (d, J = 5.0 Hz, 2 H), 5.67–6.33 (m, 2 H); ^{13}C NMR δ 1.2 (q), 11.6 (q), 22.1 (t), 22.3 (t), 27.1 (t), 30.0 (t), 42.6 (t), 132.1 (d), 132.6 (s), 141.4 (s), 143.4 (d), 196.0 (s).

Anal. Calcd for $C_{14}H_{24}OSSi$: C, 62.63; H, 9.01. Found: C, 62.74; H, 9.04.

***S*-Methyl 2,3-Dimethyl-2-pentenethioate (31a).** General procedure E afforded thiol ester **31a** in 68% yield as a 78:22 mixture of E and Z geometrical isomers: NMR (60 MHz, CCl_4) E isomer δ 1.87 (s, 2-CH_3, 6 H), 2.07 (q, J = 7.5 Hz, 2 H); Z isomer δ 1.70 (s, 2-CH_3, 6 H).

Anal. Calcd for $C_8H_{14}OS$: C, 60.71; H, 8.92. Found: C, 60.60; H, 8.93.

***S*-Methyl 2-Methyl-2-pentenethioate (31b).** Procedure E afforded **31b** in 79% yield after purification by TLC (petroleum ether/5% ether, R_f 0.73): IR 3290 (w), 2960 (s), 2920 (s), 1655 (vs), 1455 (m), 1430 (m), 1380 (m), 1210 (s), 1105 (m), 1040 (s), 1000 (s), 985 (m), 925 (m), 865 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.10 (t, J = 7.8 Hz, 3 H), 1.86 (d, J = 2.0 Hz, 3 H), 2.29 (s, 3 H), 2.23 (q, J = 7.8 Hz, 2 H), 6.60 (tq, J = 7.8 Hz, J = 2.0 Hz, 1 H); ^{13}C NMR δ 11.6, 12.3, 13.0, 22.0, 135.3, 142.1, 194.2.

Anal. Calcd for $C_7H_{12}OS$: C, 58.29; H, 8.39. Found: C, 58.33; H, 8.40.

***S*-Methyl 3-Ethyl-2-methyl-6-(trimethylsilyl)-2,5-hexadienethioate (31c).** General procedure E (3.00 mmol scale, 7–10 days) afforded 283 mg (40%) of **31c** as a 42:58 E:Z mixture of geometrical isomers after purification by MPLC (petroleum ether/2% ethyl acetate): IR (neat) 1670 (s), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) E isomer δ 0.97 (t, J = 7.0 Hz, 3 H), 1.87 (s, 3 H), 2.30 (s, 3 H), 2.90 (d, J = 4.0 Hz, 2 H); Z isomer δ 1.00 (t, J = 7.0 Hz, 3 H), 1.90 (s, 3 H), 2.30 (s, 3 H), 3.00 (d, J = 4.5 Hz, 2 H).

***S*-Methyl 3,4-Dimethyl-2-pentenethioate (33a).** General procedure A was employed with the exception that the allylic alcohol was not isolated. 10% aqueous HBF_4 was added at −70 °C and the solution was allowed to slowly warm to room temperature, stirred for 2 h, and then extracted with ether. The ether extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo to afford the thiol ester in 73% yield as a mixture of E and Z diastereomers which could be separated by GC (10% OV 101, 10 ft, 130 °C column temperature). E isomer: IR 2970 (s), 2935 (s), 1672 (vs), 1620 (vs), 1095 (s), 1045 (vs), 890 (s), 845 (s) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.08 (d, J = 7.0 Hz, 6 H), 2.13 (d, J = 1.0 Hz, 3 H), 2.23–2.55 (m, 1 H), 2.33 (s, 3 H), 5.97 (br s, 1 H). Z isomer: NMR (90 MHz, $CDCl_3$) δ 1.02 (d, J = 7.0 Hz, 6 H), 1.78 (d, J = 1.0 Hz, 3 H), 2.31 (s, 3 H), 3.90 (hep, J = 7.0 Hz, 1 H), 5.92 (br s, 1 H).

***S*-Methyl 3-(1-Methylethyl)-6-(trimethylsilyl)-2,5-hexadienethioate (33b).** General procedure E (3.00 mmol scale) afforded 419 mg (56%) of **33b** as a 40:60 E:Z mixture of geometrical isomers after purification by MPLC (petroleum ether/2–5% ethyl acetate gradient): IR (neat) 1670 (s), 1250 (s) cm^{-1}; NMR (60 MHz, CCl_4) E isomer δ 1.07 (d, J = 7.0 Hz, 6 H), 2.12 (s, 3 H), 2.93 (d, J = 4.0 Hz, 2 H); Z isomer δ 1.13 (d, J = 7.0 Hz, 6 H), 2.33 (s, 3 H), 3.48 (d, J = 4.5 Hz, 2 H).

***S*-Methyl 3,4,4-Trimethyl-2-pentenethioate (34a).** General procedure A was employed by using *tert*-butyllithium as the alkyllithium reagent (0.92 mmol scale), followed by hydrolysis according to general procedure E afforded 92 mg (58%) of **34a** as a 85:15 E:Z mixture of geometrical isomers after purification by MPLC (petroleum ether/2% ethyl acetate): IR 2960 (s), 1675 (s), 1610 (s), 1465 (m), 1430 (w), 1370 (m-s), 1255 (m-s), 1070 (s), 1015 (s), 970 (m), 835 (s) cm^{-1}; NMR (60 MHz, CCl_4) E isomer δ 1.17 (s, 9 H), 2.15 (s, 3 H); Z isomer δ 0.93 (s, 9 H), 1.97 (s, 3 H).

***S*-Methyl 3-Methyl-2-octen-4-ynethioate (34b).** 1-Lithio-1-pentyne was generated by addition of *n*-butyllithium to a THF solution of 1-pentyne. General procedures A and E were then employed to afford **34b** after purification by MPLC (petroleum ether/1% ethyl acetate): IR 2960 (vs), 2920 (vs), 2200 (s), 1675 (vs), 1630 (vs), 1590 (vs), 1440 (s), 1370 (s), 1195 (s), 1070 (vs) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.05 (t, J = 7.0 Hz, 3 H), 1.65 (sex, J = 7.0 Hz, 2 H), 2.01 (d, J = 1.0 Hz, 3 H), 2.40 (s, 3 H), 2.45 (t, J = 7.0 Hz, 2 H), 6.23 (q, J = 1.0 Hz, 1 H).

Anal. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found: C, 65.66; H, 7.75.

General Procedure H. Hydrolysis of α-Hydroxy Ketene Dithioacetals to α,β-Unsaturated Carboxylic Acids. To a solution of the α-hydroxy ketene dithioacetal (0.25 mmol) in 4.0 mL of THF and 1.0 mL of H_2O was added powdered red HgO (108.3 mg, 0.50 mmol) and 1.0 mL of 48% aqueous HBF_4. The red HgO powder gradually dissolved and the color of the solution turned to a pale yellow and became clear in 1 h. The reaction mixture was diluted with water, extracted with ether, and the ether extracts were washed with 10% NaOH. The aqueous phase was neutralized with 2 N HCl and extracted with ether. The ether extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude product.

2-Methylcyclohexene-1-carboxylic Acid (35c). General procedure H afforded **35c** in 63% yield: IR 3300–2500 (br, s), 2930 (s), 2860 (s), 1675 (vs), 1630 (s), 1280 (s), 1260 (s) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.41–1.84 (m, 4 H), 2.07 (s, 3 H), 2.07–2.56 (m, 4 H), 10.90 (br s, 1 H); ^{13}C NMR δ 22.23 (3 C atoms), 26.08, 34.37, 123.43, 150.46, 174.62.

Cyclohexene-1-carboxylic Acid (35d). General procedure H afforded **35d** in 75% yield: IR 3300–2500 (br, s), 2930 (s), 2855 (s), 1686 (vs), 1280 (s), 1260 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.40–1.95 (m, 4 H), 1.96–2.55 (m, 4 H), 7.13 (br s, 1 H), 12.38 (s, 1 H).

2,3-Dimethyl-2-pentenoic Acid (36). General procedure H afforded **36** in 62% yield as a 56:44 mixture of E/Z geometrical isomers: NMR (60 MHz, CCl_4) δ 1.09 (t, J = 7.0 Hz, 3 H), 1.90 [br s, CH_3(C2) E isomer + 2 CH_3 (C2 and C3) Z isomer], 2.13 (q, J = 1.0 Hz, CH_3(C3) E isomer), 2.34 (q, J = 7.0 Hz, CH_2 E isomer), 2.53 (q, J = 7.0 Hz, CH_2 Z isomer), 12.70 (br s, 1 H).

4-(Methylthio)-6-methylindan (24). General procedure E afforded **24** in 55% yield after purification by MPLC (petroleum ether/3–10% ethyl acetate gradient): IR (CCl_4), 1600 (m), 1575 (s), 840 (s) cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 2.10 (p, J = 7.0 Hz, 2 H), 2.23 (s, 3 H), 2.40 (s, 3 H), 2.77 (t, J = 7.0 Hz, 2 H), 2.90 (t, J = 7.0 Hz, 2 H), 6.77 (s, 2 H); ^{13}C NMR δ 15.1, 21.3, 24.8, 31.3, 33.0, 121.7, 122.9, 133.7, 136.7, 139.0, 144.4.

Anal. Calcd for $C_{11}H_{14}S$: C, 74.10; H, 7.91. Found: C, 74.21; H, 7.95.

***S*-Methyl 2-(2-methyl-2-propenyl)cyclopentene-1-thioate (22e)** was also isolated in 20% yield: IR (neat) 1660 (s), 1640 (w), 890 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.70 (s, 3 H), 1.73–2.13 (m, 2 H), 2.13–3.00 (m, 4 H), 2.23 (s, 3 H), 3.27 (d, J = 1.5 Hz, 2 H), 4.63 (d, J = 2.0 Hz, 2 H); ^{13}C NMR δ 11.2, 21.9, 22.5, 33.4, 38.0, 38.4, 111.5, 134.8, 142.7, 154.3, 189.8.

5-(Methylthio)-7-methyl-1,2,3,4-tetrahydronaphthalene (29). General procedure E afforded **29** in 87% yield after purification by MPLC (petroleum ether/3% ethyl acetate): IR (neat) 1620 (m), 1600 (m), 1570 (m), 840 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.83–2.37 (m, 4 H), 2.62 (s, 3 H), 2.72 (s, 3 H), 2.82–3.30 (m, 4 H), 7.02 (s, 1 H), 7.13 (s, 1 H); ^{13}C NMR δ 15.0 (q), 21.0 (q), 22.8 (t), 23.3 (t), 26.3 (t), 29.9 (t), 122.2 (d), 126.4 (d), 131.3 (s), 135.1 (s), 137.2 (s), 137.5 (s).

Anal. Calcd for $C_{12}H_{16}S$: C, 74.94; H, 8.39. Found: C, 74.82; H, 8.42.

***S*-Methyl 2-Methyl-4-oxo-2-cyclohexene-1-thioate (40).** Trifluoroacetic acid (0.4 mL, 5.19 mmol) was added to ketene dithioacetal **30a** (53.2 mg, 0.24 mmol). The solution immediately turned pink in color and then purple and was stirred at room temperature for 40 min whereupon water (0.8 mL) was added and the solution stirred overnight. The reaction mixture was diluted with H_2O, extracted with ether (4 × 6 mL), washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo to afford 44.5 mg of crude material. Purification by TLC (silica gel, 1000 μ, petroleum ether/2% ethyl acetate) afforded 29.5 mg (67%) of **40**: IR 3340 (w), 2930 (s), 1665 (vs), 1460 (s), 1375 (s), 1335 (s), 1245 (s), 1040 (s), 990 (s), 890 (s), 840 (s) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.99 (br s, 3 H), 2.00–2.78 (m, 4 H), 2.37 (s, 3 H), 3.51 (br t, J = 6.0 Hz, 1 H), 6.01 (br s, 1 H); ^{13}C NMR δ 11.83, 23.10, 27.00, 33.82, 54.08, 129.17, 156.20, 197.86, 198.35.

1,6-Bis(methylthio)-7,8-dihydro-3*H*-2-benzopyran-3-one (41). Ketene dithioacetal **30b** (101.8 mg, 0.32 mmol) was treated with trifluoroacetic acid as described above for **30a**. The crude material (57.3 mg) was purified by TLC (silica gel, petroleum ether/20% ethyl acetate, v/v) to afford 4.4 mg of **40** [7.4%, R_f 0.27] and 13.7 mg of **41** [18%, R_f 0.12]: IR 3430 (w), 2925 (m), 2830 (w), 1725 (vs), 1608 (s), 1580 (s), 1540 (s), 1410 (s), 1310 (s), 1040 (s), cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 2.23–2.90 (m, 4 H), 2.41 (s, 3 H), 2.57 (s, 3 H), 5.65 (s, 1 H), 5.91 (s, 1 H); ^{13}C NMR δ 12.97 (q), 13.86 (q), 21.42 (t), 28.53 (t), 101.23 (d), 109.24 (s), 113.27 (d), 148.59 (s), 153.03 (s), 154.81 (s), 163.93 (s).

Anal. Calcd for $C_{11}H_{12}O_2S_2$: C, 54.97; H, 5.03. Found: C, 54.73; H, 5.06.

General Procedure I. Synthesis of Phenols by Intramolecular Cyclization of Vinylsilanes. Dimethyl(methylthio)sulfonium fluoroborate[30] (215.7 mg, 1.1 mmol) was added to a solution of the appropriate thiol ester (**22d**, **27c**, **31c**, or **33b**) in 10 mL of methylene chloride or acetonitrile at room temperature under nitrogen. The progress of the reaction was followed by TLC (silica gel, petroleum ether/3% ethyl acetate). After 20 h, 25 mL of saturated aqueous NH_4Cl was added, the organic phase separated, and the aqueous phase extracted with 3 25-mL portions of ether. The organic phase was dried over $MgSO_4$ and concentrated in vacuo to afford crude products which were purified by column chromatography (silica gel, petroleum ether/1–5% ethyl acetate, v/v) or preparative TLC (silica gel, 1000 μ, petroleum ether/3–5% ethyl acetate, v/v).

4-Hydroxyindan (42a). General procedure I with methylene chloride as solvent afforded **42a** in 17% yield (R_f 0.30–0.38, petroleum ether/10% ethyl acetate): IR (CH_2Cl_2) 3580 (s), 3420 (m), 3040 (w), 1620 (w), 1580 (s), 1470 (s), 1205 (s), 785 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.70–2.27 (p, J = 7.0 Hz, 2 H), 2.53–2.98 (m, 4 H), 4.60 (br s, 1 H), 6.23–7.03 (m, 3 H).

S-Methyl 2-(2-propenyl)cyclopentene-1-thioate (**43a**) was also formed in 11% yield (R_f 0.79–0.85): IR (CH_2Cl_2) 1670 (s), 1645 (s), 1610 (m), 1430 (m), 995 (m), 925 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.46–2.08 (p, J = 7.0 Hz, 2 H), 2.22 (s, 3 H), 2.22–2.83 (m, 4 H), 3.23 (d, J = 6.0 Hz, 2 H), 4.72–5.20 (m, 2 H), 5.20–6.08 (m, 1 H).

General procedure I with acetonitrile as solvent also afforded **44a,b** in addition to **43a**. 2-(2-Propenyl)cyclopentene-1-carboxylic acid (**44a**) was formed in 9% yield (R_f 0.17–0.21): IR (CH_2Cl_2) 3430–2720 (br s), 1675 (s), 1630 (s), 1420 (s), 990 (m), 924 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.46–2.17 (p, J = 7.0 Hz, 2 H), 2.33–3.00 (m, 4 H), 3.37 (d, J = 4.0 Hz, 2 H), 4.83–5.30 (m, 2 H), 5.30–6.10 (m, 1 H), 12.27 (br s, 1 H).

2-[3-(Trimethylsilyl)-2-propenyl]cyclopentene-1-carboxylic acid (**44b**) was formed in 15% yield (R_f 0.21–0.26): IR (CH_2Cl_2) 3440–2730 (br s), 1670 (s), 1630 (s), 1280 (m), 840 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.46–2.13 (p, J = 7.0 Hz, 2 H), 2.33–2.90 (m, 4 H), 3.43 (d, J = 4.0 Hz, 2 H), 5.68–6.00 (m, 2 H), 12.25 (br s, 1 H).

5-Hydroxy-1,2,3,4-tetrahydronaphthalene (42b). General procedure I with acetonitrile as solvent afforded **42b** in 61% yield (R_f 0.36–0.42, petroleum ether/10% ethyl acetate, v/v): mp 67–69 °C; IR (neat) 3620 (s), 3460 (m), 3040 (w), 1610 (w), 1590 (s), 1465 (s), 1450 (m), 1320 (m), 1270 (s), 770 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.57–1.90 (m, 4 H), 2.40–2.93 (m, 4 H), 5.52 (br s, 1 H), 6.27–7.00 (m, 3 H).

***S*-Methyl 2-(2-propenyl)cyclohexene-1-thioate (43b)** was also formed in 22% yield (R_f 0.70–0.80): IR (neat) 1670 (s), 1630 (m), 1610 (m), 1430 (m), 995 (m), 920 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.46–1.93 (m, 4 H), 1.93–2.20 (m, 4 H), 2.28 (s, 3 H), 3.00 (d, J = 6.0 Hz, 2 H), 4.77–5.53 (m, 2 H), 5.53–6.10 (m, 1 H).

5-Hydroxy-6-(methylthio)-1,2,3,4-tetrahydronaphthalene (45). To a solution of phenol (49.0 mg, 0.33 mmol) in 3.5 mL of dry CH_2Cl_2 under a nitrogen atmosphere was added dimethyl (methylthio)sulfonium fluoroborate (70.6 mg, 0.36 mmol) and the mixture was left to stir at room temperature for 4 h. The reaction mixture was diluted with H_2O and extracted three times with 10 mL of ether, and the organic phase was washed with brine, dried over $MgSO_4$ and concentrated in vacuo to afford 61.1 mg of a yellow liquid. Purification by TLC (silica gel, 1000 μ, petroleum ether/3% ethyl acetate, v/v, 2×) gave three fractions. Fraction I (R_f 0.76, petroleum ether/5% ethyl acetate) afforded 30.2 mg (47%) of **45**: IR (neat) 3410 (s), 1615 (m), 1600 (m), 1570 (s), 1480 (m), 830 (m) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.48–1.89 (m, 4 H), 2.21 (s, 3 H), 2.51–2.77 (m, 4 H), 6.58 (d, J = 8.2 Hz, 1 H), 6.82 (s, 1 H), 7.23 (d, J = 8.2 Hz, 1 H); ^{13}C NMR δ 20.1, 22.6 (2C atoms), 23.5, 29.7, 116.4, 121.3, 123.8, 131.3, 140.4, 154.2.

Fraction II (R_f 0.63) afforded 5.1 mg (6.4%) of 5-hydroxy-6,8-bis(methylthio)-1,2,3,4-tetrahydronaphthalene (**46**): IR (neat) 3415 (s), 1615 (s), 1565 (m), 1445 (m), 880 (w) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.42–1.87 (m, 4 H), 2.27 (s, 3 H), 2.36 (s, 3 H), 2.50–2.84 (m, 4 H), 6.72 (s, 1 H), 7.27 (s, 1 H); ^{13}C NMR δ 16.8, 20.2, 22.1, 22.6, 24.1, 27.5, 117.3, 124.7, 128.2, 130.0, 139.2, 152.6.

Fraction III (R_f 0.18) afforded 2.5 mg (4%) of 5-hydroxy-8-(methylthio)-1,2,3,4-tetrahydronaphthalene: IR (CCl_4) 3600 (br, s), 2910 (s), 1575 (m), 1455 (s), 1435 (s), 1300 (s), 1265 (s), 1205 (s), 1030 (s), 970 (m) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.70–1.97 (m, 4 H), 2.46–2.86 (m, 4 H), 2.38 (s, 3 H), 4.58 (br s, 1 H), 6.64 and 7.00 (d, J = 8.3 Hz, 2 H).

3-Ethyl-2-methylphenol (47a). General procedure I (0.40 mmol scale) with acetonitrile afforded **47a** (R_f 0.42–0.49, petroleum ether/10% ethyl acetate, v/v) in 37% yield: IR (CH_2Cl_2) 3580 (s), 3420 (s), 3040 (w), 1610 (m), 1585 (m), 1493 (m), 1450 (s), 1315 (s), 1190 (s), 770 (s) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.18 (t, J = 7.5 Hz, 3 H), 2.18 (s, 3 H), 2.62 (q, J = 7.6 Hz, 2 H), 4.64 (br s, 1 H), 6.54–7.00 (m, 3 H).

3-Ethyl-2-methyl-6-(trimethylsilyl)-2,5-hexadienoic acid **48a** (R_f 0.54–0.61) was also isolated in 27% yield: NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.23 (t, J = 7.0 Hz, 3 H), 1.87 (s, 3 H), 2.43 (q, J = 7.0 Hz, 2 H), 2.92 (d, J = 4.0 Hz, 2 H), 5.67–5.94 (m, 2 H), 10.42 (br s, 1 H).

3-Ethyl-2-methyl-2,5-hexadienoic acid **49a** (R_f 0.28–0.34) was also isolated in 28% yield: NMR (60 MHz, CCl_4) δ 1.20 (t, J = 7.0 Hz, 3 H), 1.93 (s, 3 H), 2.46 (q, J = 7.0 Hz, 2 H), 3.00 (d, J = 4.0 Hz, 2 H), 4.83–5.23 (m, 2 H), 5.37–5.58 (m, 1 H), 11.57 (br s, 1 H).

3-Isopropylphenol (47b). General procedure I (0.81 mmol scale) with acetonitrile as solvent afforded **47b** (R_f 0.28–0.38, petroleum ether/10% ethyl acetate) in 14% yield: IR (neat) 3400 (br, s), 3040 (w), 1610 (m), 1595 (s), 1490 (s), 1455 (m), 1310 (m), 1270 (m), 870 (s), 780 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.20 (d, J = 7.0 Hz, 6 H), 2.78 (hep, J = 7.0 Hz, 1 H), 5.63 (br s, 1 H). 6.40–7.23 (m, 4 H).

3-(1-Methylethyl)-6-(trimethylsilyl)-2,5-hexadienoic acid (**48b**) (R_f 0.38–0.50) was isolated as a mixture of 2*E* and 2*Z* geometrical isomers in 13% yield: IR (CH_2Cl_2) 3420–2740 (v br, s), 1685 (s), 1630 (s), 1245 (m), 870 (s), 845 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.03 (s, 9 H), 1.03 (d, J = 7.0 Hz, 6 H), 2.30 (hep, J = 7.0 Hz, 1 H), 2.93 (d, J = 5.0 Hz, 2 H), 5.43–5.98 (m, 3 H), 10.33 (br s, 1 H).

3-(1-Methylethyl)-2,5-hexadienoic acid **49b** (R_f 0.20–0.28) was also isolated in 18% yield; IR (CH_2Cl_2) 3460–2735 (br, s), 1685 (s), 1630 (s), 1415 (s), 995 (m), 920 (s), 880 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.10 (d, J = 7.0 Hz, 6 H), 2.27 (hep, J = 7.0 Hz, 1 H), 3.33 (d, J = 7.0 Hz, 2 H), 5.68–6.85 (m, 2 H), 6.85–8.12 (m, 2 H), 11.22 (br s, 1 H).

1-[(Trimethylsilyl)oxy]-3-methylcyclopentene. The procedure was adapted from that reported by Clark and Heathcock.[32] 2-Cyclopentenone (820 mg, 10 mmol) was added dropwise to a solution of lithium dimethylcuprate (2.48 g CuI and 19.0 mL of 1.37 M methyllithium, 13 mmol) in 50 mL of ether at −40 °C under nitrogen. The resulting mixture was stirred at −40 °C for 0.5 h,

warmed to −10 °C, (over 1.5 h), and stirred at −10 °C for 1.5 h. The enolate anion was trapped by the sequential addition of 2.51 g (14 mol) of HMPT, 1.42 g (14 mmol) of triethylamine, and 1.52 g (14 mmol) of chlorotrimethylsilane. The reaction was allowed to warm to room temperature over 1.5 h, diluted with 100 mL of pentane, stirred an additional 15 min, filtered thru Celite, and concentrated in vacuo to afford 1.48 g (87% yield) of silyl enol ether which was used without further purification. IR (neat) 1645 cm^{-1}; NMR (60 MHz, CCl_4) δ 0.13 (s, 9 H), 0.87 (d, J = 7.0 Hz, 3 H), 1.70–2.33 (m, 4 H), 2.33–2.83 (m, 1 H), 4.37 (d, J = 2.0 Hz, 1 H).

2-[Bis(methylthio)methylene]-3-methylcyclopentanone (4). Methyllithium (3.5 mL, 1.48 M, 5.2 mmol) was added to a solution of 1-[(trimethylsilyl)oxy]-3-methylcyclopentene (852 mg, 5.0 mmol) and HMPT (930 mg, 5.2 mmol) in 20 mL of THF at room temperature under nitrogen. After 1 h the reaction mixture was cooled to −78 °C and 0.40 g (5.2 mmol) of carbon disulfide was added. The solution was warmed to 0 °C over 2 h and cooled to −78 °C, and a solution of LHMDS (868 mg HMDS, 2.5 mL of 2.12 M n-BuLi, 5.3 mmol) was added via cannula. After the solution had stirred at −78 °C for 2 h, 2.27 g (16 mmol) of methyl iodide was added. The reaction mixture was slowly warmed to room temperature over 2 h and stirred at room temperature for 3.5 h. The reaction mixture was diluted with 30 mL of saturated NH_4Cl and extracted with ether (4 × 25 mL), and the ether extracts were washed with H_2O and dried over $MgSO_4$. Concentration in vacuo and Kugelrohr distillation (60–92 °C, (0.05 mmHg)) of the crude red-orange liquid afforded 764 mg (76% yield) of 4: IR (neat) 1690 (s), 1530 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.23 (d, J = 7.5 Hz, 3 H), 1.50–2.23 (m, 2 H), 2.23–2.67 (m, 2 H), 2.40 (s, 3 H), 2.47 (s, 3 H), 3.37 (p, J = 7.0 Hz, 1 H); ^{13}C NMR δ 17.9 (2C atoms), 19.8, 27.2, 37.7, 39.0, 141.6, 149.4, 202.1.

Anal. Calcd for $C_9H_{14}OS_2$: C, 53.42; H, 6.99. Found: C, 53.50; H, 7.02.

Purification of the pot residue by preparative TLC (silica gel, 1000 μ, petroleum ether/5% ethyl acetate, v/v) afforded 187.8 mg (12% yield) of bis(ketene dithioacetal) 5: IR (neat) 1645 (s), 1515 (s) cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.17 (d, J = 7.0 Hz, 3 H), 2.45 (s, 12 H), 2.41–2.97 (m, 2 H), 3.22 (p, J = 7.0 Hz, 1 H); ^{13}C NMR δ 18.1 (4C atoms), 22.2, 35.7, 38.3, 138.4, 146.7, 148.6, 150.0, 186.3.

Anal. Calcd for $C_{12}H_{18}OS_4$: C, 47.02; H, 5.93. Found: C, 47.15; H, 5.97.

***S*-Methyl 2-(3-Furyl)-5-methylcyclopentene-1-thioate (50).** n-Butyllithium (1.84 mL, 2.28 M, 4.2 mmol) was added dropwise to a solution of 3-bromofuran[35] (680 mg, 4.6 mmol) in 10 mL of ether at −78 °C under a nitrogen atmosphere. After 1 h a solution of 4 (607 mg, 3.0 mmol) in 5.0 mL of ether was added dropwise and the resultant solution was stirred at −78 °C for 0.5 h and then allowed to warm to 0 °C over 2 h. The reaction mixture was diluted with 30 mL of saturated aqueous NH_4Cl and extracted with 4 × 25 mL ether. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated in vacuo to afford 830 mg of crude α-hydroxy ketene dithioacetal which was used without further purification. IR (neat) 3510 (br, m), 1535 (m), 1520 (m), 1475 (m), 1460 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.23 (d, J = 7.0 Hz, 3 H), 1.60–2.67 (m, 4 H), 2.12 (s, 3 H), 2.23 (s, 3 H), 3.17 (p, J = 5.0 Hz, 1 H), 4.35 (br s, 1 H), 6.40 (m, 1 H), 7.03 (s, 1 H), 7.35 (m, 1 H).

The crude α-hydroxy ketene dithioacetal (830 mg, 3 mmol) was treated with 10% aqueous HBF_4 (12 mL) in 60 mL of THF/H_2O (80:20, v/v) at room temperature for 16 h. The reaction was monitored by TLC (petroleum ether/5% ethyl acetate). The reaction mixture was diluted with 25 mL of H_2O and extracted 4 times with 25 mL of ether. The organic phase was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by MPLC (silica gel, petroleum ether/2% ethyl acetate, v/v) afforded 473 mg of pure **50** as a yellow oil in 71% yield: IR (neat) 1635 (s), 1582 (m), 1500 (m), 1450 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.23 (d, J = 7.0 Hz, 3 H), 1.40–1.97 (m, 1 H), 1.97–2.57 (m, 1 H), 2.33 (s, 3 H), 2.80 (dt, J = 7.0 Hz, J = 2.0 Hz, 2 H), 3.08–3.68 (m, 1 H), 6.63 (t, 1 H), 7.30 (m, 1 H), 7.98 (s, 1 H); ^{13}C NMR δ 11.2, 19.8, 30.8, 35.5, 42.3, 110.0, 120.6, 137.2, 139.0, 142.3, 143.0, 191.9.

Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.83; H, 6.36. Found: C, 64.61; H, 6.39.

(±)-Myodesmone (51). The procedure of Anderson was employed.[31] Isobutyllithium was prepared from isobutyl bromide and lithium dispersion and used as an ether solution.[36] Isobutyllithium (3.85 mL, 0.52 M, 2.0 mmol) was added dropwise to a suspension of 190 mg (1.0 mmol) of CuI in 10 mL of ether at −50 to −40 °C under a nitrogen atmosphere. After 1.5 h a solution of thiol ester **50** (222 mg, 1.0 mmol) in 5.0 mL of ether was added rapidly to the diisobutylcuprate solution. The resultant mixture was stirred at −50 to −40 °C for 2.5 h, quenched with 25 mL of saturated NH_4Cl, warmed to 0 °C, and filtered through Celite. The Celite was washed with 25 mL each of ether, petroleum ether, and H_2O. The organic phase was separated and the aqueous phase was extracted with 3 25-mL portions of ether. The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude product. Preparative TLC (silica gel, 1000 μ, petroleum ether/5% ethyl acetate, v/v) afforded 123.1 mg of pure (±)-myodesmone as a yellow oil in 53% yield: UV λ_{max} (CH_3OH) 278 (ϵ 4830), 230 (ϵ 5610), 223 (ϵ 6170) nm; IR (neat) 3145, 2960, 2935, 2870, 2845, 1675 (s), 1620, 1560, 1505, 1465, 1399, 1388, 1363, 1335, 1308, 1285, 1250, 1233, 1200, 1165, 1135, 1105, 1085, 1055, 1020, 995, 975, 955, 935, 875, 843, 805, 788, 730 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 0.90 (d, J = 6.6 Hz, 6 H), 1.13 (d, J = 6.8 Hz, 3 H), 1.34–1.72 (m, 1 H), 1.78–2.19 (m, 1 H), 2.19–2.47 (m, 3 H), 2.70 (t, J = 7.0 Hz, 2 H), 3.20 (br q, J = 7.0 Hz, 1 H), 6.41 (m, 1 H), 7.36 (t, J = 1.7 Hz, 1 H), 7.72 (br s, 1 H).

The 90-MHz ^1H NMR spectrum of synthetic (±)-myodesmone was virtually identical with a 100-MHz spectrum of the natural material kindly provided by Professor M. D. Sutherland. Literature:[4] UV λ_{max} (EtOH) 282 (ϵ 5380), 232 sh (ϵ 5600), 226 (ϵ 5700) nm; NMR (100 MHz, CCl_4) δ 0.90 (d, J = 7.0 Hz, 6 H), 1.13 (d, J = 7.0 Hz, 3 H), 1.2–1.8 (m, 1 H), 1.8–2.2 (m, 1 H), 2.2–2.4 (m, 3 H), 2.73 (finely split t, J = 7.0 Hz, 2 H), 3.0–3.5 (br q, J = 7.0 Hz, 1 H), 6.59 (m, 1 H), 7.37 (t, 1 H), 7.76 (br s, 1 H).

3-Methyl-2-[1-(methylthio)-3-methylbutylidene]cyclopentanone (52). n-Butyllithium (1.6 mL, 2.26 M solution in hexane, 3.6 mmol) was added to thiophenol (0.40 g, 3.6 mmol) in 15.0 mL of THF at 0 °C under nitrogen. After 20 min cuprous iodide (0.69 g, 3.6 mmol) was added and the resulting clear yellow solution was stirred for an additional 20 min. The (phenylthio)copper solution was cooled to −78 °C and 6.9 mL of a 0.52 M hexane solution of isobutyllithium[36] was added dropwise and the resulting solution was stirred at −78 °C for 1.5 h. 2-[Bis(methylthio)methylene]-3-methylcyclopentanone (4) (0.607 g, 3.0 mmol) in 10 mL of THF was added via cannula. After stirring at −78 °C for 1 h the mixture was slowly warmed to −60 °C over 1 h whereupon 15 mL of MeOH was added dropwise, followed by the addition of 30 mL of saturated aqueous NH_4Cl. The solution was diluted with 50 mL of ether and filtered thru Celite. The Celite was washed with 30 mL each of petroleum ether, ether, and water and the organic phase separated. The aqueous phase was extracted with 3 25-mL portions of ether. The combined organic phase was washed with 1 M NaOH, dried over $MgSO_4$ and concentrated in vacuo. Purification by MPLC (silica gel, petroleum ether/5% ethyl acetate, v/v) afforded 344 mg (54%) of **52** (R_f 0.35–0.43): IR (neat) 1690 (s), 1575 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.88 (d, J = 6.0 Hz, 3 H), 1.00 (d, J = 6.0 Hz, 3 H), 1.13 (d, J = 7.0 Hz, 3 H), 1.40–2.07 (m, 3 H), 2.07–2.40 (m, 2 H), 2.33 (s, 3 H), 2.40–3.17 (m, 2 H), 3.23 (p, J = 6.5 Hz, 1 H); ^{13}C NMR δ 13.3, 17.8, 21.0, 22.0, 27.1, 29.1, 35.2, 36.8, 37.7, 135.5, 154.1, 203.0.

The reduction product **3-methyl-2-[(methylthio)-methylene]cyclopentanone** was also isolated in 25% yield (117.2 mg, R_f 0.30–0.39, petroleum ether/10% ethyl acetate, v/v); IR (neat) 1690 (s), 1580 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 1.20 (d, J = 7.0 Hz, 3 H), 1.45–1.77 (m, 1 H), 1.77–2.17 (m, 1 H), 2.17–2.57 (m, 2 H), 2.47 (s, 3 H), 2.87 (p, J = 6.0 Hz, 1 H), 7.17 (d, J = 1.0 Hz, 1 H).

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1-(3-Furyl)-3-methyl-2-[1-(methylthio)-3-methylbutylidene]-1-cyclopentanol (53). *n*-Butyllithium (0.37 mL of a 2.00 M hexane solution) was added dropwise to a solution of 3-bromofuran (120 mg, 0.85 mmol) in 10 mL of ether at −78 °C under nitrogen. After 2 h, a solution of **52** in 5 mL of ether was added dropwise. The resulting solution was stirred at −78 °C for 0.5 h and then slowly warmed to 0 °C (over 2 h) whereupon the solution was diluted with 30 mL of saturated aqueous NH_4Cl. The aqueous phase was extracted with 4 25-mL portions of ether and the combined ether extracts were washed with H_2O, dried over $MgSO_4$, and concentrated in vacuo to afford 167.6 mg of crude **53**: IR (neat) 3480 (br, m), 1565 (m), 1520 (m), 1465 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.87 (d, J = 6.0 Hz, 6 H), 1.23 (d, J = 7.0 Hz, 3 H), 1.27–1.90 (m, 3 H), 1.90–2.50 (m, 4 H), 2.20 (s, 3 H), 3.13 (p, J = 6.5 Hz, 1 H), 3.53 (br s, 1 H), 6.37 (s, 1 H), 7.17 (s, 1 H), 7.35 (split s, 1 H).

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Registry No. 1, 90968-96-0; 2, 87711-77-1; 3, 90968-97-1; (±)-4, 89295-78-3; (±)-5, 89295-80-7; 8, 17649-89-7; 9, 84307-81-3; 10, 17649-90-0; 11, 79300-00-8; 12, 51507-08-5; 13, 87615-87-0; 14, 17649-86-4; 15a, 19429-40-4; 15b, 84307-82-4; 15c, 84307-83-5; 15d, 90968-98-2; 15e, 90968-99-3; 16a, 84333-35-7; 16b, 84307-84-6; 17a, 84307-85-7; 17b, 15081-74-0; 17c, 90969-00-9; 17d, 90969-01-0; 19a, 84307-87-9; 19b, 84307-86-8; 19c, 90969-02-1; 20b, 90969-03-2; 22a, 84307-90-4; 22b, 84307-91-5; 22c, 84307-93-7; 22d, 90969-04-3; 22e, 90969-05-4; 23b, 84307-92-6; 24, 90969-06-5; 25a, 84307-96-0; 25b, 84307-94-8; 26a, 84307-97-1; *cis*-26b, 90969-07-6; *trans*-26b, 90990-51-5; 27a, 84307-98-2; 27b, 5828-09-1; 27c, 90969-36-1; 28b, 90969-08-7; 29, 90969-09-8; 30a, 84308-01-0; 30b, 84308-02-1; (*E*)-31a, 90969-10-1; (*Z*)-31a, 90969-11-2; (*E*)-31b, 86467-33-6; 31c, 90969-12-3; (*E*)-33a, 90969-13-4; (*Z*)-33a, 90990-52-6; 33b, 90969-14-5; (*E*)-34a, 90969-15-6; (*Z*)-34a, 90969-16-7; 34b, 90969-17-8; 35a, 67209-77-2; 35b, 1560-11-8; 35c, 13148-94-2; 35d, 636-82-8; (*E*)-36, 90969-18-9; (*Z*)-36, 81911-91-3; 37, 16957-70-3; 40, 90969-19-0; 41, 90969-20-3; 42a, 1641-41-4; 42b, 529-35-1; 43a, 90969-21-4; 43b, 90969-22-5; 44a, 90969-23-6; 44b, 90969-24-7; 45, 90969-25-8; 46, 90969-26-9; 47a, 1123-73-5; 47b, 618-45-1; 48a, 90969-27-0; (*E*)-48b, 90969-28-1; (*Z*)-48b, 90969-29-2; 49a, 90969-30-5; 49b, 90969-31-6; (±)-50, 89295-81-8; 50 (α-hydroxy dithioacetal), 90969-34-9; (±)-51, 89362-67-4; (±)-52, 90969-32-7; 53, 90969-33-8; $CH_3CO(CH_2)_5CH_3$, 111-13-7; 5-hydroxy-8-(methylthio)-1,2,3,4-tetrahydronaphthalene, 54899-76-2; (±)-1-[(trimethylsilyl)oxy]-3-methylcyclopentene, 89295-85-2; 3-bromofuran, 22037-28-1; (±)-3-methyl-2-[(methylthio)methylene]cyclopentanone, 90969-35-0.

Ergoline Synthons: Synthesis of 3,4-Dihydro-6-methoxybenz[*cd*]indol-5(1*H*)-one (6-Methoxy-Uhle's Ketone) and 3,4-Dihydrobenz[*cd*]indol-5(1*H*)-one (Uhle's Ketone) via a Novel Decarboxylation of Indole-2-carboxylates

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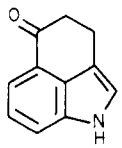
An efficient synthesis of a new substituted ergoline synthon, 3,4-dihydro-6-methoxybenz[*cd*]indol-5(1*H*)-one, is described. The general synthetic strategy has also been applied to the preparation of the known 3,4-dihydrobenz[*cd*]indol-5(1*H*)-one, Uhle's ketone. The key step, a formal decarboxylation of intermediate 2-carboxy-3,4-dihydrobenz[*cd*]indol-5(1*H*)-one, is accomplished by reduction of the carboxylate ethyl ester to the indole-2-carboxaldehyde followed by catalytic decarbonylation to the parent indole using in situ generated Rh(1,3-bis(diphenylphosphino)propane)$_2^+Cl^-$ catalyst. The catalytic decarbonylation reaction was extended to several other indole-2-carboxaldehydes and appears to be a general reaction of indole aldehydes.

The ergot alkaloids interact with dopamine,[1] serotonin,[2] norepinephrine,[3] and histamine[4] receptors to produce a complex spectrum of pharmacological activities.[5] As part of an investigation of selective 5-hydroxytryptamine receptor agents,[6] we became interested in preparing synthetic ergot substructures which contain the serotonin molecule in its entirety. The successful elaboration of 3,4-dihydrobenz[*cd*]indol-5(1*H*)-one (Uhle's ketone), 1, to a host



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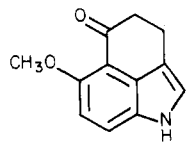

2

of more complex compounds[7] suggested the 6-methoxy congener 2 as an intermediate for the preparation of ring oxygenated relatives. We report here a convenient, high yield synthesis of 2 and the parent ketone 1 via a novel decarboxylation of intermediate indole-2-carboxylates 12 and 13 under mild, neutral, nonoxidizing conditions. This

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