Control of Chemo- and Stereoselectivity in the Reactions of Organocuprates with α-Oxoketene Dithioacetals

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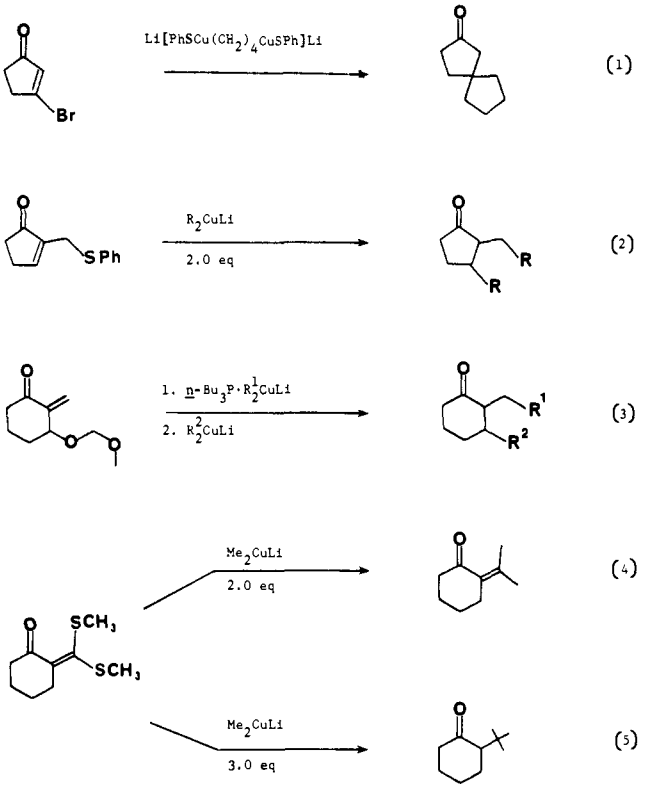
Abstract: α-Oxoketene dithioacetals can be induced to undergo a selective substitution reaction with organocopper reagents to afford β-alkylthio-α,β-enones. The effect of substrate structure, transferable copper ligand, copper reagent, and solvent upon the chemo- and stereoselectivity of the reaction was examined. Cyclic and acyclic substrates afforded the *E* β-alkylthio-α,β-enones in good to excellent yields with generally high stereoselectivity (i.e., >90:10) upon reaction with (PhSCuR)Li and ($MeOCMe_2C{\equiv}CCuR$)Li mixed cuprates containing Me, *n*-Bu, *sec*-Bu, and *t*-Bu transferable ligands with the exception of acyclic substrates **5** and **6** which afforded the *Z* isomer upon reaction with *t*-Bu cuprates. Ester and lactone derivatives generally undergo preferential reduction of the carbon–sulfur bond without alkyl substitution unless a carbanion stabilizing group is located at the α-carbon atom. Reaction of α-oxoketene dithioacetals **13a** and **13b** containing two different alkylthio substituents with lithium dimethylcuprate occurred with stereospecific substitution of the alkylthio substituent syn to the ketone carbonyl. The stereoselectivity of the reaction is accounted for in terms of an addition–elimination pathway.

Introduction

We have, over the past several years, investigated the chemistry of α-oxoketene dithioacetals[1] as potentially versatile substrates for the sequential regioselective construction of new carbon–carbon bonds.[2] During the course of this investigation, we discovered that α-oxoketene dithioacetals could be induced to undergo a selective reaction with organocopper reagents to afford β-alkylthio-α,β-enones (vinylogous thiol esters) with some degree of stereoselectivity.[3] We now report the results of an extensive study on the stereo- and chemoselectivity[4] of this reaction as a function of solvent, organocuprate, and substrate structure. The geometry about the carbon–carbon double bond in one of the vinylogous thiol esters has been firmly established by an X-ray diffraction study, and trends in the UV and NMR spectra have been established which permit assignment of olefin configuration throughout the series. A model is proposed to account for the observed stereoselectivities, and an examination of 2-carboalkoxyketene dithioacetals has established a correlation between substrate structure and reactivity. Studies examining the configurational stabilities of the vinylogous thiol esters and the equilibrium *E*/*Z* isomer distribution are also described. Synthetic applications involve a regiospecific synthesis of α-pyrones which has been reported[2b] and a stereoselective synthesis of α,β-unsaturated ketones that will be detailed in a subsequent paper.

The reaction of organocopper reagents with α,β-unsaturated carbonyl compounds containing a good leaving group at the β-carbon atom has been actively investigated over the past decade.[3,5-7] The substitution of the leaving group by the alkyl ligand of the cuprate generally affords β-alkyl-α,β-unsaturated carbonyl compounds in a chemoselective fashion, although bis-conjugate addition to afford β,β-dialkyl carbonyl compounds may be competitive with the more reactive cuprates and substrates.[5a] The reaction has been assumed to proceed by an addition–elimination mechanism,[5b,c] and substrates have been designed to undergo sequential conjugate addition–elimination–conjugate addition events that afford spiro[6a] (eq 1) and vicinally disubstituted cycloalkanones (eq 2 and 3).[6b,c] Utilization of substrates that yield less reactive β-alkyl-substituted α,β-enones has facilitated the use of a different organocopper reagent in the second substitution reaction (eq 3).[6c] Few studies, however, have examined substrates containing two good leaving groups at the β-carbon atom of the α,β-unsaturated carbonyl compound. Although the addition of organocuprates to α-oxoketene dithioacetals[7a,b] (eq 4 and 5) and bis(methylthio)methylene malonates[7c] has been reported, the transformations have involved the addition of either two or three alkyl groups to afford α-alkylidene or α-tertiary alkyl ketones and



malonates. To our knowledge, a preliminary report[3] from our laboratory described the first successful addition of a single alkyl

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(1) β,β-Dialkylthio-α,β-unsaturated ketones have been described in the literature by several convenient and simple descriptive names. These include α-oxoketene dithioacetals (Marino, J. P.; Kostusyk, J. L. *Tetrahedron Lett.* **1979**, 2489), α-keto ketene mercaptals (Shahak, I.; Sasson, Y. *Ibid.* **1973**, 4207), α-di(alkylmercapto)methylene ketones (Arjona, O.; Cereceda, J. A.; Quiroga, M. L. *Tetrahedron* **1980**, *36*, 2137), and α-dithiomethylene ketones (see ref 7a).

(2) (a) Dieter, R. K.; Jenkitkasemwong, Y. *Tetrahedron Lett.* **1982**, *23*, 3747. (b) Dieter, R. K.; Fishpaugh, J. R. *J. Org. Chem.* **1983**, *48*, 4439. (c) Dieter, R. K.; Dieter, J. W. *J. Chem. Soc., Chem. Commun.* **1983**, 1378. (d) Dieter, R. K.; Jenkitkasemwong, Y.; Dieter, J. W. *J. Org. Chem.* **1984**, *49*, 3183.

(3) Dieter, R. K.; Fishpaugh, J. R.; Silks, L. A. *Tetrahedron Lett.* **1982**, *23*, 3751 and references cited therein.

(4) The term chemoselectivity is employed to describe the selective reaction of α-oxoketene dithioacetals with organocuprates in the presence of the product vinylogous thiol esters. See: Warren, S. "Organic Synthesis: The Disconnection Approach"; Wiley: Chichester, England, 1982; Chapter 5, p 34.

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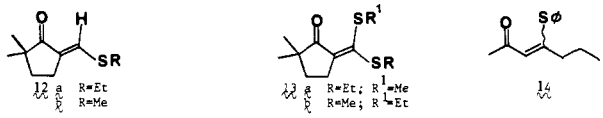
group from organocuprates to an α,β-unsaturated carbonyl compound containing two good leaving groups at the β-carbon atom.

Preparative Experiments

α-Oxoketene dithioacetals **1–7**, lactone **9**, and carbomethoxyketene dithioacetals **10** and **11** were prepared by an established procedure[8] involving the sequential addition of carbon disulfide, lithium diisopropylamide (LDA), or lithium hexamethyldisilyl azide (LHMDS) as THF solutions, and iodomethane to the appropriate ketone or ester enolate anion.

The β,β-dichloro enone **8** was prepared by Friedel–Crafts acylation of vinylidene dichloride with acetyl chloride.[9] The two diastereomers of an α-oxoketene dithioacetal containing two different alkylthio substituents were required to probe the stereospecificity of the reaction. Deprotonation of **12a** according



to the procedure of Marino[10] followed by quenching with methylsulfinyl chloride afforded **13a** and **13b** as a nearly 1:1 mixture. Considering a possible role of the chloride ion in the isomerization process, sulfenylating reagents containing less nucleophilic leaving groups were examined. Deprotonation of **12a** and reaction of the carbanion with methyl methylthiosulfonate[11] afforded **13a** stereoselectively. Attempted purification on silica gel, however, afforded a mixture of **13a** and **13b** ($\sim$1:1). For this reason an unpurified sample of **13a** containing a small amount of **12a** (12%) was employed in the organocopper substitution reaction. In a similar manner **12b** was converted into **13b** employing ethyl ethylthiosulfonate[11] as the sulfenylating reagent.

The β-phenylthio derivative **14** was obtained in 71% yield as a mixture of *E* and *Z* geometrical isomers by reaction of 3-heptyn-2-one[12] with thiophenol in THF.[13] The diastereomers were separated by column chromatography and the configurations determined by NMR chemical shifts [olefinic proton: δ 5.60 (*E*), 6.30 (*Z*); methylene protons: δ 2.70 (*E*), 2.08 (*Z*)]. The chemical shift trends were consistent with those reported for the *E* and *Z* isomers of ethyl 3-(phenylthio)-2-butenoate.[5c]

Results

In an initial experiment it was discovered that some degree of chemoselectivity could be achieved by simply controlling the reaction temperature. Treatment of **1** with lithium dimethylcuprate at −50 °C afforded the *E* vinylogous thiol ester **15a** in 46% yield which could be increased to 65% yield by lowering the reaction temperature to −78 °C. Reasoning that a greater degree of chemoselectivity could be achieved by utilization of less reactive cuprates, the phenylthio heterocuprate[14] of Posner and the acetylenic mixed cuprate of Corey[15] were examined. The methyl(phenylthio)cuprate afforded a mixture of *E* (79%) and *Z* (2%) stereoisomers in good yield while the methylacetylenic cuprate was more efficient, affording the *E* isomer in 96% yield (Table I, entries 2 and 3).

Table I reveals that the addition of organocopper reagents to α-oxoketene dithioacetals afforded the *E* vinylogous thiol esters as the predominant stereoisomer with the exception of acyclic substrates **5** and **6** which afforded the *Z* isomer upon reaction with *t*-Bu cuprates (Table I, entries 20, 21, 27). The stereoselectivity of the reaction is dependent upon the substrate structure and organocuprate. Although there is considerable variation in the isomer ratios and chemical yields consistent with the simultaneous influence of several reaction parameters, several patterns do emerge. First, the cyclopentanone derivative **1**, cyclohexenone derivatives **3** and **4**, and the acyclic substrates **5–7** exhibited very good to excellent stereoselectivity for organocuprates containing primary, secondary, and tertiary alkyl ligands. The stereoselectivities (*E*:*Z* isomer ratios) and chemical yields for the reactions of **1**, **5**, and **6** were uniformly high along the phenylthio mixed organocuprate series CH_3, *n*-Bu, *sec*-Bu, and *t*-Bu (Table I, entries 2, 4, 6, 7, 17–19, 21, 22, 24, and 26), although reaction of the acyclic substrate **5** with the *t*-Bu cuprate in THF afforded predominantly a product arising from reduction of the carbon–sulfur bond and low yields of the substitution product (entry 20). Reaction of **5** and **6** with the *tert*-butyl(phenylthio)cuprate in diethyl ether afforded vinylogous thiol esters **20d** and **22d** in good to excellent yields, although **22d** was formed with modest stereoselectivity (entries 21 and 27). It should also be noted that in three instances the acetylenic mixed cuprates afforded higher yields of vinylogous thiol esters than the corresponding phenylthio mixed cuprates (entries 3, 9, 25 vs. 2, 8, 24) although this was not always the case (entries 5, 23 vs. 4, 22). Several experiments revealed the dependence of the chemical yield upon both the substrate and organocuprate (Table I, compare entries 2–6, 20–25). Cyclohexenones **3** and **4** (entries 14–16) reacted with organocuprates containing a primary alkyl ligand in a highly stereoselective manner. Reaction of the *sec*-Bu and *t*-Bu organocuprates with **3** and **4** was not examined. The acyclic derivative **7** containing a tetrasubstituted olefin also reacted with the methyl- and *n*-butyl(phenylthio)cuprates to afford the *E* isomers with a high degree of stereoselectivity. Second, the cyclohexanone derivative **2** gave consistently lower stereoselectivities and chemical yields for the CH_3 and *sec*-Bu cuprates but better results for the *n*-Bu and *t*-Bu cuprates (Table I, entries 10–13). Third, addition of lithium cyclopropyl(phenylthio)cuprate to **1** afforded the vinylogous thiol ester **15e** as a 70:30 *E*:*Z* mixture of stereoisomers (entry 8). Although addition of lithium *tert*-butyl(phenylthio)cuprate to **1** was initially observed to afford a 1:1 mixture of *E* and *Z* stereoisomers, it was eventually discovered that this ratio resulted from isomerization during the purification procedure (silica gel, column chromatography). Utilization of careful work-up conditions afforded crude *tert*-butyl vinylogous thiol ester (**15d**) as a 95:5 mixture of *E* and *Z* stereoisomers. Reaction of **1** with the cyclopropyl cuprate, however, always afforded a mixture of *E* and *Z* stereoisomers and the stereoselectivity of this reaction could not be improved. The *E* and *Z* cyclopropyl vinylogous thiol esters (*E*)-**15e** and (*Z*)-**15e** could be separated by column chromatography but were configurationally unstable. The *Z* isomer underwent partial isomerization within 0.5 h at room temperature in $CDCl_3$ while the *E* isomer could be stored in a frozen benzene matrix. In general, the vinylogous thiol esters exhibited good configurational stability with the exception of the highly unstable *tert*-butyl and cyclopropyl vinylogous thiol esters **15d** and **15e**, respectively. The vinylogous thiol esters derived from the cy-

(5) (a) Posner, G. H.; Brunelle, D. J. *J. Chem. Soc., Chem. Commun.* **1973**, 907. (b) Casey, C. P.; Marten, D. F.; Boggs, R. A. *Tetrahedron Lett.* **1973**, 2071. (c) Kobayashi, S.; Takei, H.; Mukaiyama, T. *Chem. Lett.* **1973**, 1097. (d) Sum, F.-W.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1431, and references cited therein. (e) Piers, E.; Cheng, K. F.; Nagakura, I. *Ibid.* **1982**, *60*, 1256, and references cited therein. (f) Dieter, R. K.; Silks, L. A. *J. Org. Chem.* **1983**, *48*, 2786, and references cited therein.

(6) (a) Wender, P. A.; Eck, S. L. *Tetrahedron Lett.* **1977**, 1245. (b) Smith, A. B., III; Wexler, B. A.; Slade, J. S. *Ibid.* **1980**, *21*, 3237. (c) Takahashi, T.; Hori, K.; Tsuji, J. *Ibid.* **1981**, *22*, 119.

(7) (a) Corey, E. J.; Chen, R. H. K. *Tetrahedron Lett.* **1973**, 3817. (b) Johansen, O. H.; Undheim, K. *Acta Chem. Scand., Ser. B* **1979**, *33*, 460. (c) Ittah, Y.; Shahak, I. *Synthesis* **1976**, 320.

(8) Dieter, R. K. *J. Org. Chem.* **1981**, *46*, 5031.

(9) Heilbron, I.; Jones, E. R. H.; Julia, M. *J. Chem. Soc.* **1949**, 1430.

(10) Marino, J. P.; Katterman, L. C. *J. Chem. Soc., Chem. Commun.* **1979**, 946.

(11) The procedure of Trost for the preparation of benzene phenylthiosulfonate was employed: Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405.

(12) 3-Heptyn-2-one was prepared by reaction of 1-lithiopentyne with acetyl chloride in THF at −76 °C. For an alternative preparation see: Castro, C. E.; Havlin, R.; Honwad, V. K.; Malte, A.; Moje, S. *J. Am. Chem. Soc.* **1969**, *91*, 6464.

(13) Reaction of 3-heptyn-2-one with thiophenol and triethylamine in THF afforded **14** as an *E*:*Z* mixture in 67–71% yield. For an alternative synthetic procedure see: Kobayashi, S.; Meguro-ku, O.; Mukaiyama, T. *Chem. Lett.* **1974**, 705.

(14) Posner, G. H.; Whitten, C. E.; Sterling, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 7788.

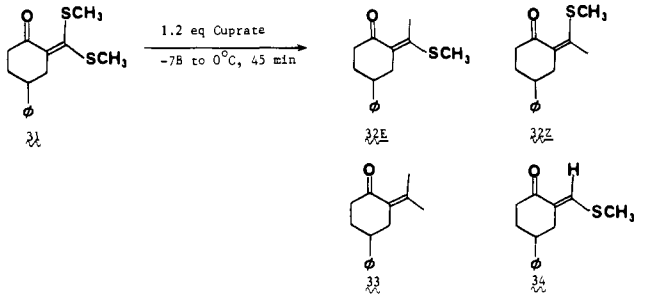
(15) Corey, E. J.; Floyd, D.; Lipshutz, B. H. *J. Org. Chem.* **1978**, *43*, 3418.

clohexanone substrate displayed moderate stability and did undergo partial isomerization over several days when stored neat or as solutions.

In view of the moderate to high configurational instability of some of the product vinylogous thiol esters, several control experiments were performed. Treatment of vinylogous thiol ester (*E*)-**17a** with lithium methyl(phenylthio)cuprate [(i) THF, −78 to 0 °C; (ii) satd aq NH_4Cl)] afforded pure (*E*)-**17a** and a minor amount of 2-(1-methylethylidene)cyclohexanone. In this instance, isomerization of (*E*)-**17a** under these reaction conditions was not significant. However, reaction of vinylogous thiol ester (*E*)-**15a** and (*E*)-**22c** with the higher order cuprate, di-*tert*-butylcyanocuprate,[16] in diethyl ether afforded (*Z*)-**15a** and (*Z*)-**22c** as the principal products in 64 and 70% yield, respectively, indicating that isomerization is quite possible under certain conditions. This isomerization process was examined in greater detail for (*E*)-**22c** and (*Z*)-**22c**. Treatment of (*E*)-**22c** with 0.1, 0.2, and 2.0 equiv of di-*tert*-butylcyanocuprate afforded 95:5, 89:11, and 17:83 mixtures, respectively, of *E* and *Z* stereoisomers while treatment of (*Z*)-**22c** with 2.0 equiv of the cuprate afforded a 19:81 *E*:*Z* isomer ratio. Vinylogous thiol esters (*E*)-**22c** and (*Z*)-**22c** did not undergo isomerization in THF under the same reaction conditions.

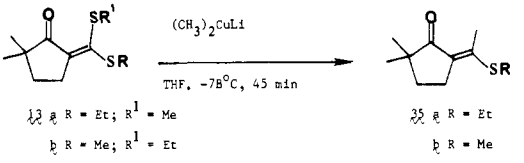
The configurational instabilities of some of the vinylogous thiol esters and the isomerization of (*E*)-**15a** and (*E*)-**22c** under the reaction conditions prompted a brief examination of the equilibrium stereoisomer ratios. The thermodynamic stability of the *E* and *Z* geometrical isomers of vinylogous thiol esters **14**, **15a**, **17a**, **20a**, **20c**, **22c**, and **24a** was examined. Each purified isomer was dissolved in $CDCl_3$ in an NMR tube to which a trace of HCl was added. The isomerization process was monitored by NMR until equilibrium was obtained as indicated by identical isomer compositions from either the *E* or *Z* geometrical isomer. The results (Table II) indicate considerable variation but are consistent with literature reports of *E* β-alkylthio derivatives[17] being more stable than the *Z* isomers, while *Z* β-arylthio derivatives are generally more stable than the corresponding *E* isomers.

A series of organocopper reagents were examined in order to explore the effect of specific organocuprate reagent upon product distributions and stereoselectivity. The ketene dithioacetal of 4-phenylcyclohexanone (**31**) was chosen as substrate since all of the possible products would be relatively nonvolatile and material balance could be easily determined. Reaction of **31** with nine



organocopper reagents was examined in THF and, where organocuprate solubility permitted, in diethyl ether, toluene, or benzene. The reaction afforded the *E* and *Z* vinylogous thiol esters (*E*)-**32** and (*Z*)-**32**, α-alkylidene ketone **33**, reduction product **34**, and recovered starting material. The results are listed in Table III and several patterns emerge. First, $(CH_3)_2CuLi$, $[(CH_3)_2CuSCN]Li_2$, $[(C_6H_{11})_2PCuCH_3]Li$, and $[(CH_3)_2CuCN]Li_2$ gave substantial quantities of bis-substitution product **33** (i.e., >14%) when 1.2 equiv of organocopper reagent was utilized. The yield of **33** increased along the solvent series THF, Et_2O, $PhCH_3$ when $(CH_3)_2CuLi$ (21, 33, 65%), $[(CH_3)_2CuCN]Li_2$ (51, 65, 75%), and $[(C_6H_{11})_2PCuCH_3]Li$ (39, 65, 66%) were employed and decreased along the solvent series when $[(CH_3)_2CuSCN]Li_2$ (37, 19, 14%) was employed (Table III, entries 1, 2, 4, 12–20). These results for $[(C_6H_{11})_2PCuCH_3]Li$ were obtained when the reagent was generated by warming the solution to 0 °C over a 40-min period and then cooling to −78 °C before the addition of **31**. Attempted generation of this reagent at −40 °C afforded different yields of **32**, **33**, and **31** in THF (67, 11, 10%), ether (46, 32, 1%), and toluene (31, 41, 16%) than the reagent generated at 0 °C. Second, the mixed cuprates $(PhSCuCH_3)Li$ and $(CH_3OCMe_2C{\equiv}CCuCH_3)Li$ afforded good yields of vinylogous thiol esters (*E*)-**32** and (*Z*)-**32** and low yields of **33** (<6%) in THF (Table III, entries 5, 10). The mixed cuprate $(PhSCuCH_3)Li$ afforded poor results in Et_2O as a result of limited solubility. Third, the acetylenic mixed cuprate afforded the highest yield of reduction product **34** (14%) in diethyl ether (Table III, entry 11) consistent with earlier observations involving other α-oxoketene dithioacetals (Table I, entry 5). The phosphine complexed cuprates $Ph_3P{\cdot}(CH_3)_2CuLi$ and $n\text{-}Bu_3P{\cdot}(CH_3)_2CuLi$ afforded good yields of vinylogous thiol ester **32** in THF while the latter cuprate afforded increased yields of **33** in Et_2O and $PhCH_3$ (Table III, entries 6–9). Fourth, the lower order cyanocuprate, $(CH_3CuCN)Li$, did not effect substitution under the reaction conditions (Table III, entries 21, 22). Fifth, the stereoselectivity of the reaction showed some variation with organocuprate reagent and solvent utilized. In general the *E*:*Z* distribution hovered around a 70:30 ratio and the influence of solvent was not uniform but depended on the specific organocuprate employed (Table III; compare entries 1–4, 12–14, and 18–20 vs. 7, 8, and 15–17). The phosphine complexed cuprate $Ph_3P{\cdot}(CH_3)_2CuLi$ afforded the highest selectivity (80:20) paralleling an earlier report on the effectiveness of $n\text{-}Bu_3P{\cdot}(CH_3)_2CuLi$ in stereoselective substitution reactions.[19]

Having established the stereoselectivity of the reaction, α-oxoketene dithioacetals **13a** and **13b** having two different alkylthio substituents were examined in order to explore the stereospecificity of the reaction. Reaction of **13a** with lithium dimethylcuprate



(6)

afforded **35a** (67%) stereospecifically while reaction of **13b** afforded **35b** (45%) (eq 6). Similarly, reaction of **13a** with methyl(phenylthio)cuprate afforded **35a** (64%) stereospecifically. In all instances, the alkylthio substituent syn to the ketone carbonyl was replaced by the cuprate ligand in a stereospecific process.

The β,β-dichloro enone **8** underwent the substitution reaction with lithium dimethylcuprate to cleanly afford the *E* β-chloro enone **25** stereoselectively in 84% yield (Table I, entry 30).[20]

Finally, the ester derivatives **9–11** were briefly examined to explore the generality of the reaction. Treatment of lactone **9** with lithium dimethylcuprate afforded the reduction product **26** cleanly in 60% yield (Table I, entry 31), while the methyl ester **10** upon reaction with lithium dialkylcuprates afforded primarily reduction product **28**. Reaction of ester **10** with *n*-BuCu[18d] or *t*-BuCu afforded primarily recovered starting material along with small amounts of substitution product **27** and reduction product **28**. The yield of **27a** could not be increased by use of $CH_3Cu{\cdot}BF_3$.[18e] However, reaction of **10** with lithium *tert*-butyl(phenylthio)cuprate in diethyl ether afforded **27c** in 90% yield with excellent stereoselectivity (entry 35). Methyl ester **11** which

(16) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Tetrahedron Lett.* **1982**, *23*, 3755.

(17) (a) Furukawa, N.; Fukumura, M.; Nishio, T.; Oae, S. *Phosphorus Sulfur*, **1978**, *5*, 191. (b) Nishio, T.; Omote, Y. *J. Chem. Soc., Perkin Trans. 1* **1981**, 934. (c) Cavalchi, B.; Landini, D.; Montanari, F. *J. Chem. Soc. C* **1969**, 1204.

(18) (a) Hooz, J.; Layton, R. B. *Can. J. Chem.* **1970**, *48*, 1626. (b) Bertz, S.; Dabbagh, G. *J. Org. Chem.* **1984**, *49*, 1119. (c) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. *Ibid.* **1983**, *48*, 546. (d) Corey, E. J.; Chen, R. H. K. *Tetrahedron Lett.* **1973**, 1611. (e) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.* **1982**, *47*, 119. (f) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675.

(19) Casey, C. P.; Marten, D. F. *Tetrahedron Lett.* **1974**, 925.

(20) Barrett, A. G. M.; Morris, T. M.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2272.

Table I. Reactions of α-Oxoketene Dithioacetals with Organocuprates

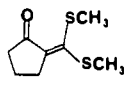
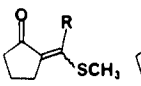
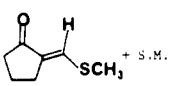
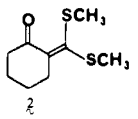
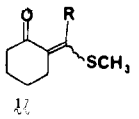
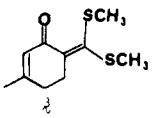
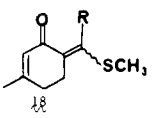
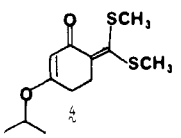
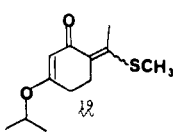
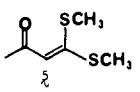
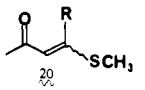
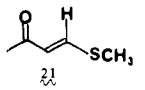
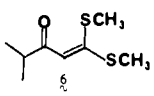
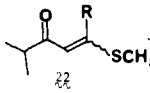
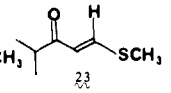
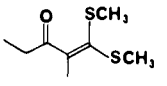
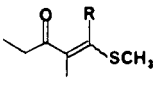
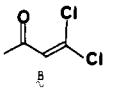
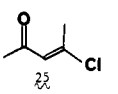
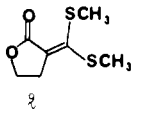
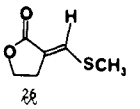
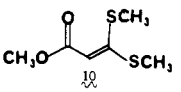
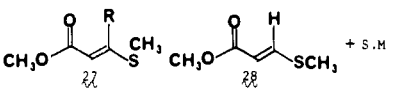
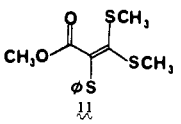
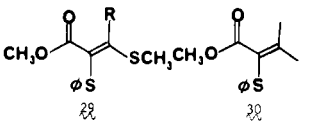
Entry	Substrate	Cuprate Ligand R	Cuprate[a]	Products (E:Z)[b] % Yield[c]		
	 1			 15	 16	+ S.M.
1		a Me	A	65[d]		
2			B	(97:3) 81	-	
3			C	(98:2) 96	-	
4		b n-Bu	B	(92:8)[e] 83	9	
5			C	(92:8) 55	12	38
6		c sec-Bu	B	(97:3) 93		
7		d tert-Bu	B	(95:5)[e] 96		
8		e C_3H_5	B	(70:30) 64		
9			C	(70:30) 77		
	 2			 17		
10		a Me	B	(77:23) 75		
11		b n-Bu	B	(90:10) 70		
12		c sec-Bu	B	(79:21)[e] 62		
13		d tert-Bu	B	(95:5)[e] 96		
	 3			 18		
14		a Me	B	(94:6)[e] 79		
15		b $Me_2CH{=}CHCH_2CH_2$	B	(96:4) 75		
	 4			 19		
16		Me	B	(93:7) 84		
	 5			 20	 21	S.M.
17		a Me	B	(95:5) 92		
18		b n-Bu	B	(91:9) 88		
19		c sec-Bu	B	(91:9) 87		
20		d tert-Bu	B	(8:92)[e] 14	65	14
21			B[f]	(8:92)[e] 89		
	 6			 22	 23	
22		a Me	B	(94:6) 87	2.5	
23			C	(96:4) 51		
24		b n-Bu	B	(93:7) 69		
25			C	(89:11) 93		
26		c sec-Bu	B	(94:6) 97		
27		d tert-Bu	B[f]	(20:80)[c] 53		

Table I (*Continued*)

Entry	Substrate	Cuprate Ligand R	Cuprate[a]	Products (*E*:*Z*)[b] % Yield[c]		
	 7			 24		
28		a Me	B	(97:3) 88		
29		b n-Bu	B	(96:4) 47		
	 8			 25		
30		Me	A	> (95:5)[e] 84		
	 9			 26		
31		a Me	B	60[d]		
	 10			 27 28		+ S.M
32		a Me	A	13[d]	61	B
33		b n-Bu	D[f]	18[d]	-	67
34		c tert-Bu	D[f]	24[d]	15	46
35			B[f]	(94:6)[e] 90		
	 11			 29 30		+ S.M.
36		a Me	B	(24:76) 86	11	-
37		b n-Bu	B	< (5:95)[e] 84	-	13

[a] The following organocopper reagents were employed: A = R_2CuLi, B = (PhSCuR)Li, C = $(MeOCMe_2C{\equiv}CCuR)Li$, D = RCu. The reactions were run in THF unless otherwise noted. [b] *E*:*Z* isomer ratios were determined by NMR and GLC peak areas unless otherwise noted. [c] Yields are based upon isolated products purified by medium-pressure liquid chromatography (MPLC) on silica gel. [d] Only the *E* isomer was isolated. [e] *E*:*Z* isomer ratio was determined by NMR integration only. [f] Et_2O was used as solvent.

Table II. Acid-Catalyzed Isomerization of *E* and *Z* Vinylogous Thiol Esters

entry	substrate[a]	*E*:*Z* ratio at equil[b]
1	14 *E*	42:58
2	*Z*	43:57
3	15a *E*	84:16
4	*Z*	85:15
5	17a *E*	60:40
6	*Z*	64:36
7	20a *E*	73:27
8	*Z*	73:27
9	20c *E*	82:18
10	*Z*	81:19
11	22c *E*	81:19
	Z	81:19
12	24a *E*	55:45
	Z	56:44

[a] Substrate was treated with a trace of HCl in $CDCl_3$. [b] Ratios were determined by NMR integration at 90 or 300 MHz.

contains an α-phenylthio substituent underwent clean reaction with lithium dialkylcuprates to afford the substitution products **29** in a stereoselective fashion.

Assignment of Double-Bond Configuration

The geometry about the carbon–carbon double bond was rigorously established by an X-ray diffraction study for (*E*)-**15d** which was obtained pure by fractional crystallization. The ORTEP drawing[21] is provided in Figure 1 and the torsion angles in the ring, bond angles and bond distances are listed in Table IV. Table V provides the fractional crystal coordinates. There is a high degree of strain in the molecule, with a torsion angle about the C2–C6 double bond of 15.9°. The bulky *tert*-butyl group has a close, nonbonded contact from C10 to the oxygen of 3.04 Å. The five-membered ring is also highly strained, with an approximate C_2 axis through the carbonyl group.

(21) Johnson, C. K. "ORTEPII", Oak Ridge National Laboratory Technical Report ORNL-5138, Oak Ridge, Tenn.

Table III. Product Distributions as a Function of Solvent and Cuprate in the Reactions of α-Oxoketene Dithioacetal **31** with Organocopper Reagents

			products (*E*:*Z*), % yield[a]					
entry	cuprate	solvent	(**32***E* + **32***Z*)[b]	**33**	**34**	**31**	total yield	ref[c]
1	$(CH_3)_2CuLi$	THF	(74:26) 73	21		5	99	
2		Et_2O	(76:24) 62	33		1	96	
3		PhH	(59:41) 34	54		7	95	
4		$PhCH_3$	(65:35) 12	65		4	81	
5	$(PhSCuCH_3)Li$	THF	(67:33) 82	4		5	91	14
6	$Ph_3P{\cdot}(CH_3)_2CuLi$	THF	(80:20) 75	10		5	90	18a
7	$n\text{-}Bu_3P{\cdot}(CH_3)_2CuLi$	THF	(69:31) 61	6	1	18	86	18a
8		Et_2O	(68:32) 41	29	4	23	97	
9		$PhCH_3$	(73:27) 40	19	5	31	95	
10	$(CH_3OCMe_2C{\equiv}CCuCH_3)Li$	THF	(76:24) 86	6		7	99	15
11		Et_2O	(71:29) 68	11	14	3	96	
12	$[(C_6H_{11})_2PCuCH_3]Li$	THF	(70:30) 41	39		10	84	18b
13		Et_2O	(65:35) 28	65		1	93	
14		$PhCH_3$	(45:55) 22	66			88	
15	$[(CH_3)_2CuSCN]Li_2$	THF	(59:41) 46	37	8	19	91	18c
16		Et_2O	(71:29) 51	19		19	89	
17		$PhCH_3$	(73:27) 67	14		18	99	
18	$[(CH_3)_2CuCN]Li_2$	THF	(79:29) 34	51		4	89	16
19		Et_2O	(30:70) 27	65			91	
20		$PhCH_3$	(56:44) 9	75			91	
21	$(CH_3CuCN)Li$	THF				95		18f
22		Et_2O				98		

[a] Yields are based upon isolated products purified by TLC on silica gel. [b] Isomer ratios were determined from the NMR spectra of the crude reaction mixture and the purified mixture of (*E*)-**32** and (*Z*)-**32**. [c] Literature reference for preparation of the cuprate.

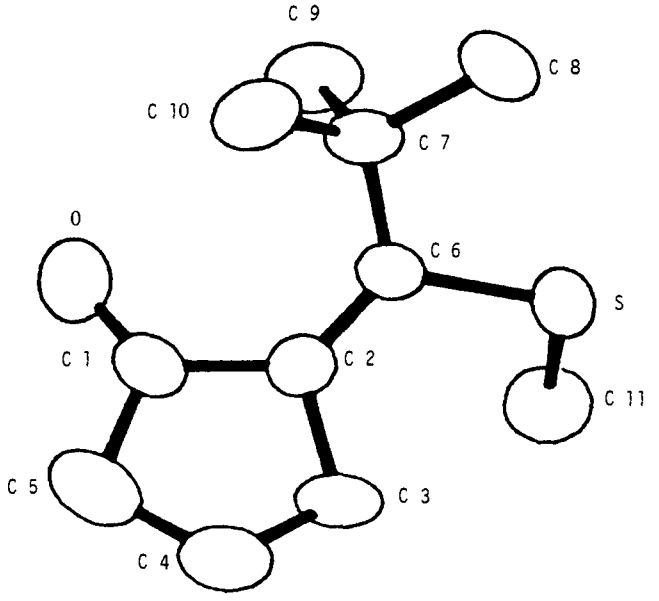


Figure 1. ORTEP drawing of vinylogous thiol ester (*E*)-**15d**.[21]

A consistent set of empirical patterns was obtained from UV and NMR spectral data that permits assignment of olefin geometry. Separation and purification of the *E* and *Z* stereoisomers of 17 vinylogous thiol esters revealed that the *E* isomers exhibit a more intense absorption in the UV spectrum at shorter wavelengths then the corresponding *Z* isomers (Table VI). This pattern had been previously reported for several vinylogous thiol esters[17a,b] and it was suggested[17a] that the UV data were indicative of an interaction between the carbonyl group and the sulfur atom in the *Z* isomer. In this regard, it is interesting to note that (*E*)-**22c** (λ_{max} 297, 290, 288) and (*Z*)-**22c** (λ_{max} 308, 302, 300) display virtually identical shifts to shorter wavelengths along the solvent series ethanol, ether, and hexane, respectively. In addition, the β-methyl or β-methylene protons syn to the ketone carbonyl in the *E* isomers display NMR absorptions downfield relative to the corresponding absorptions for the *Z* isomers (Table VI). This pattern is also in accord with a well-established trend for the β protons or β-methyl substituents of α,β-unsaturated esters and ketones.[22] The *E* isomers of **15c**, **15e**, **20c**, and **22c** exhibit γ-methine absorptions downfield relative to those of the *Z* isomers while the γ-methyl substituent in the *E* isomers of **15c**, **20c**, and

Table IV. Bond Distances, Bond Angles, and Torsion Angles for (*E*)-**15d** Determined by X-ray Diffraction[a]

bond type	distance, Å	bond type	angle, deg	bond	torsion angle, deg
S-C6	1.763	C6-S-C11	105.42	C1-C2	+13.6
S-C11	1.801	O-C1-C2	127.33	C2-C3	-31.4
O-C1	1.219	O-C1-C5	123.56	C3-C4	+37.4
C1-C2	1.481	C2-C1-C5	108.87	C4-C5	-29.0
C1-C5	1.507	C1-C2-C3	104.86	C1-C5	+9.5
C2-C3	1.524	C1-C2-C6	130.02	C2-C6	+15.9
C2-C6	1.358	C3-C2-C6	125.09		
C3-C4	1.513	C2-C3-C4	103.58		
C4-C5	1.510	C3-C4-C5	104.14		
C6-C7	1.546	C1-C5-C4	104.88		
C7-C8	1.545	S-C6-C2	119.41		
C7-C9	1.532	S-C6-C7	113.89		
C7-C10	1.522	C2-C6-C7	126.70		
		C6-C7-C8	110.55		
		C6-C7-C9	108.87		
		C6-C7-C10	112.03		
		C8-C7-C9	107.55		
		C8-C7-C10	106.32		
		C9-C7-C10	111.41		

[a] The estimated standard deviation in bond lengths is 0.001 to 0.002 Å, and in bond angles it is 0.02 to 0.04 deg.

Table V. Fractional Crystal Coordinates for Compound (*E*)-**15d**[a]

atom	*x*	*y*	*z*
S	0.79971	0.19633	0.73528
O	0.85824	0.00635	1.17260
C1	0.95406	0.05392	1.18344
C2	0.92992	0.11305	1.04799
C3	1.10397	0.14150	1.08587
C4	1.19360	0.12657	1.30002
C5	1.12733	0.05710	1.33153
C6	0.78790	0.13985	0.91938
C7	0.60869	0.12643	0.91461
C8	0.49392	0.18737	0.81697
C9	0.54094	0.06190	0.79159
C10	0.60020	0.11950	1.11876
C11	0.94952	0.15823	0.64297

[a] The estimated standard deviation in the coordinates is between 0.00001 and 0.00003.

Table VI. UV and NMR Spectral Data for Assignment of Olefin Configuration in β-Alkylthio-α,β-enones

enone	UV (MeOH), λ_{max} ($\epsilon \times 10^4$)	NMR, δ α-(=CH)	β-CH_3	β-CH_2	γ-H	γ-CH_3
14 *E*	296 (1.40)[a]	5.58		2.70		
Z	303 (1.20)[a]	6.30		2.08		
15a *E*	311 (2.40)		2.56			
Z	322 (1.60)		2.11			
15b *E*	312 (1.85)			2.95		
Z	322 (1.35)			2.69		
15c *E*	313 (1.25)[a]				4.17	1.09
Z	321 (0.65)[a]				2.76	1.17
15e *E*	317 (1.13)				≃2.66	
Z	320 (0.65)[a]				≃1.65	
17a *E*	307 (1.80)		2.40			
Z	320 (1.20)		2.14			
17b *E*	307 (1.40)					
Z	318 (0.79)[a]					
18b *E*	331 (0.90)			2.83		
Z	339 (0.67)			≃2.50		
19 *E*	321 (1.50)		2.36			
Z	332 (1.25)		2.14			
20a *E*	294 (0.80)	5.89	2.37			
Z	307 (0.60)	6.30	2.22			
20b *E*	294 (0.60)	5.82		2.80		
Z	304 (0.46)	6.26		2.40		
20c *E*	299 (1.60)	5.74			4.09	1.07
Z	309 (0.99)	6.24			3.65	1.17
22a *E*	294 (1.80)	5.91	2.40			
Z	308 (0.67)	6.37	2.25			
22b *E*	295 (1.09)	5.87		2.73		
Z	303 (0.78)	6.31		≃2.49		
22c *E*	297 (1.60)	5.80			4.12	1.14
Z	308 (0.65)	6.27			≃2.66	1.19
24a *E*	296 (0.85)		2.10			
Z	310 (0.24)[a]		2.07			
24b *E*	296 (0.57)			2.55		
Z	304 (0.54)			2.40		

[a] Measured in 95% ethanol.

22c appears upfield relative to the γ-methyl absorption in the *Z* isomers. Similarly, the *E* stereoisomers containing a *tert*-butyl group syn to the ketone carbonyl generally exhibit absorptions in the NMR upfield relative to the *tert*-butyl absorption of the *Z* isomer. The difference in chemical shift between the γ-methyls of a β *sec*- or *tert*-butyl group of *E* and *Z* vinylogous thiol esters is much smaller than that found for the β protons or methyl groups in similar substrates. The *tert*-butyl groups in vinylogous thiol esters (*E*)-**15d** and (*Z*)-**15d** have virtually the same chemical shift. Finally, the *E* trisubstituted enones[23] **20a–c** and **22a–c** exhibit an upfield absorption for the α-olefinic proton relative to the olefinic absorption of the *Z* isomer.[17a,b] This undoubtedly reflects shielding by the spacially proximate sulfur heteroatom, and a similar trend is observed for the allylic methylene group in the *E* and *Z* isomers of **15d**. The downfield absorptions of the vinyl proton in the spectra of **20d** and **22d** (δ 6.40 and 6.44, respectively) is consistent with the *Z* configuration. This was confirmed by difference NOE experiments in which irradiation of the *t*-Bu group affords an NOE enhancement in the vinyl absorptions of **20d** and **22d**. These patterns are consistent throughout all the pairs of *E* and *Z* stereoisomers examined and should provide a reliable guide for the assignment of olefin geometry in vinylogous thiol esters. There is, however, a substantial variation in the absolute values of the absorption maxima, extinction coefficient, and chemical shift for individual substrates so that assignment of geometry in the absence of a mixture or pair of isomers is difficult.[24]

Vinylogous thiol ester **17d** was isolated as a single stereoisomer, and the olefin was assigned the *E* configuration by analogy with (*E*)-**15d**. In an effort to confirm this assignment **17d** was treated with $LiAlH_4$, DIBAL, or methyllithium to afford the corresponding allylic alcohols. Reduction of **17d** gave two allylic alcohols[25] while addition of methyllithium afforded a single allylic alcohol. The ^1H NMR spectra of the allylic alcohols were recorded as benzene solutions containing 0–0.5 equiv of the $Eu(fod)_3$ chemical shift reagent, and plots of log Δδ vs. log *r* afford a scatter of points for the structures containing a *Z* olefin and lines of negative slope for structures containing the *E* olefin consistent with the original assignment.[26] It was also observed that addition of alkyllithium reagents to α-oxoketene dithioacetal **2**, in which the two methylthio substituents exhibit the same chemical shift ($CDCl_3$, δ 2.36), afforded α-hydroxyketene dithioacetals in which the methylthio substituent presumably syn to the hydroxyl group is shifted upfield (the methylthio absorptions for the α-hydroxyketene dithioacetals were δ 2.33 and 2.23 for the methyllithium addition product and δ 2.36 and 2.28 for the allyllithium addition product). The methylthio substituent in **17d** and the reduction and methyllithium addition products derived from it display similar chemical shifts ($CDCl_3$, δ 2.17, 2.19, and 2.19, respectively) suggesting the *E* stereoisomer.

Discussion

The actual mechanism involved in the conjugate addition of organocuprates to α,β-unsaturated carbonyl compounds has not yet been fully elucidated despite intensive investigations over the past decade. Nucleophilic addition[27] of the organocuprate to the β-carbon atom of the enone has been suggested as an alternative to the original proposal of House involving electron transfer.[28] Both views postulate a copper(III) species that has never been detected spectroscopically and which is presumed to undergo very rapid reductive elimination to afford an enolate anion. Alternatively, the copper(III) intermediate can be avoided by involving participation of both copper atoms of the cuprate dimer.[29] Direct addition of the cuprate across the carbon–carbon double bond to afford an α-cuprio ketone has also been proposed.[30] Investigations by House have provided evidence for the formation of intermediate lithium enolate anions at 0 °C or above although it could not be determined whether the conjugate adduct insoluble at low temperatures (−44 to −78 °C) was a lithium or copper enolate.[31] The nature of the enolate anion generated by organocopper conjugate addition remains a point of controversy.[32] Regardless of the actual

(22) 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, and references cited therein.

(23) Although (*Z*)-4-methylthio-3-penten-2-one has been reported [Duus, F.; Anthonsen, J. W. *Acta Chem. Scand., Ser. B* **1977**, *31*, 40. Fabian, J. *Tetrahedron* **1973**, *29*, 2449], the mode of preparation and the UV and NMR spectra data appear to be more consistent with the *E* isomer: UV max (C_6H_{12} 286; NMR (60 MHz, CCl_4) δ 5.73 olefinic proton). Comparison of the vinyl proton absorption with those reported in Table VI and ref 17a,b suggests that the *E* isomer was actually obtained.

(24) The initial assignment of the *Z* configuration to the major stereoisomer of **24a** was tentatively determined from the UV spectrum of the single isomer and subsequently shown to be incorrect. See ref 3.

(25) The conformational mobility of cyclohexane derivatives would suggest that the two allylic alcohols are the *E* and *Z* double-bond geometrical isomers, although the difference in chemical shift between the methylthio substituents ($CDCl_3$, δ 2.19 and 2.16) is smaller than expected. Presumably, isomerization of the olefin could occur under the reaction conditions or during the work-up procedure since the addition of methyllithium to **17d** afforded a single product.

(26) Kime, K. A.; Sievers, R. E. *Aldrichimica Acta* **1977**, *10*, 54, and references cited therein.

(27) (a) Whitesides, G. M.; Kendall, P. E. *J. Org. Chem.* **1972**, *37*, 3718. (b) Casey, C. P.; Cesa, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4236. (c) Krauss, S. R.; Smith, S. G. *Ibid.* **1981**, *103*, 141. (d) Frejaville, C.; Jullien, R.; Stahl-Lariviere, H.; Wanat, M.; Zann, D. *Tetrahedron* **1982**, *38*, 2671.

(28) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.

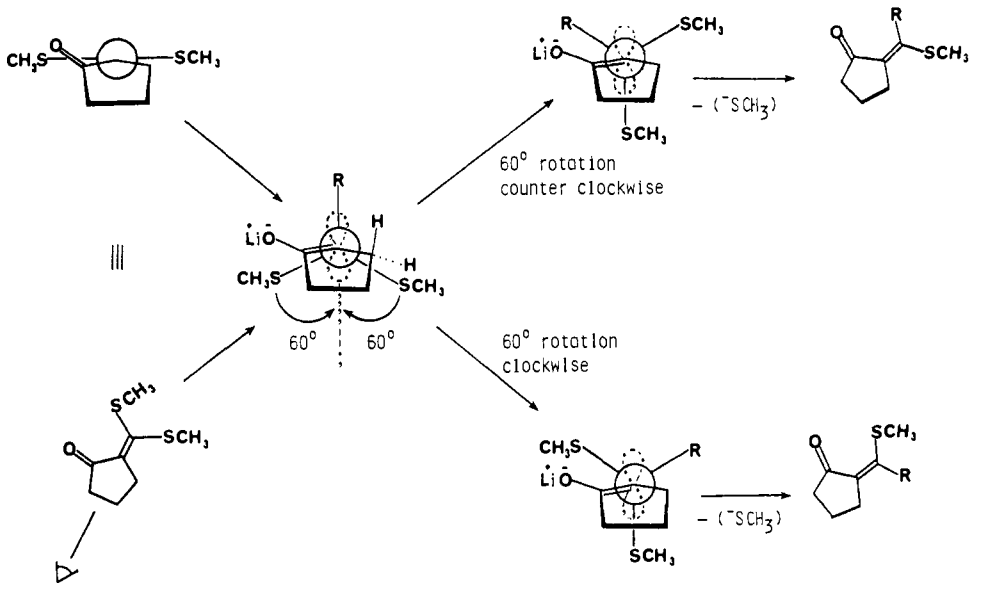
(29) (a) Alexakis, A.; Chuit, C.; Commercon-Bourgain, M.; Foulon, J. P.; Jabri, N.; Mangeney, P.; Normant, J. F. *Pure Appl. Chem.* **1984**, *56*, 91. (b) Pearson, R. G.; Gregory, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 4098. (c) Cabaret, D.; Welvart, *Z. J. Organomet. Chem.* **1979**, *177*, 75.

(30) Berlan, J.; Battioni, J.-P.; Koosha, K. *Bull. Soc. Chim. Fr.* **1979**, 183. Four, P.; Riviere, H.; Tang, P. W. *Tetrahedron Lett.* **1977**, 3879.

(31) (a) House, H. O.; Wilkins, J. M. *J. Org. Chem.* **1978**, *43*, 2443. (b) House, H. O.; Wilkins, J. M. *Ibid.* **1976**, *41*, 4031.

(32) Posner, G. H. "An Introduction to Synthesis Using Organocopper Reagents"; Wiley: New York, 1980; Chapter 2, pp 42–47, and references cited therein.

Scheme I



mechanistic pathway, formation of an intermediate enolate anion is established by trapping with a wide range of electrophiles.[32] Although a direct substitution reaction cannot be ruled out,[33] the addition–elimination pathway originally proposed by Casey[5b] provides a rational model that is consistent with the present results. A similar mechanism has been invoked for the reaction of 1-halogeno-2-phenylsulfonylethylenes with lithium dimethylcuprate.[33b] α-Oxoketene dithioacetal **7**, lactone **9**, and ester **10** undergo the substitution reaction with a general trend toward diminished yields as expected for a conjugate addition process involving these less electrophilic or less easily reduced α,β-unsaturated carbonyl compounds. Introduction of an α-phenylthio substituent into **10** (e.g., **11**) increases the electrophilicity of the enoate and the efficiency of the substitution reaction. For the lactone **9** and ester **10**, reduction of the C–S bond becomes the predominant reaction pathway, although reaction of lithium *tert*-butyl(phenylthio)cuprate with **10** in Et_2O did afford the substitution product in 90% yield.

The initial organocopper conjugate addition event would lead after reductive elimination to an enolate anion containing two good leaving groups at the γ-carbon atom (β-carbon of the original enone). In order for facile elimination to occur, there must be a rotation about the γ-carbon atom of the enolate such that the carbon–sulfur bond of the leaving group achieves a trans periplanar arrangement with the enolate π cloud (Scheme I). This can be achieved by either a 60 or 120° rotation, and the concept of minimum motion in the transition state would favor a 60° motion. There are, however, two good leaving groups at the γ-carbon atom which can rotate 60° in opposite directions, thereby decreasing the likelihood of a stereoselective process. Rotation of 60° in a clockwise direction would require motion of an alkylthio substituent past the enolate oxygen atom and its attendant solvent shell. This would be expected to be disfavored as a result of either steric or dipolar interactions. Indeed, α-oxoketene dithioacetals **13a** and **13b** containing two different alkylthio substituents undergo a stereospecific substitution reaction with loss of the alkylthio substituent syn to the ketone carbonyl consistent with motion of the syn alkylthio substituent away from the enolate oxygen atom in a counterclockwise direction. The reaction displays a high degree of stereoselectivity for organocuprates containing primary, secondary, and tertiary alkyl ligands and for cyclic and acyclic α-oxoketene dithioacetals. Although the organocopper substitution reactions were carried out in THF or ether, the isomerization studies (Table II) would seem to indicate that the isomer distributions in these reactions generally reflect kinetic control. The formation of the *Z* isomers from the reaction of **5** and **6** with the *t*-Bu cuprate may arise from isomerization events or reflect the larger *A* value (4.4) of the *t*-Bu group in the rotation process.[34] Reaction of the cyclic substrates **1** and **2** with a *t*-Bu cuprate would be expected to afford the *E* isomers of **15d** and **17d** predominantly during either the initial elimination sequence or during subsequent isomerization events as a result of $A^{1,3}$ strain[35] present in the *Z* isomer. The variation in stereoselectivity for reaction of a given substrate with various cuprates, the stereoselective isomerization of several vinylogous thiol esters under the reaction conditions, and the configurational instability of several vinylogous thiol esters suggest that partial isomerization of products under the reaction conditions or during workup and isolation may account for those reactions displaying moderate stereoselectivity. The isomerization of (*E*)-**15a** to (*Z*)-**15a** and (*E*)-**22c** to (*Z*)-**22c** is intriguing as the apparently less stable isomer is formed stereoselectively. Complexation of the sulfur substituent with the organocuprate[33b,36] prior to formation of the carbon–copper (III) bond and collapse of an intermediate copper complex may account for these results.[37] Finally, this substitution reaction exhibits modest to high stereoselectivity depending upon the specific organocuprate reagent and solvent utilized (Table III). The range of isomer ratios obtained, however, reflects relatively small differences in transition state and solvation energies.

The chemoselectivity of the reaction is dependent upon a delicate balance between α-oxoketene dithioacetal, vinylogous thiol ester, and organocuprate reactivity. This is most clearly seen in the study of product distributions as a function of organocuprate and solvent (Table III). Reaction of 1.18–1.20 equiv of lithium dimethylcuprate with **31** afforded substantial quantities of bis-substitution product **33** which increases along the solvent series THF < Et_2O < PhH ~ $PhCH_3$. The composite yields of substitution products

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(37) Evidence for the initial formation of an olefin–copper(I) π complex in these conjugate addition reactions has recently been obtained by a ^{13}C NMR study. See: Hallnemo, G.; Olsson, T.; Ullenius, C. *J. Organomet. Chem.* **1984**, *265*, C22. A referee's suggestion that this isomerization occurs by removal of the γ proton by a base in the reaction mixture seems unlikely since organocuprates undergo conjugate addition reactions to reasonably strong carbon acids such as Hagemann's ester (see: Kametani, T.; Nemoto, H. *Tetrahedron Lett.* **1979**, 3309). Although the presence of an equilibrium concentration of free *tert*-butyllithium cannot be ruled out (see ref 38), a mechanism involving base-promoted isomerization must also account for the selective formation of the *Z* isomer.

in these reactions require 1.14, 1.28, 1.40, and 1.41 equiv of organocopper reagents indicating that 0–20% of the products are arising from either CH_3Cu or a heterocuprate [$(CH_3SCuCH_3)Li$] formed in the reaction mixture from CH_3Cu and $LiSCH_3$. Good coordinating solvents such as THF and DME slow down organocopper conjugate addition reactions,[31a] and this would account for the observed solvent effect. As the coordinating ability of the solvent decreases, the organocopper reagent becomes more reactive and less selective toward the α-oxoketene dithioacetal and product vinylogous thiol ester. Although $(PhSCuCH_3)Li$ was ineffective in diethyl ether and toluene owing to limited solubility, the mixed organocuprate $(CH_3SCuCH_3)Li$, presumably generated in situ, appears to be influenced by these solvents in the same manner since the excess substitution products increase from 0 to 20% along the solvent series. Chemoselectivity can also be achieved by modulating the reactivity of the organocuprate by utilization of cuprates containing nontransferable [e.g., $(PhSCuCH_3)Li$ and $(MeOCMe_2C{\equiv}CCuCH_3)Li$] or coordinating [e.g., $Ph_3P{\cdot}(CH_3)_2CuLi$ and $n\text{-}Bu_3P{\cdot}(CH_3)_2CuLi$] ligands. The higher order cuprates $[(CH_3)_2CuSCN]Li_2$ and $[(CH_3)_2CuCN]Li_2$ also afford substantial quantities of bis-substitution product **33** which increase along the solvent series THF < Et_2O < $PhCH_3$ for the latter and decreases for the former. The structure of these higher order cuprates is not known and the influence of solvent upon the extent of aggregation may have some bearing on the product distributions.[38]

In summary, α-oxoketene dithioacetals undergo a chemo- and stereoselective substitution reaction with organocuprates to afford vinylogous thiol esters. The reaction proceeds well with organocopper reagents containing primary, secondary, and tertiary alkyl ligands and with cyclic and acyclic α-oxoketene dithioacetals. The reaction generally affords the *E* vinylogous thiol ester with generally high stereoselectivity (i.e., >90:10), and instances of low stereoselectivity appear to be related to configurational instability of the products.

Experimental Section

Proton NMR spectra were recorded as $CDCl_3$ solutions, unless otherwise noted, on either a Varion EM-360L or JEOL-FX90Q instrument. Chemical shifts are reported as values in parts per million relative to tetramethylsilane as internal standard. Unless otherwise noted, the carbon NMR (^{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 spectrophotometer as CCl_4 solutions unless otherwise noted. Melting points were determined on a Thomas-Hoover melting-point apparatus and are uncorrected. Elemental analyses were determined by Atlantic Microlab Inc., Atlanta, GA.

CuI was freshly purified by dissolving an appropriate quantity of CuI in boiling saturated NaI(aq) over a period of 30 min. Pure CuI was produced by cooling and diluting the solution with H_2O followed by filtration and washing sequentially with H_2O, EtOH, EtOAc, ether, and pentane and drying in vacuo for 24 h.[39] CuBr was purified according to a procedure employed for CuCl that was slightly modified.[40] Commercial CuBr (Alfa) was dissolved in 48% HBr, precipitated by the addition of water, and filtered. The precipitate was washed sequentially with H_2O, EtOH, and Et_2O and then dried in vacuo. CuSCN was prepared according to an established procedure.[41] CuCN was obtained from Matheson Coleman and Bell, and $(C_6H_{11})_2PH$ was obtained from Aldrich. These reagents were used without further purification. The concentration of alkyllithium reagents in commercial or prepared solutions was determined by titration of diphenylacetic acid to the yellow end point.[42] (4-Methylpent-3-en-1-yl)lithium was prepared according to an established procedure.[43] Thiophenol was distilled and stored over 3-Å molecular sieves. Tetrahydrofuran and Et_2O were distilled from sodium/benzophenone prior to use.

General Procedure A: Substitution Using Lithium Alkyl(phenylthio)cuprates, (RCuSPh)Li. *n*-Butyllithium (0.53 mL, 2.40 M, 1.25 mmol) was added dropwise to a 0 °C solution of thiophenol (0.13 mL, 1.27 mmol) and 7 mL of tetrahydrofuran (THF) in a three-neck flask equipped with a N_2 inlet, solid addition funnel, and septum; the solution was stirred for 10 min. Copper iodide (243 mg, 1.27 mmol) was added via the solid addition funnel and the solution was stirred for 15 min. The resulting clear yellow solution was cooled to −78 °C and the appropriate alkyllithium (1.27 mmol) was added by syringe. The solution slowly changed to a clear (R = Me) or a light brown, opaque (R = *n*-Bu, *sec*-Bu) solution over a 1-h period. A −78 °C solution of ketene dithioacetal (1.00 mmol) in 2 mL of THF was added via a double-tipped needle into the −78 °C alkyl(phenylthio)cuprate solution. The reaction was monitored by TLC until starting material was consumed and then quenched at −78 °C with 2 mL of methanol and warmed to room temperature. The reaction mixture was then poured into a mixture of 50 mL of ether (Et_2O) and NH_4Cl (satd) and stirred for 15 min. The copper salts were filtered off, the filtrate was extracted with 2 × 25 mL of Et_2O, washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford the crude vinylogous thiol ester, which was purified by medium-pressure liquid chromatography (MPLC) (petroleum ether/2–20% ethyl acetate, v/v).

(*E*)-5,5-Dimethyl-2-(1-ethylthio-1-methylthiomethylene)cyclopentanone (13a). 2-Formylcyclopentanone[44] was converted to (*E*)-1-(ethylthiomethylene)cyclopentanone (i) according to the procedure of Ireland and Marshall.[45] Treatment of 2-formylcyclopentanone with 1.1 equiv of *p*-TsCl in pyridine at 0 °C for 0.5 h followed by the addition of 3.0 equiv of ethanethiol afforded i in 32% yield after purification by MPLC (R_f 0.29, petroleum ether/5% ethyl acetate, v/v): IR ($CHCl_3$) 3020 (w), 2970 (s), 2930 (m), 1695 (s), 1585 (vs), 1455 (m), 1440 (m), 1410 (m), 1290 (s), 1265 (s), 1240 (s), 1195 (s) cm^{-1}; NMR (90 MHz) δ 1.37 (t, *J* = 7.3 Hz, 3 H), 1.65–2.08 (m, 2 H), 2.12–2.70 (m, 4 H), 2.88 (q, *J* = 7.3 Hz, 2 H), 7.37 (t, *J* = 2.3 Hz, 1 H); ^{13}C NMR δ 202.1, 136.0, 132.2, 37.7, 28.0, 27.5, 18.9, 15.2.

n-Butyllithium (22.0 mL, 2.3 M, 50.6 mmol) was added dropwise to a solution of 2,6-di-*tert*-butyl-4-methylphenol (11.20 g, 51 mmol) in 300 mL of THF cooled to 0 °C. The solution was stirred at 0 °C for 15 min, and then a solution of (*E*)-1-(ethylthiomethylene)cyclopentanone (2.65 g, 17 mmol) in 10 mL of THF was added via cannula; the solution was stirred for an additional 15 min. Methyl iodide (3.40 mL, 55 mmol) was syringed into the red solution maintained at 0 °C and the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was diluted with saturated aqueous NH_4Cl and extracted with 2 × 50 mL of Et_2O. The Et_2O extracts were washed with brine and dried over $MgSO_4$. Purification by MPLC (R_f 0.43, petroleum ether/5% ethyl acetate, v/v) gave 563 mg (18%) of **12a**: IR ($CHCl_3$) 3020 (w), 2990 (m), 2960 (s), 2920 (m), 1690 (s), 1580 (vs), 1440 (m), 1380 (m), 1300 (m), 1280 (m), 1265 (s), 1120 (s) cm^{-1}; NMR (90 MHz) δ 1.06 (s, 6 H), 1.17 (t, *J* = 7.3 Hz, 3 H), 1.78 (t, *J* = 7.4 Hz, 2 H), 2.35 (dt, *J* = 7.4 Hz, *J* = 2.6 Hz, 2 H), 2.84 (q, *J* = 7.3 Hz, 2 H), 7.46 (t, *J* = 2.6 Hz, 1 H); ^{13}C NMR δ 206.6, 137.8, 131.8, 45.4, 35.0, 28.2, 24.2, 23.7 (2 C), 15.5.

n-Butyllithium (0.26 mL, 2.3 M, 0.6 mmol) was added to a solution of diisopropylamine (90 μL, 0.61 mmol) in 4 mL of THF cooled to 0 °C. After 15 min the solution was cooled to −78 °C and hexamethylphosphoramide (0.12 mL, 0.61 mmol) was added and stirring was continued for 30 min. A solution of **12a** (55 mg, 0.30 mmol) in 1 mL of THF was added and the solution was stirred at −78 °C for 45 min whereupon methylthio methylsulfonate (110 mg, 0.90 mmol) was added neat to the orange solution. The reaction mixture was slowly warmed to −30 °C over a 1-h period, diluted with saturated aqueous $NaHCO_3$, and extracted with 2 × 30 mL of petroleum ether. The organic phase was washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo to afford 67 mg of a crude oil which by NMR consisted of 12% **12a** and 87% **13a** (R_f 0.46, petroleum ether/5% ethyl acetate, v/v). Attempted purification resulted in isomerization of **13a** so the crude mixture was used in the substitution reaction. The NMR absorptions of **13a** were readily apparent in the spectra of the crude material: NMR (90 MHz) δ 1.08 (s, 6 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.75 (t, *J* = 7.4 Hz, 2 H), 2.46 (s, 3 H), 2.75 (t, *J* = 7.4 Hz, 2 H), 2.92 (q, *J* = 7.2 Hz, 2 H); ^{13}C NMR δ 206.0, 150.2, 134.5, 47.4, 35.1, 29.3, 24.3, 24.1 (2 C), 18.4, 17.5; mass spectrum *m/e* 230.0834 (M^+) (calcd for $C_{11}H_{18}OS_2$: 230.0799).

(*Z*)-5,5-Dimethyl-2-(1-ethylthio-1-methylthiomethylene)cyclopentanone (13b). 2-Formylcyclopentanone[44] was converted into **13b** in three steps by procedures analogous to those described for the synthesis of **13a**.

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(*E*)-1-(Methylthiomethylene)cyclopentanone (R_f 0.25, petroleum ether/5% ethyl acetate, v/v) was obtained in 66% yield: mp 43–44 °C; IR ($CHCl_3$) 3010 (w), 2970 (m), 2930 (m), 1700 (s), 1585 (vs), 1435 (m), 1410 (m), 1285 (s), 1190 (s) cm^{-1}; NMR (90 MHz) δ 1.80–2.13 (m, 2 H), 2.20–2.62 (m, 4 H), 2.47 (s, 3 H), 7.31 (t, J = 2.6 Hz, 1 H); ^{13}C NMR δ 202.1, 136.0, 132.1, 37.8, 27.6, 19.1, 17.0.

12b (R_f 0.36 petroleum ether/5% ethyl acetate, v/v) was obtained in 7% yield: IR ($CHCl_3$) 3025 (w), 3000 (m), 2960 (s), 2930 (s), 2870 (m), 1695 (s), 1585 (vs), 1460 (m), 1300 (m), 1285 (s), 1020 (s) cm^{-1}; NMR (90 MHz) δ 1.07 (s, 6 H), 1.78 (t, J = 7.2 Hz, 2 H), 2.33–2.52 (m, 2 H), 2.47 (s, 3 H), 7.36 (t, J = 2.6 Hz, 1 H); ^{13}C NMR δ 206.0, 138.9, 131.5, 45.2, 35.0, 24.0, 23.7 (2 C), 17.0.

13b (R_f 0.46, petroleum ether/5% ethyl acetate, v/v) was obtained in 72% yield: IR ($CHCl_3$) 2960 (s), 2930 (s), 2860 (m), 1680 (s), 1530 (vs), 1455 (m), 1260 (m), 1230 (m), 1200 (m) cm^{-1}; NMR (90 MHz) δ 0.99 (s, 6 H), 1.25 (t, J = 7.6 Hz, 3 H), 1.75 (t, J = 7.4 Hz, 2 H), 2.47 (s, 3 H), 2.72 (t, J = 7.4 Hz, 2 H), 2.94 (q, J = 7.6 Hz, 2 H); ^{13}C NMR δ 205.5, 149.5, 134.9, 47.1, 34.8, 29.0, 24.0 (2 C), 23.8, 17.3, 14.3.

(*E*)-5,5-Dimethyl-2-(1-ethylthio)ethylidenecyclopentanone (35a). Methyllithium (0.50 mL, 1.60 M, 0.80 mmol) was added dropwise to a suspension of CuI (72 mg, 0.40 mmol) in 5 mL THF at 0 °C and then stirred for 10 min. The clear cuprate solution was cooled to −78 °C and then a solution of **13a** (69 mg crude) and 2 mL of THF was added via cannula to the −78 °C cuprate solution. The reaction mixture was stirred at −78 °C for 30 min and then quenched with methanol. The reaction mixture was worked up as in general procedure A and purified by column chromatography to yield **35a** (R_f 0.50, petroleum ether/5% ethyl acetate, v/v) in 67% yield: IR ($CHCl_3$) 2970 (s), 2935 (m), 2870 (m), 1685 (s), 1575 (vs), 1455 (m), 1380 (m), 1370 (m) cm^{-1}; NMR (90 MHz) δ 1.04 (s, 6 H), 1.32 (t, J = 7.33 Hz, 3 H), 1.71 (t, J = 7.20 Hz, 2 H), 2.36–2.60 (m, 2 H), 2.56 (s, 3 H), 2.91 (q, J = 7.33 Hz, 2 H); ^{13}C NMR δ 208.0, 151.5, 127.8, 47.1, 34.9, 26.6, 24.2 (2 C), 23.9, 15.9, 14.9; mass spectrum m/e 198.1073 (M^+) (calcd for $C_{11}H_{18}OS$: 198.1078).

(*E*)-5,5-Dimethyl-2-(1-methylthioethylidene)cyclopentanone (35b). Reaction of **13b** with 1.4 equiv of lithium dimethylcuprate as described above afforded **35b** after purification by column chromatography (R_f 0.50, petroleum ether/5% ethyl acetate, v/v) in 45% yield: IR ($CHCl_3$) 2990 (m), 2970 (s), 2940 (s), 2830 (m), 1690 (s), 1580 (vs), 1460 (m), 1370 (m), 1260 (s) cm^{-1}; NMR (90 MHz) δ 1.05 (s, 6 H), 1.72 (t, J = 7.2 Hz, 2 H), 2.07–2.60 (m, 2 H), 2.38 (s, 3 H), 2.56 (s, 3 H); ^{13}C NMR δ 207.9, 151.9, 127.6, 47.2, 34.9, 26.6, 24.3 (2 C), 15.7, 13.5; mass spectrum m/e 184.0913 (M^+) (calcd for $C_{10}H_{16}OS$: 184.0922).

2-[1-(Methylthio)ethylidene]cyclopentanone (15a). A light yellow solution of lithium methyl(phenylthio)cuprate (39 mmol) was generated in 300 mL of THF according to general procedure A. A solution of 5.59 g (29.7 mmol) of **1** in 20 mL of THF was added to the clear, cold (−78 °C) cuprate solution via cannula, stirred for 45 min at −78 °C, warmed to −40 °C over a 15-min period, and then quenched with 20 mL of methanol. The solution was warmed to room temperature and worked up as described above. Purification by column chromatography afforded the *E* isomer, **(*E*)-15a** (R_f 0.40, petroleum ether/5% ethyl acetate, v/v) in 78% yield: UV max (CH_3OH) 311 (ϵ 24 000); IR ($CHCl_3$) 2960 (s), 2920 (s), 2880 (s), 1680 (vs), 1580 (vs), 1410 (vs), 1360 (s), 1230 (vs), 1080 (m), 995 (m), 980 (m) cm^{-1}; NMR (90 MHz) δ 1.80 (p, J = 7.0 Hz, 2 H), 2.35 (t, J = 7.0 Hz, 2 H), 2.38 (s, 3 H), 2.56 (s, 3 H), 2.30–2.70 (m, 2 H); ^{13}C NMR δ 204.0, 163.6, 128.3, 40.7, 30.5, 19.3, 15.6, 13.5.

Anal. Calcd for $C_8H_{12}OS$: C, 61.50; H, 7.74. Found: C, 61.41; H, 7.62.

Purification by column chromatography afforded the *Z* isomer, **(*Z*)-15a** (R_f 0.14, petroleum ether/5% ethyl acetate, v/v) in 3% yield: UV max (CH_3OH) 332 (ϵ 16 000); IR 2920 (m), 1690 (s), 1560 (s), 1430 (m), 1243 (m), 1142 (s), 905 (w) cm^{-1}; NMR (90 MHz) δ 1.60–2.10 (m, 2 H), 2.11 (t, J = 1.2 Hz, 3 H), 2.30 (s, 3 H), 2.31 (t, J = 7.3 Hz, 2 H), 2.63 (t, J = 6.5 Hz, 2 H); ^{13}C NMR δ 204.5, 148.7, 128.5, 39.5, 30.4, 19.9, 19.7, 13.9.

2-[1-(Methylthio)pentylidene]cyclopentanone (15b). A light brown solution of lithium *n*-butyl(phenylthio)cuprate (14.8 mmol) was generated in 75 mL of THF according to procedure A. A solution of 2.0 g (10.6 mmol) of **1** in 20 mL of THF was added to the cold (−78 °C) cuprate solution via cannula. The reaction was stirred at −78 °C for 30 min, warmed to −60 °C over 30 min, quenched with 20 mL of methanol and then warmed to room temperature. The general work-up procedure was followed. Purification by column chromatography afforded the *E* isomer, **(*E*)-15b** (R_f 0.21, petroleum ether/2% ethyl acetate, v/v) in 78% yield: UV max (CH_3OH) 312 (ϵ 18 500); IR 2960 (s), 2921 (s), 2870 (m), 1672 (s), 1560 (s), 1425 (m), 1230 (s), 1200 (s) cm^{-1}; NMR (60 MHz, CCl_4) δ 0.87 (t, J = 7.0 Hz, 3 H), 1.03–1.53 (m, 4 H), 1.82 (p, J = 6.8 Hz, 2 H), 2.31 (s, 3 H), 2.00–2.40 (m, 2 H), 2.51 (t, J = 6.8 Hz, 2 H), 2.95 (t, J = 7.0 Hz, 2 H); ^{13}C NMR δ 203.0, 155.7, 127.8, 40.5, 31.8, 30.5, 28.0, 22.4, 19.1, 13.7, 13.0.

Anal. Calcd for $C_{11}H_{18}OS$: C, 66.70; H, 9.18. Found: C, 66.55; H, 9.14.

Purification by column chromatography afforded the *Z* isomer, **(*Z*)-15b** (R_f 0.03, petroleum ether/2% ethyl acetate, v/v) in 2% yield: UV max (CH_3OH) 322 (ϵ 13 500); IR 2960 (s), 2920 (s), 2860 (m), 1680 (s), 1545 (s), 1454 (m), 1434 (m), 1239 (m), 1134 (s) cm^{-1}; NMR (90 MHz) δ 0.96 (t, J = 5.0 Hz, 3 H), 1.03–1.62 (m, 4 H), 1.96 (app q, J = 7.0 Hz, 2 H), 2.34 (s, 3 H), 2.13–2.34 (m, 4 H), 2.69 (t, J = 7.0 Hz, 2 H); ^{13}C NMR δ 205.0, 153.2, 128.4, 39.6, 32.7, 30.8, 30.2, 22.7, 20.2, 13.8 (2 C).

Purification also afforded **16** (R_f 0.04) in 9% yield: IR 2920 (s), 1700 (vs), 1590 (vs), 1430 (m), 1280 (s), 1190 (vs) cm^{-1}; NMR (90 MHz) δ 1.93 (app q, J = 7.0 Hz, 2 H), 2.18–2.60 (m, 4 H), 2.44 (s, 3 H), 7.33 (t, J = 3.0 Hz, 1 H); ^{13}C NMR δ 195.4, 136.8, 131.2, 37.4, 27.7, 20.0, 18.0.

2-(2-Methyl-1-methylthiobutylidene)cyclopentanone (15c). A light brown solution of lithium *sec*-butyl(phenylthio)cuprate (4.8 mmol) was generated in 40 mL of THF according to general procedure A. A solution of 800 mg (4.25 mmol) of **1** in 6.0 mL of THF was added via cannula to the cold (−78 °C) cuprate solution. The solution was stirred at −78 °C for 40 min, quenched with 6.0 mL of methanol, warmed to room temperature, and worked up as described above. Purification by column chromatography afforded **(*E*)-15c** in 90% yield (R_f 0.20, petroleum ether/2% ethyl acetate, v/v): UV max (C_2H_5OH) 313 (ϵ 12 500); IR 3015 (m), 2975 (s), 2940 (m), 1700 (s), 1570 (m), 1460 (m), 1380 (w), 1220 (s), 1090 (w), 800 (m), 720 (m) cm^{-1}; NMR (90 MHz) δ 0.83 (t, J = 6.9 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 1.30–1.75 (m, 2 H), 1.90 (p, J = 6.8 Hz, 2 H), 2.20–2.60 (m, 2 H), 2.30 (s, 3 H), 2.40 (t, J = 6.8 Hz, 2 H), 4.17 (sext, J = 6.8 Hz, 1 H); ^{13}C NMR δ 204.8, 161.0, 135.5, 40.5, 37.1, 33.1, 28.1, 19.8, 18.9, 17.5, 12.0; mass spectrum m/e 198.1059 (M^+) (calcd for $C_{11}H_{18}OS$: 198.1078).

The *Z* isomer, **(*Z*)-15c**, was obtained in 2.8% yield (R_f 0.09, petroleum ether/2% ethyl acetate, v/v): UV max (C_2H_5OH) 321 (ϵ 6500); IR ($CHCl_3$) 3015 (s), 2980 (s), 2940 (s), 2880 (m), 1680 (s), 1560 (s), 1230 (m), 1180 (m), 1140 (m), 835 (m) cm^{-1}; NMR (90 MHz) δ 0.87 (t, J = 7.0 Hz, 3 H), 1.17 (d, J = 6.8 Hz, 3 H), 1.58 (q, J = 7.0 Hz, 2 H), 1.94 (app q, J = 6.8 Hz, 2 H), 2.34 (s, 3 H), 2.20–2.54 (m, 2 H), 2.58–2.83 (m, 1 H), 2.76 (t, J = 6.8 Hz, 2 H); ^{13}C NMR δ 203.8, 158.0, 131.3, 42.0, 40.0, 31.2, 27.7, 19.8, 18.8, 18.2, 12.2.

(*E*)-2-[Methylthio(2,2-dimethyl)propylidene]cyclopentanone ((*E*)-(15d)). A beige solution of lithium *tert*-butyl(phenylthio)cuprate (5.70 mmol) in 20 mL of THF was generated according to procedure A. A solution of 536 mg (2.85 mmol) of **1** in 4.0 mL of THF was added via cannula to the cold (−78 °C) cuprate solution. The solution was stirred for 40 min at −60 °C, quenched with 5.0 mL of methanol, warmed to room temperature, and worked up as described in general procedure A. No purification was necessary on the crude product. The product crystallized upon standing to give a 96% yield of **15d** (R_f 0.33, petroleum ether/10% methylene chloride, 10% diethyl ether, v/v): UV max (CH_3OH) 320 (ϵ 8900); IR 2960 (s), 2920 (s), 2850 (m), 1690 (s), 1545 (vs), 1525 (s), 1170 (s), 1070 (m) cm^{-1}; NMR (90 MHz) δ 1.31 (s, 9 H), 1.88 (app q, J = 6.8 Hz, 2 H), 2.24 (s, 3 H), 2.30 (t, J = 6.8 Hz, 2 H), 2.68 (t, J = 6.8 Hz, 2 H); ^{13}C NMR δ 205.5, 166.9, 137.5, 40.6, 39.5, 37.2 (2 C), 29.2 (3 C), 20.6.

Anal. Calcd for $C_{11}H_{18}OS$: C, 66.61; H, 9.15. Found: C, 66.39; H, 9.17.

(*E*)-2-(1-Methylthio-1-cyclopropylmethylene)cyclopentanone (15e). *sec*-Butyllithium (1.70 M, 6.64 mL) was added in one portion via syringe to a cold (−78 °C) solution of cyclopropyl bromide (682 mg, 5.65 mmol) in 10 mL of THF. The resultant light yellow solution became clear upon warming to room temperature, whereupon it was added via cannula to a cold (−78 °C) solution of phenylthiocopper (5.65 mmol) and stirred for 30 min. A solution of **1** (530 mg, 2.82 mmol) in 3.0 mL of THF was added to the cuprate solution which was stirred at −60 °C for 45 min, quenched with 5.0 mL of methanol, and warmed to room temperature. The general work-up procedure was employed. Purification afforded a 64% yield of both **(*E*)-15e** and **(*Z*)-15e**. **(*E*)-15e** (R_f 0.40, petroleum ether/10% ethyl acetate, v/v): UV max (CH_3OH) 317 (ϵ 11 300); IR 2920 (m), 1690 (s), 1560 (s), 1410 (w), 1340 (w), 1230 (m), 1190 (m), 1170 (m), 1140 (m), 960 (w) cm^{-1}; NMR (90 MHz) δ 0.63–1.00 (m, 4 H), 1.89 (p, J = 6.8 Hz, 2 H), 2.22 (s, 3 H), 2.20–2.40 (m, 2 H), 2.66 (t, J = 6.5 Hz, 2 H + CH, 1 H); ^{13}C NMR δ 204.0, 156.0, 135.0, 40.7, 32.6, 19.8, 16.4, 14.0 (2 C), 8.8.

Anal. Calcd for $C_{10}H_{14}OS$: C, 65.91; H, 7.74. Found: C, 65.93; H, 7.76.

(*Z*)-15e (R_f 0.25, petroleum ether/10% ethyl acetate, v/v): UV max (C_2H_5OH) 320 (ϵ 6500); IR 3080 (w), 2960 (s), 2880 (m), 1685 (s), 1547 (s), 1435 (m), 1410 (m), 1345 (m), 1230 (s), 1210 (s), 1140 (s), 960 (m), 865 (m) cm^{-1}; NMR (90 MHz) δ 0.59–1.13 (m, 4 H),

1.41–2.09 (m, 3 H), 2.19–2.47 (m, 2 H), 2.41 (s, 3 H), 2.73 (t, J = 6.8 Hz, 2 H); ^{13}C NMR δ 200.5, 152.7, 132.1, 39.3, 31.1, 20.3, 15.7, 15.2, 8.4.

2-(1-Methylthioethylidene)cyclohexanone (17a). General procedure A was employed, with the exception that 15.4 g (76.2 mmol) of **2** was reacted with 99 mmol of lithium methyl(phenylthio)cuprate in 600 mL of THF. Purification by column chromatography afforded (*E*)-**17a** (R_f 0.40, petroleum ether/5% ethyl acetate, v/v) in a 58% yield: UV max (CH_3OH) 307 (ϵ 18 000); IR 2950 (s), 2870 (m), 1662 (s), 1535 (s), 1430 (m), 1280 (vs), 1140 (m), 960 (m) cm^{-1}; NMR (90 MHz) δ 1.53–1.73 (m, 4 H), 2.35 (s, 3 H), 2.40 (t, J = 1.6 Hz, 3 H), 2.40–2.80 (m, 4 H); ^{13}C NMR δ 199.6, 149.6, 129.7, 41.6, 30.2, 23.6(2C), 18.5, 14.1.

Anal. Calcd for $C_9H_{14}OS$: C, 63.48; H, 8.29. Found: C, 63.36; H, 8.32.

Purification by column chromatography afforded (*Z*)-**17a** (R_f 0.19, petroleum ether/5% ethyl acetate, v/v) in 17% yield: UV max (CH_3OH) 320 (ϵ 12 000); IR 2925 (s), 2860 (m), 1635 (s), 1495 (s), 1430 (m), 1320 (m), 1285 (s), 1170 (m), 960 (w) cm^{-1}; NMR (90 MHz) δ 1.61–1.72 (m, 4 H), 2.14 (t, J = 1.0 Hz, 3 H), 2.29 (s, 3 H), 2.31–2.65 (m, 4 H); ^{13}C NMR δ 198.4, 153.3, 127.1, 39.5, 29.7, 23.5, 22.4, 18.2, 15.8.

2-(1-Methylthiopentylidene)cyclohexanone (17b). General procedure A was employed, with the exception that 3.0 g (14.8 mmol) of **2** was treated with 19.2 mmol of lithium *n*-butyl(phenylthio)cuprate in 75 mL of THF. Purification by column chromatography afforded (*E*)-**17b** (R_f 0.40, petroleum ether/5% ethyl acetate, v/v) in 63% yield: UV max (CH_3OH) 308 (ϵ 14 000); IR 2900 (s), 2840 (m), 1645 (m), 1440 (w), 1420 (m), 1260 (s), 1130 (m), 1110 (m), 1095 (m), 960 (w), 900 (w) cm^{-1}; NMR (90 MHz) δ 0.94 (t, J = 6 Hz, 3 H), 1.21–1.48 (m, 4 H), 1.48–1.82 (m, 4 H), 2.32 (s, 3 H), 2.02–2.88 (m, 6 H); ^{13}C NMR δ 199.2, 153.9, 129.4, 41.7, 31.8, 30.7, 30.3, 23.6, 22.6(2C), 13.7, 13.5.

Anal. Calcd for $C_{12}H_{20}OS$: C, 67.87; H, 9.49. Found: C, 67.86; H, 9.54.

The *Z* isomer, (*Z*)-**17b** (R_f 0.14, petroleum ether/5% ethyl acetate, v/v), was also obtained in 7% yield after purification: UV max (CH_3OH) 318 (ϵ 7900); IR 2920 (s), 2860 (m), 1638 (m), 1490 (m), 1430 (m), 1290 (m), 1270 (m), 1142 (m), 960 (w) cm^{-1}; NMR (90 MHz) δ 0.95 (t, J = 6.1 Hz, 3 H), 1.25–1.56 (m, 4 H), 1.56–1.88 (m, 4 H), 2.26 (s, 3 H), 2.20–2.65 (m, 6 H); ^{13}C NMR δ 198.0, 156.0, 127.0, 40.0, 31.0, 30.5, 29.0, 24.0, 23.0, 22.9, 15.0, 14.0.

2-(2-Methyl-1-methylthiobutylidene)cyclohexanone (17c). General procedure A was employed, with the exception that 3.0 g (14.8 mmol) of **2** was treated with 19.2 mmol of lithium *sec*-butyl(phenylthio)cuprate in 75 mL of THF. Purification by column chromatography afforded (*E*)-**17c** (R_f 0.41, petroleum ether/5% ethyl acetate, v/v) in 62% yield: UV max (C_2H_5OH) 298 (ϵ 4000); IR 2960 (s), 2920 (s), 2850 (m), 1685 (s), 1570 (w), 1450 (m), 1270 (m), 1130 (m) cm^{-1}; NMR (90 MHz) δ 0.77 (t, J = 7.1 Hz, 3 H), 1.09 (d, J = 6.6 Hz, 3 H), 1.16–1.52 (m, 2 H), 1.56–1.94 (m, 4 H), 2.16 (s, 3 H), 2.19–3.00 (m, 5 H); ^{13}C NMR δ 204.9, 150.2, 143.2, 43.9, 40.7, 34.2, 27.5, 26.1, 25.7, 19.5, 18.7, 11.9; mass spectrum m/e 212.1247 (M^+) (calcd for $C_{12}H_{20}OS$: 212.1235).

The *Z* isomer could not be isolated pure.

(*E*)-2-[Methylthio(2,2-dimethyl)propylidene]cyclohexanone (17d). General procedure A was employed, with the exception that 3.0 g (14.8 mmol) of **2** was treated with 19.2 mmol of lithium *tert*-butyl(phenylthio)cuprate in 75 mL of THF. Purification by column chromatography afforded **17d** in a 96% yield (R_f 0.24, petroleum ether/2% ethyl acetate, v/v): UV max (CH_3OH) 285 (ϵ 9700); IR 2930 (s), 2850 (m), 1683 (s), 1480 (w), 1430 (w), 1350 (w), 1300 (w), 1260 (w), 1220 (w), 1130 (m), 1110 (m), 1060 (m), 960 (w), 925 (w) cm^{-1}; NMR (90 MHz) δ 1.17 (s, 9 H), 1.59–2.00 (m, 4 H), 2.14 (s, 3 H), 2.59 (t, J = 6.0 Hz, 2 H), 2.88 (t, J = 6.0 Hz, 2 H); ^{13}C NMR δ 210.7, 150.0, 128.0, 45.0, 40.3, 38.7, 29.9 (3 C), 28.5, 26.8, 20.8; mass spectrum m/e 212.1234 (M^+) (calcd for $C_{12}H_{20}OS$: 212.1235).

Anal. Calcd for $C_{12}H_{20}OS$: C, 67.87; H, 9.49. Found: C, 68.02; H, 9.50.

The other isomer could not be isolated by chromatography.

3-Methyl-6-(1-methylthioethylidene)cyclohex-2-enone (18a). Purification by column chromatography afforded the *E* isomer, (*E*)-**18a** (R_f 0.36, petroleum ether/20% ethyl acetate, v/v) in 79% yield: IR (CH_2Cl_2) 2950 (s), 2930 (s), 2870 (s), 1640 (s), 1620 (m), 1460 (m), 1420 (m), 1380 (m), 1320 (m), 1190 (m), 900 (m), 860 (m); NMR (90 MHz) δ 1.92 (s, 3 H), 2.35 (s, 3 H), 2.07–2.47 (m, 2 H), 2.46 (s, 3 H), 2.80 (t, J = 6.0 Hz, 2 H), 5.88 (br s, 1 H); ^{13}C NMR δ 187.8, 158.9, 147.2, 128.6, 127.1, 30.7, 28.7, 23.6, 18.3, 13.9; mass spectrum m/e 182.0764 (M^+) (calcd for $C_{10}H_{14}OS$ 182.0765).

3-Methyl-6-(1-methylthio-5-methyl-4-hexenylidiene)cyclohex-2-enone (18b). Purification by column chromatography afforded the *E* isomer, (*E*)-**18b** (R_f 0.40, petroleum ether/10% ethyl acetate, v/v) in 73% yield: UV max (CH_3OH) 331 (ϵ 9000), 246 (ϵ 11 000); IR 2970 (m), 2910 (s), 1545 (s), 1430 (m), 1285 (s), 1220 (s), 970 (w) cm^{-1}; NMR (90 MHz) δ 1.66 (s, 6 H), 1.92 (s, 3 H), 2.32 (s, 3 H), 2.20–2.40 (m, 4 H), 2.68–2.95 (m, 4 H), 5.19 (t, J = 7.1 Hz, 1 H), 5.85 (br s, 1 H); ^{13}C NMR δ 187.4, 158.2, 150.9, 132.0, 128.7, 127.8, 123.3, 30.8, 30.7, 29.1, 28.1, 25.5, 23.5, 17.5, 13.8.

The *Z* isomer, (*Z*)-**18b** (R_f 0.13, petroleum ether/10% ethyl acetate, v/v), was obtained in 2% yield: UV max (CH_3OH) 339 (ϵ 6700), 245 (8600); IR 2960 (s), 2905 (s), 1330 (m), 1300 (s), 1225 (s), 1190 (s), 970 (w), 880 (w) cm^{-1}; NMR (90 MHz) δ 1.62 (s, 3 H), 1.69 (s, 3 H), 1.93 (s, 3 H), 2.29 (s, 3 H), 2.02–2.85 (m, 8 H), 5.20 (t, J = 7.1 Hz, 1 H), 5.95 (br s, 1 H); ^{13}C NMR δ 188.0, 157.8, 151.7, 133.0, 128.2, 124.9, 122.3, 31.1, 30.8, 28.0 (2 C), 25.6, 23.6, 17.6, 15.1.

3-(1-Methylethoxy)-6-(1-methylthioethylidene)cyclohex-2-enone (19). General procedure A was employed and the reaction was quenched at −78 °C with 2.0 mL of methanol. Purification by column chromatography afforded (*E*)-**19** (R_f 0.40, petroleum ether/18% ethyl acetate, v/v) in 78% yield: UV max (CH_3OH), 321 (ϵ 15 000), 266 (10 500), 258 (10 100); IR ($CHCl_3$) 3000 (s), 2940 (m), 1620 (vs), 1570 (s), 1370 (s), 1290 (s), 1190 (s), 1110 (s) cm^{-1}; NMR (90 MHz) δ 1.18 (d, J = 6.1 Hz, 6 H), 2.25 (s, 3 H), 2.36 (t, J = 1.0 Hz, 3 H), 2.73 (t, J = 6.0 Hz, 4 H), 4.32 (sept, J = 6.1 Hz, 1 H), 5.23 (s, 1 H); ^{13}C NMR δ 188.8, 174.8, 145.2, 127.3, 104.6, 70.7, 29.4, 27.7, 21.4 (2 C), 18.3, 14.0.

Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.69; H, 8.02. Found: C, 63.68; H, 8.06.

Purification by column chromatography afforded the *Z* isomer, (*Z*)-**19** (R_f 0.20, petroleum ether/18% ethyl acetate, v/v), in 6% yield: UV max (CH_3OH), 332 (ϵ 12 500), 260 (9600), 254 (8800), 248 (7500), 241 (6200); IR ($CHCl_3$) 3000 (m), 2940 (m), 2860 (m), 1610 (s), 1550 (m), 1385 (s), 1330 (s), 1310 (s), 1195 (vs), 1110 (s), 995 (m), 925 (w), 845 (m) cm^{-1}: NMR (90 MHz) δ 1.25 (d, J = 6.1 Hz, 6 H), 2.14 (s, 3 H), 2.25 (s, 3 H), 2.34 (t, J = 6.8 Hz, 2 H), 2.72 (t, J = 6.4 Hz, 2 H), 4.40 (sept, J = 6.1 Hz, 1 H), 5.36 (s, 1 H); ^{13}C NMR δ 188.6, 173.1, 146.2, 124.7, 103.9, 70.7, 29.4, 26.9, 21.5 (2 C), 18.2, 15.4.

4-Methylthiopent-3-en-2-one (20a). General procedure A was employed, with the exception that 3.0 g (18.5 mmol) of **5** was treated with 20.3 mmol of lithium methyl(phenylthio)cuprate in 150 mL of THF. Purification by column chromatography afforded an 87% yield of the *E* isomer, (*E*)-**20a** (R_f 0.40, petroleum ether/10% ethyl acetate, v/v): UV max (CH_3OH) 294 (ϵ 8100); IR 2960 (m), 2908 (m), 1666 (s), 1550 (s), 1420 (s), 1370 (s), 1350 (s), 1190 (s), 1110 (s), 1000 (m), 960 (m) cm^{-1}; NMR (90 MHz) δ 2.17 (s, 3 H), 2.31 (s, 3 H), 2.37 (d, J = 0.74 Hz, 3 H), 5.89 (s, 1 H); ^{13}C NMR δ 193.2, 162.9, 112.6, 30.0, 16.8, 14.4.

Purification by column chromatography afforded a 5% yield of the *Z* isomer, (*Z*)-**20a** (R_f 0.10, petroleum ether/10% ethyl acetate, v/v): UV max (CH_3OH) 307 (ϵ 6000); IR 3000 (s), 2920 (w), 1652 (s), 1540 (s), 1440 (m), 1425 (s), 1190 (s), 1010 (m), 955 (m) cm^{-1}; NMR (90 MHz) δ 2.16 (s, 3 H), 2.22 (d, J = 0.9 Hz, 3 H), 2.34 (s, 3 H), 6.30 (s, 1 H); ^{13}C NMR δ 195.5, 159.0, 120.1, 29.9, 23.4, 14.0.

4-Methylthiooct-3-en-2-one (20b). General procedure A was employed, with the exception that 3.0 g (18.5 mmol) of **5** was treated with 20.3 mmol of lithium *n*-butyl(phenylthio)cuprate in 150 mL of THF. Purification by column chromatography afforded the *E* isomer, (*E*)-**20b** (R_f 0.37, petroleum ether/10% ethyl acetate, v/v), in an 80% yield: UV max (CH_3OH) 294 (ϵ 6000); IR 2900 (s), 2827 (s), 1660 (s), 1540 (s), 1415 (s), 1340 (s), 1165 (s), 950 (m) cm^{-1}; NMR (90 MHz) δ 0.92 (t, J = 6.4 Hz, 3 H), 1.20–1.67 (m, 4 H), 2.15 (s, 3 H), 2.30 (s, 3 H), 2.80 (t, J = 7.5 Hz, 2 H), 5.82 (s, 1 H); ^{13}C NMR δ 192.9, 165.0, 114.8, 33.9, 31.6, 31.1, 22.3, 14.4, 13.3.

Anal. Calcd for $C_9H_{16}OS$: C, 62.74; H, 9.36. Found: C, 62.86; H, 9.38.

Purification by column chromatography afforded the *Z* isomer, (*Z*)-**20b** (R_f 0.10, petroleum ether/10% ethyl acetate, v/v) in an 8% yield: UV max (CH_3OH) 304 (ϵ 4600); IR 2950 (s), 2860 (m), 1651 (s), 1525 (s), 1425 (s), 1350 (s), 1190 (s), 960 (m) cm^{-1}; NMR (90 MHz) δ 0.95 (t, J = 7.0 Hz, 3 H), 1.25–1.60 (m, 4 H), 2.17 (s, 3 H), 2.32 (s, 3 H), 2.40 (t, J = 7.4 Hz, 2 H), 6.26 (s, 1 H); ^{13}C NMR δ 195.8, 163.0, 119.6, 35.6, 31.8, 30.3, 22.2, 13.8 (2 C).

5-Methyl-4-methylthiohept-3-en-2-one (20c). General procedure A was followed, with the exception that 4.03 g (24.9 mmol) of **5** was treated with 46.9 mmol (1.88 equiv) of lithium *sec*-butyl(phenylthiocuprate) in 300 mL of THF. After 1 h the reaction mixture was allowed to warm to −30 °C over a period of 20 min. The reaction was quenched after 45 min at −30 °C. Purification by column chromatography afforded the *E* isomer, (*E*)-**20c** (R_f 0.14, petroleum ether/2% ethyl acetate, v/v), in 79% yield: UV max (CH_3OH) 299 (ϵ 16 000); IR 2960 (m), 2920 (m), 2860 (w), 1670 (s), 1543 (s), 1450 (w), 1420 (w), 1353 (m), 1185 (s), 1140 (m), 973 (w) cm^{-1}; NMR (90 MHz) δ 0.81 (t, J = 7.0 Hz, 3 H), 1.07 (d, J = 6.85 Hz, 3 H), 1.25–1.60 (m, 2 H), 2.12 (s, 3 H), 2.19 (s, 3 H), 4.09 (sext, J = 7.0 Hz, 1 H), 5.74 (s, 1 H); ^{13}C NMR δ 193.5, 170.8, 115.2, 44.5, 37.0, 28.5, 19.2, 13.9, 11.2; mass spectrum m/e 172.0916

(M^+) (calcd for $C_9H_{16}OS$: 172.0922).

Purification by column chromatography afforded the *Z* isomer, (*Z*)-**20c** (R_f 0.05, petroleum ether/2% ethyl acetate, v/v) in 7.5% yield: UV max (CH_3OH) 309 (ϵ 9900); IR 3040 (s), 2995 (s), 2940 (s), 2895 (m), 1680 (s), 1540 (vs), 1440 (s), 1370 (s), 1205 (s), 1065 (m) cm^{-1}; NMR (90 MHz) δ 0.94 (t, J = 7.1 Hz, 3 H), 1.17 (d, J = 6.8 Hz, 3 H), 1.35–1.75 (m, 2 H), 2.20 (s, 3 H), 2.31 (s, 3 H), 3.65 (sext, J = 6.9 Hz, 1 H), 6.24 (s, 1 H); ^{13}C NMR δ 195.6, 167.9, 116.9, 38.3, 30.4, 29.7, 20.3, 13.9, 11.4.

(*Z*)-5,5-Dimethyl-4-methylthiohex-3-en-2-one (20d). General procedure A was followed, with the exception that 444 mg (2.74 mmol) of **5** was treated with 7.89 mmol (2.88 equiv) of lithium *tert*-butyl(phenylthio)cuprate in 50 mL of THF, and the reaction mixture was warmed to −60 °C over a period of 60 min. Purification by TLC (silica gel, 1000 μ) afforded **20d** (R_f 0.19, petroleum ether/2% ethyl acetate, v/v) in 14% yield: IR ($CHCl_3$) 2960 (s), 1665 (s), 1545 (s), 1365 (s), 1335 (m), 1285 (s), 895 (w) cm^{-1}; NMR (90 MHz) δ 1.24 (s, 9 H), 2.38 (s, 3 H), 2.33 (s, 3 H), 6.43 (s, 1 H); ^{13}C NMR δ 196.8, 166.6, 123.0, 39.8, 31.1, 29.0 (3 C), 20.2; mass spectrum m/e 172.0924 (M^+) (calcd for $C_9H_{16}OS$: 172.0922).

Purification also afforded **21** in 65% yield: NMR (90 MHz) δ 2.23 (s, 3 H), 2.37 (s, 3 H), 6.03 (d, J = 15 Hz, 1 H), 7.71 (d, J = 15 Hz, 1 H).

In a different experiment (entry 21) general procedure A was followed, except that 2.50 equiv of lithium *tert*-butyl(phenylthio)cuprate was used and THF was replaced by ether as the solvent. Purification afforded an 89% yield of **20d** without any detection of the reduction product **21**.

2-Methyl-5-methylthiohex-4-en-3-one (22a). General procedure A was employed, with the exception that the reaction mixture was stirred at −50 °C for 1.5 h and then quenched with 2.0 mL of methanol. Purification by column chromatography (R_f 0.44, petroleum ether/5% ethyl acetate v/v) afforded the *E* isomer, (*E*)-**22a**, in 82% yield: UV max (CH_3OH) 294 (ϵ 18 000); IR 2960 (s), 2920 (s), 2880 (m), 1670 (s), 1560 (s), 1455 (m), 1420 (m), 1370 (s), 1350 (m), 1060 (s), 950 (w), 890 (w) cm^{-1}; NMR (90 MHz) δ 1.09 (d, J = 6.9 Hz, 6 H), 2.31 (s, 3 H), 2.40 (d, J = 0.97 Hz, 3 H), 2.67 (sept, J = 6.9 Hz, 1 H), 5.91 (s, 1 H); ^{13}C NMR δ 200.2, 159.6, 114.2, 41.2, 21.2, 18.3 (2 C), 14.7.

The isomer (*Z*)-**22a** (R_f 0.18, petroleum ether/5% ethyl acetate v/v) was also obtained in 5% yield after purification: UV max (CH_3OH) 308 (ϵ 6700): IR 2960 (s), 2920 (s), 1647 (s), 1530 (vs), 1440 (m), 1180 (m), 1130 (s), 1080 (m) cm^{-1}; NMR (90 MHz) δ 1.09 (d, J = 6.9 Hz, 6 H), 2.25 (d, J = 1.2 Hz, 3 H), 2.32 (s, 3 H), 2.61 (sept, J = 6.5 Hz, 1 H), 6.37 (m, 1 H); ^{13}C NMR δ 190.3, 159.5, 118.7, 40.4, 23.6, 18.6 (2 C), 14.3.

Purification also afforded **23** (R_f 0.19) in 2.5% yield: IR ($CDCl_3$) 2960 (s), 2920 (s), 2860 (m), 1650 (s), 1545 (vs), 1460 (m), 1300 (m), 1070 (s), 945 (m) cm^{-1}; NMR (90 MHz) δ 1.11 (d, J = 6.8 Hz, 6 H), 2.36 (s, 3 H), 2.77 (sept, J = 6.8 Hz, 1 H), 6.11 (d, J = 15 Hz, 1 H), 7.75 (d, J = 15 Hz, 1 H); ^{13}C NMR δ 199.8, 146.1, 120.1, 38.8, 18.4 (2 C), 14.3.

2-Methyl-5-methylthionon-4-en-3-one (22b). General procedure A was employed, with the exception that 6.01 g (31.6 mmol) of **6** was treated with 39.5 mmol of lithium *n*-butyl(phenylthio)cuprate in 325 mL of THF. Purification by column chromatography afforded a 64% yield of the *E* isomer, (*E*)-**22b** (R_f 0.57, petroleum ether/10% ethyl acetate, v/v): UV max (CH_3OH) 295 (ϵ 10 900); IR 2940 (s), 2900 (s), 2840 (m), 1663 (s), 1543 (s), 1450 (m), 1420 (m), 1370 (m), 1345 (m), 1105 (m), 1060 (s) cm^{-1}; NMR (90 MHz) δ 0.91 (t, J = 7.0 Hz, 3 H), 1.09 (d, J = 7.0 Hz, 6 H), 1.25–1.75 (m, 4 H), 2.27 (s, 3 H), 2.58 (sept, J = 7.0 Hz, 1 H), 2.73 (t, J = 7.0 Hz, 2 H), 5.87 (s, 1 H); ^{13}C NMR δ 203.2, 164.6, 118.8, 41.5, 34.4, 31.7, 22.4, 18.4 (2 C), 14.8, 14.0; mass spectrum m/e 200.1236 (M^+) (calcd for $C_{11}H_{20}OS$: 200.1235).

Purification by column chromatography afforded a 5% yield of the *Z* isomer, (*Z*)-**22b** (R_f 0.25, petroleum ether/10% ethyl acetate, v/v): UV max (CH_3OH) 303 (ϵ 7800); IR 2940 (s), 2910 (s), 2833 (m), 1655 (s), 1525 (s), 1450 (m), 1420 (s), 1170 (m), 1120 (s), 1090 (s) cm^{-1}; NMR (90 MHz) δ 0.98 (t, J = 7.0 Hz, 3 H), 1.13 (d, 6.8 Hz, 6 H), 1.25–1.75 (m, 4 H), 2.31 (s, 3 H), 2.09–2.80 (m, 3 H), 6.31 (s, 1 H); ^{13}C NMR δ 201.8, 163.2, 117.6, 40.2, 35.5, 31.5, 21.9, 18.3(2C), 13.5, 13.4.

2,6-Dimethyl-5-methylthiooct-4-en-3-one (22c). General procedure A was employed, with the exception that 1.41 g (7.4 mmol) of **6** was treated with 14.8 mmol (2.00 equiv) of lithium *sec*-butyl(phenylthio)cuprate in 75 mL of THF and the solution was allowed to warm to −30 °C over a 1-h period. Purification by column chromatography afforded the *E* isomer, (*E*)-**22c** (R_f 0.60, petroleum ether/10% ethyl acetate, v/v) in a 91% yield: UV max (CH_3OH) 297 (ϵ 16 000); IR 2940 (s), 2900 (m), 2840 (m), 1660 (m), 1535 (s), 1445 (m), 1350 (m), 1105 (w), 1054 (s) cm^{-1}; NMR (90 MHz) δ 0.87 (t, J = 7.2 Hz, 3 H), 1.10 (d, J = 6.8 Hz, 6 H), 1.14 (d, J = 6.8 Hz, 3 H), 1.25–1.65 (m, 2 H), 2.3 (s, 3 H), 2.66 (sept, J = 6.8 Hz, 1 H), 4.12 (sext, J = 7.1 Hz, 1 H), 5.80 (s, 1 H); ^{13}C NMR δ 200.1, 170.8, 114.5, 41.5, 37.3, 28.8, 19.6, 18.5, 13.9, 11.7(2C).

The *Z* isomer, (*Z*)-**22c** (R_f 0.24, petroleum ether/10% ethyl acetate, v/v), was also obtained by column chromatography in 6% yield: UV max (CH_3OH) 321 (ϵ 6500); IR 3020 (m), 2980 (s), 2940 (m), 2880 (m), 1660 (s), 1540 (vs), 1470 (m), 1385 (m), 1135 (m), 1075 (m) cm^{-1}; NMR (90 MHz) δ 0.94 (t, J = 7.0 Hz, 3 H), 1.11 (d, J = 6.8 Hz, 6 H), 1.19 (d, J = 6.7 Hz, 3 H), 1.53 (p, J = 7.0 Hz, 2 H), 2.30 (s, 3 H), 2.40–2.80 (m, 2 H), 6.27 (s, 1 H); ^{13}C NMR δ 202.3, 168.3, 115.5, 40.8, 38.6, 30.0, 20.6, 18.6, 14.2, 11.6(2C).

2,6,6-Trimethyl-5-methylthiohept-4-en-3-one (22d). General procedure A was followed, with the exception that the reaction mixture was stirred at −78 °C for 1 h, warmed to −55 °C over a 30-min period, and then quenched with 2.0 mL of methanol. Purification yielded **16** in 53%, in which both isomers were present and inseparable by chromatography (R_f 0.55, petroleum ether/10% diethyl ether, v/v). By NMR, the ratio of *E*/*Z* isomers was 1:4. *Z* isomer: UV max (CH_3OH) 305 (ϵ 8600); IR 2960 (s), 1673 (s), 1540 (s), 1455 (m), 1360 (m), 1161 (s) cm^{-1}; NMR (90 MHz) δ 1.04 (d, J = 7.0 Hz, 6 H), 1.18 (s, 9 H), 2.17 (s, 3 H), 2.65 (sept, J = 7.0 Hz, 1 H), 6.39 (s, 1 H); ^{13}C NMR δ 203.3, 167.6, 121.5, 41.6, 40.3, 29.4, 28.8, 18.5. *E* isomer: NMR (90 MHz) δ 1.27 (s, 9 H), 5.60 (s, 1 H).

4-Methyl-5-methylthiohex-4-en-3-one (24a). General procedure A was followed, with the exception that 2.83 g (14.9 mmol) of **7** was treated with 23.8 mmol of lithium methyl(phenylthio)cuprate in 150 mL of THF and the reaction was allowed to warm to −30 °C. Purification afforded the *E* isomer, (*E*)-**24a** (R_f 0.39, petroleum ether/2% ethyl acetate, v/v), in 88% yield: UV max (CH_3OH) 297 (ϵ 8500); IR 2980 (s), 2905 (s), 2860 (m), 1670 (s), 1550 (s), 1430 (s), 1370 (s), 1340 (s), 1230 (s), 1020 (s), 970 (m), 907 (s) cm^{-1}; NMR (90 MHz) δ 0.95 (t, J = 7.3 Hz, 3 H), 1.88 (q, J = 1.5 Hz, 3 H), 2.10 (q, J = 1.5 Hz, 3 H), 2.21 (s, 3 H), 2.42 (q, J = 7.3 Hz, 2 H); ^{13}C NMR δ 203.3, 142.4, 129.6, 34.2, 18.2, 16.3, 13.7, 7.9.

Anal. Calcd for $C_8H_{14}OS$: C, 60.71; H, 8.92. Found C: 60.81; H, 8.94.

The *Z* isomer, (*Z*)-**24a** (R_f 0.11, petroleum ether/2% ethyl acetate, v/v), was also obtained in 6.5% yield after purification: UV max (C_2H_5OH) 304 (ϵ 5400); IR ($CHCl_3$) 2995 (s), 2940 (s), 2880 (m), 1700 (s), 1660 (s), 1530 (m), 1460 (m), 1435 (m), 1380 (m), 1150 (m), 1095 (m), 1030 (m), 985 (m) cm^{-1}; NMR (90 MHz) δ 1.06 (t, J = 7.1 Hz, 3 H), 1.93 (s, 3 H), 2.07 (s, 3 H), 2.21 (s, 3 H), 2.51 (q, J = 7.1, 2 H); ^{13}C NMR δ 203.7, 144.1, 133.4, 34.3, 18.5, 16.5, 15.7, 8.0.

4-Methyl-5-methylthionon-4-en-3-one (24b). General procedure A was followed, with the exception that 915 mg (4.8 mmol) of **7** was treated with 6.33 mmol of lithium *n*-butyl(phenylthio)cuprate in 55 mL of THF and the reaction mixture was stirred at −78 °C for 30 min, warmed to −60 °C over a 30-min period, and then quenched with 5.0 mL of methanol. Purification by column chromatography afforded the *E* isomer, (*E*)-**24b** (R_f 0.36 petroleum ether/2% ethyl acetate, v/v), in 45% yield: UV max (CH_3OH) 296 (ϵ 5700); IR 2960 (s), 1667 (s), 1540 (s), 1450 (s), 1425 (s), 1370 (m), 1331 (m), 1230 (s), 970 (s) cm^{-1}; NMR (90 MHz) δ 0.81–1.00 (m, 3 H), 1.07 (t, J = 7.3 Hz, 3 H), 1.16–1.69 (m, 4 H), 1.99 (s, 3 H), 2.28 (s, 3 H), 2.25–2.69 (m, 4 H); ^{13}C NMR δ 203.4, 159.0, 146.1, 34.3, 31.6, 30.7, 22.2, 16.5, 13.5 (2 C), 7.9; mass spectrum m/e 200.1250 (M^+) (calcd for $C_{11}H_{20}OS$: 200.1235).

Purification by column chromatography afforded a 2% yield of the *Z* isomer, (*Z*)-**24b** (R_f 0.21, petroleum ether/2% ethyl acetate, v/v): UV max (CH_3OH) 310 (ϵ 2400); IR ($CHCl_3$) 2960 (s), 2920 (s), 2860 (m), 1688 (s), 1510 (w), 1455 (m), 1430 (m), 1370 (m), 1335 (m), 1225 (w), 1135 (w), 950 (w) cm^{-1}; NMR (90 MHz) δ 0.95 (t, J = 7.0 Hz, 3 H), 1.11 (t, J = 7.8 Hz, 3 H), 1.16–1.69 (m, 4 H), 1.95 (s, 3 H), 2.20 (s, 3 H), 2.41 (t, J = 7.8 Hz, 2 H), 2.61 (q, J = 7.8 Hz, 2 H); ^{13}C NMR δ 204.9, 143.0, 133.2, 34.3, 30.7, 30.4, 22.2, 16.0, 15.5, 13.6, 7.9.

2-[1-Methylthioethylidene]-γ-butyrolactone (26). General procedure A was followed, with the exception that 1.5 equiv of methyl (phenylthio)cuprate was used and the reaction mixture was warmed over 60 min from −78 to 0 °C. Purification by column chromatography afforded the reduction product **26** (R_f 0.23, petroleum ether/20% ethyl acetate, v/v) in 60% yield: IR 3000 (m), 2950 (s), 2870 (w), 1770 (s), 1635 (s), 1450 (m), 1390 (s), 1310 (s), 1200 (s), 1070 (m), 1040 (s), 870 (s), 740 (m) cm^{-1}; NMR (60 MHz, CCl_4) δ 2.50–2.93 (m, 2 H), 2.55 (s, 3 H), 4.33 (t, J = 6.5 Hz, 2 H), 7.31 (t, J = 3.0 Hz, 1 H); ^{13}C NMR δ 169.5, 141.5, 119.4, 65.1, 26.2, 17.4.

Anal. Calcd for $C_6H_8O_2S$: C, 49.98; H, 5.59. Found: C, 49.79; H, 5.62.

Methyl 3-Methylthio-2-butenoate (27a). Methyllithium (2.54 mmol) was added to a cold (0 °C) suspension of CuI (243 mg, 1.27 mmol) and 10.0 mL of THF in a three-neck flask fitted with a nitrogen inlet, stopper, and septum. The solution was stirred for 1 h and chilled to −78 °C; ketene dithioacetal **10** (178.0 mg, 1.00 mmol) in 4.0 mL of THF was added in one portion via syringe. The reaction mixture was monitored

by TLC, quenched at −78 °C with 2.0 mL of methanol, and warmed to room temperature. The reaction mixture was poured into a mixture of 50 mL of ether and NH_4Cl (satd) and stirred for 15 min. The copper salts were filtered off; the filtrate was extracted with 2 × 25 mL of Et_2O, washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford the crude products.

Purification by medium-pressure liquid chromatography afforded **27a**[46] (R_f 0.51 petroleum ether/5% ethyl acetate, v/v) in 13% yield: UV max (CH_3OH) 273 (ε 7300); IR ($CHCl_3$) 3030 (vw), 2970 (w), 2940 (w), 2900 (w), 2840 (vw), 1710 (s), 1605 (s), 1440 (m), 1355 (m), 1270 (vs), 1205 (s), 1110 (m) cm^{-1}; NMR (90 MHz) δ 2.29 (s, 3 H), 2.40 (d, J = 0.98 Hz, 3 H), 3.69 (s, 3 H), 5.44 (m, 1 H); ^{13}C NMR δ 165.6, 160.0, 107.7, 50.8, 20.8, 15.1.

The reduction product **28** (R_f 0.39, petroleum ether/5% ethyl acetate, v/v) was obtained in 61% yield: IR ($CHCl_3$) 3030 (w), 3010 (w), 2950 (m), 2920 (m) 2850 (w), 1710 (s), 1590 (vs), 1445 (s), 1330 (s), 1310 (s), 1290 (s), 1275 (s), 1200 (m), 1180 (s) cm^{-1}; NMR (90 MHz) δ 2.33 (s, 3 H), 3.73 (s, 3 H), 5.66 (d, J = 14.9 Hz, 1 H), 7.75 (d, J = 14.9 Hz, 1 H); ^{13}C NMR δ 165.6, 147.3, 112.8, 51.4, 14.4.

Starting material was recovered in an 8% yield.

Methyl 3-Methylthio-2-heptenoate (27b). To 0.1423 g of CuBr (0.99 mmol) were sequentially added 2.5 mL of dimethyl sulfide and 10 mL of ether. This mixture was cooled to −50 °C and 0.44 mL of *n*-butyl lithium was added (2.27 M, 0.99 mmol). The mixture was stirred for 45 min. The brown mixture was then chilled to −78 °C and **10** was added via syringe (10 mL of ether). After 1 h, the mixture was warmed to −20 °C and quenched with NH_4Cl (satd). The resulting suspension was filtered through Celite and extracted with ether (3 × 25 mL). The ether extracts were dried ($MgSO_4$) and concentrated in vacuo to give 0.0987 g of crude material. Purification by TLC (SiO_2, 1000 μ) afforded 0.0177 g (18%) of **27b** (R_f 0.47, petroleum ether/2% ethyl acetate, v/v): IR ($CDCl_3$) 2950 (s), 2920 (s), 2810 (s), 1700 (s), 1675 (s), 1590 (m), 1450 (m), 1430 (m), 1350 (m), 1280 (m), 930 (m) cm^{-1}; NMR (90 MHz) δ 0.94 (t, J = 7.0 Hz, 3 H), 1.11–1.79 (m, 4 H), 2.28 (s, 3 H), 2.86 (t, J = 7.9 Hz, 2 H), 3.75 (s, 3 H), 5.41 (s, 1 H); ^{13}C NMR δ 165.8, 165.1, 107.0, 50.8, 34.0, 32.2, 27.7, 15.0, 13.8.

Purification also gave 0.589 g of **10** (67%).

Methyl 4,4-Dimethyl-3-methylthio-2-pentenoate (27c). To a stirred solution of 2.0 mL of dimethyl sulfide in 15 mL of diethyl ether and 0.1409 g of CuBr (0.98 mmol), maintained at −78 °C, was added via syringe 0.60 mL (0.98 mmol) of *tert*-butyllithium. After the mixture was stirred for 1 h, **10** was added via syringe (5.0 mL ether). The reaction mixture was allowed to warm to 20 °C and stirring was continued overnight. The mixture was quenched with NH_4Cl (satd), filtered through Celite, and extracted with ether (3 × 25 mL). The ethereal extracts were dried over $MgSO_4$ and concentrated in vacuo to give the crude product. Purification by TLC (SiO_2, 1000 μ, petroleum ether/2% ethyl acetate, v/v) afforded 0.0220 g (24%) of **27c** (R_f 0.39): IR ($CDCl_3$) 2960 (m), 1710 (s), 1567 (s), 1430 (m), 1361 (m), 1270 (vs), 940 (m), 880 (m) cm^{-1}; NMR (90 MHz) δ 1.38 (s, 9 H), 2.20 (s, 3 H), 3.68 (s, 3 H), 5.29 (s, 1 H); ^{13}C NMR δ 171.0, 165.1, 107.6, 50.9, 38.8, 28.8 (3 C), 16.1; mass spectrum m/e 188.0860 (M^+) (calcd for $C_9H_{16}O_2S$: 188.0871).

Purification also afforded **28** in 15% yield and **10** was recovered in 46% yield.

In a separate experiment (entry 34) general procedure A was employed with 57 mg (0.32 mmol) of **10** and 1.60 mmol (5.0 equiv) of *tert*-butyl(phenylthio)cuprate in 50 mL of Et_2O at −78 °C. The reaction mixture was warmed to room temperature over 30 min, stirred for 5 h, and then quenched with 5 mL of saturated aqueous NH_4Cl. Purification afforded a 90% yield of **27c** with no detection of **28**.

Methyl 3-Methylthio-2-phenylthio-2-butenoate (29a). General procedure A was followed, with the exception that 520 mg (1.82 mmol) of **11** was treated with 1.99 mmol of lithium methyl(phenylthio)cuprate in 10 mL of THF. Purification by column chromatography afforded the *Z* isomer, (*Z*)-**29a**, in 65% yield (R_f 0.25, petroleum ether/5% ethyl acetate, v/v): UV max (CH_3OH) 286 (ε 15 500), 254 (14 500); IR ($CHCl_3$) 3070 (w), 3050 (w), 2980 (s), 2950 (m), 2930 (m), 2820 (w), 1715 (br, s), 1685 (s), 1590 (s), 1530 (br, s), 1480 (s), 1440 (s), 1375 (m), 1265 (vs), 1235 (vs), 1160 (m), 1085 (m), 1050 (m), 1030 (s), 970 (m), 950 (w) cm^{-1}; NMR (90 MHz) δ 2.29 (s, 3 H), 2.52 (s, 3 H), 3.57 (s, 3 H), 7.10–7.35 (m, 5 H); ^{13}C NMR δ 165.2, 164.5, 135.4, 128.6 (2 C), 126.9 (2C), 125.5, 114.1, 51.7, 19.8, 15.2; mass spectrum m/e 254.0425 (M^+) (calcd for $C_{12}H_{14}O_2S_2$: 254.0435).

The *E* isomer, (*E*)-**29a** (R_f 0.35, petroleum ether/5% ethyl acetate, v/v), was obtained in 21% yield: mp 60–61 °C; UV max (CH_3OH) 291 (ε 10 100), 250 (10 500); IR ($CHCl_3$) 3050 (vw), 3035 (w), 2970 (w), 2930 (m), 2900 (m), 1710 (s), 1690 (s), 1580 (m), 1550 (s), 1475 (s), 1440 (s), 1420 (m), 1330 (m), 1320 (w), 1260 (vs), 1235 (vs), 1190 (m), 1155 (s), 1050 (s), 1020 (m), 965 (w) cm^{-1}; NMR (90 MHz) δ 2.41 (s, 3 H), 2.54 (s, 3 H), 3.66 (s, 3 H), 7.06–7.35 (m, 5 H); ^{13}C NMR δ 166.4, 164.6, 137.0, 128.7 (2 C), 126.2(2C), 125.2, 113.5, 51.9, 22.0, 16.3.

The disubstituted product, **30a**, was obtained in 11% yield (R_f 0.56, petroleum ether/5% ethyl acetate, v/v): IR ($CHCl_3$) 3020 (m), 2960 (m), 2920 (w), 1715 (vs), 1585 (m), 1485 (m), 1445 (m), 1260 (s), 1230 (s), 1100 (m), 1030 (m) cm^{-1}; NMR (90 MHz) δ 2.13 (s, 6 H), 3.60 (s, 3 H), 7.19–7.55 (m, 5 H); ^{13}C NMR δ 167.4, 153.5, 135.8, 128.7 (2 C), 127.8(2C), 125.8, 120.4, 51.9, 23.9, 23.4.

Methyl 3-Methylthio-2-phenylthio-2-heptenoate (29b). General procedure A was followed, with the exception that 385 mg (1.35 mmol) of **11** was treated with 1.88 mmol of lithium *n*-butyl phenylthiocuprate in 10 mL of THF and the reaction mixture was warmed for 45 min from −78 to −25 °C. Purification by column chromatography afforded the *E* isomer, (*E*)-**28b**, in 75% yield (R_f 0.40, petroleum ether/5% ethyl acetate, v/v): UV max (C_2H_5OH) 285 (ε 11 000), 250 (10 100); IR ($CHCl_3$) 3020 (m), 2970 (m), 2940 (m), 2880 (w), 1710 (s), 1585 (w), 1520 (m), 1485 (m), 1440 (m), 1410 (s), 1240 (s), 1030 (m), 1020 (m) cm^{-1}; NMR (90 MHz) δ 0.85–1.15 (m, 3 H), 1.20–1.90 (m, 4 H), 2.34 (s, 3 H), 2.80–3.10 (m, 2 H), 3.61 (s, 3 H), 7.15–7.55 (m, 5 H); ^{13}C NMR δ 168.4, 165.6, 136.8, 129.0 (2C), 127.4 (2 C), 125.9, 114.8, 52.1, 32.4, 32.1, 22.7, 15.2, 13.9.

General Procedure for the Addition of Methylcuprates to α-Oxoketene Dithioacetal 31. A 5-mL solution of 0.12 M (1.2 equiv) cuprate solution [$(CH_3CuSPh)Li$, $(n\text{-}Bu)_3P{\cdot}(CH_3)_2CuLi$, $Ph_3P{\cdot}(CH_3)_2CuLi$, [$(CH_3)_2$-CuSCN]Li_2, [$(CH_3)_2CuCN]Li_2$, [3-methoxy-3,3-dimethylbutynyl-$CuCH_3$]Li, [$(C_6H_{11})_2PCuCH_3$]Li] was prepared according to literature procedure(s) in a 10-mL round-bottom flask that had been purged with nitrogen and flame-dried. The cuprate solution was cooled to −78 °C and then a solution of **31** (0.50 mmol) in 2 mL of THF was slowly added to the cuprate solution via a double-tipped needle. The reaction mixture was allowed to slowly warm to 0 °C over a 1-h period where it was quenched with 2 mL of methanol. The reaction mixture was poured into 30 mL NH_4Cl (satd) and 50 mL Et_2O. The ether layer was separated and the aqueous layer was extracted with 2 × 20 mL of Et_2O. The combined organic layers were washed with 20 mL of water and 20 mL of brine and dried over $MgSO_4$. Concentration in vacuo gave a crude yellow oil. Purification by column chromatography (10% ethyl acetate/petroleum ether) gave pure compounds **31**, (*E*)-**32**, (*Z*)-**32**, **33**, and **34**.

31 (R_f 0.34): IR ($CHCl_3$) 3050 (m), 3000 (s), 2930 (s), 1720 (m), 1660 (br, s), 1500 (s), 1460 (s), 1420 (s), 1230 (br s), 1140 (m) cm^{-1}; NMR (90 MHz) δ 7.46–7.05 (m, 5 H), 3.20–2.72 (m, 2 H), 2.70–1.80 (m, 5 H), 2.34 (s, 6 H); ^{13}C NMR δ 198.6, 148.3, 144.6, 137.3, 128.4 (2 C), 126.5 (2 C), 126.4, 41.6, 40.7, 40.4, 30.7, 18.1 (2 C); mass spectrum m/e 278.0800 (M^+) (calcd for $C_{15}H_{18}OS_2$: 278.0799).

(*E*)-**32** (R_f 0.30): UV max (CH_3OH) 309 (ε 14 000); IR ($CHCl_3$) 3070 (vw), 3055 (w), 3030 (m), 2920 (s), 2880 (m), 1715 (w), 1670 (br, s), 1610 (m), 1550 (s), 1530 (s), 1505 (s), 1460 (s), 1435 (s), 1375 (m), 1335 (m), 1305 (m), 1275 (s), 1240 (s), 1210 (m), 1180 (m), 1160 (m), 1080 (m), 990 (m), 965 (w) cm^{-1}; NMR (90 MHz) δ 7.44–7.05 (m, 5 H), 3.18–2.76 (m, 2 H), 2.67–2.20 (m, 3 H), 2.44 (s, 3 H), 2.32 (s, 3 H), 2.26–1.85 (m, 2 H); ^{13}C NMR δ 198.5, 151.5, 145.5, 145.1, 128.4 (2 C), 126.6 (2 C), 126.3, 41.0, 40.8, 37.9, 30.2, 18.4, 13.9.

(*Z*)-**32** (R_f 0.18): UV max (CH_3OH) 313 (ε 8900); IR ($CHCl_3$) 3070 (vw), 3050 (w), 3030 (m), 2930 (s), 2880 (m), 1710 (w), 1670 (s), 1650 (s), 1640 (s), 1605 (m), 1530 (br, s), 1500 (s), 1460 (s), 1430 (s), 1330 (m), 1310 (m), 1270 (vs), 1240 (s), 1180 (m), 1160 (m), 1080 (m), 980 (m), 960 (w) cm^{-1}; NMR (90 MHz) δ 7.43–7.08 (m, 5 H), 3.14–2.76 (m, 2 H), 2.74–2.37 (m, 3 H), 2.28 (s, 3 H), 2.17–1.85 (m, 2 H), 2.11 (s, 3 H); ^{13}C NMR δ 197.2, 154.5, 145.4, 145.0, 128.4 (2 C), 126.5 (2 C), 126.3, 41.0, 38.9, 38.1, 29.1, 18.3, 15.7.

33 (R_f 0.55): IR 3070 (w), 3050 (m), 2990 (s), 2920 (br, s), 1715 (s), 1680 (vs), 1605 (s), 1500 (m), 1460 (s), 1430 (m), 1380 (m), 1290 (m), 1275 (m), 1240 (br, m), 1175 (m), 1140 (m), 1070 (m), 1035 (m), 990 (m), 960 (w) cm^{-1}; NMR (90 MHz) δ 7.52–6.96 (m, 5 H), 3.15–2.70 (m, 2 H), 2.66–2.35 (m, 3 H), 2.31–1.89 (m, 2 H), 2.03 (d, J = 1.7 Hz, 3 H), 1.76 (d, J = 1.2 Hz, 3 H); ^{13}C NMR δ 203.2, 145.3, 143.7, 131.1, 128.4(2C), 126.5(2C), 126.3, 41.8, 41.4, 37.6, 31.1, 23.0, 22.1; mass spectrum m/e 214.1368 (M^+) (calcd for $C_{15}H_{18}O$: 214.1358).

34 (R_f 0.24): IR ($CHCl_3$) 3030 (w), 2930 (m), 1725 (br, m), 1670 (br, s), 1610 (w), 1550 (s), 1500 (m), 1460 (m), 1440 (m), 1310 (s), 1270 (vs), 1240 (m), 1190 (m), 1050 (m) cm^{-1}; NMR (90 MHz) δ 7.61 (m, 1 H), 7.45–7.10 (m, 5 H), 3.20–1.84 (m, 7 H), 2.46 (s, 3 H); ^{13}C NMR δ 195.4, 145.0, 144.6, 130.0, 128.6 (2 C), 127.6 (2 C), 126.5, 40.4, 38.5, 35.6, 30.1, 17.5.

X-ray Analysis. Vinylogous thiol ester (*E*)-**15d** crystallized as large, colorless plates. A small fragment of one such sheet extinguished cleanly in polarized light. The space group is $P2_1/c$, with cell constants of a = 8.571 (5) Å, b = 19.39 (1) Å, c = 7.298 (3) Å, β = 110.17 (4)°, V =

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1138 (1) Å. $C_{11}H_{18}OS$ has a molecular weight of 198.32 amu, and with $Z = 4$. The calculate density is 1.16 g/cm^3. Data were collected on a Syntex $P2_1$ four-circle diffractometer in the θ-2θ mode using copper radiation, λ 1.5418 Å; 1034 reflections were retained as observed, 250 rejected as unobserved. The structure was solved by direct methods[47] and refined by least-squares methods.[48] The final agreement factors were $R_1 = 0.04$, $R_2 = 0.05$. The final difference map was judged to be free of significant features. Final atomic positional parameters are given in Table V, and the bond lengths and angles are given in Table IV.

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Registry No. 1, 17649-89-7; **2**, 17649-90-0; **3**, 96898-99-6; **4**, 79300-00-8; **5**, 17649-86-4; **6**, 87615-87-0; **7**, 51507-08-5; **8**, 5780-61-0; **9**, 21441-31-6; **10**, 89489-55-4; **11**, 96899-00-2; **12a**, 96899-01-3; **12b**, 96899-02-4; **13a**, 96899-03-5; **13b**, 96899-04-6; (*E*)-**14**, 96899-05-7; (*Z*)-**14**, 86310-05-6; (*E*)-**15a**, 84308-03-2; (*Z*)-**15a**, 96899-06-8; (*E*)-**15b**, 84308-04-3; (*Z*)-**15b**, 96899-07-9; (*E*)-**15c**, 87615-88-1; (*Z*)-**15c**, 96899-08-0; (*E*)-**15d**, 84308-05-4; (*Z*)-**15d**, 84308-06-5; (*E*)-**15e**, 96899-09-1; (*Z*)-**15e**, 96899-10-4; **16**, 96899-11-5; (*E*)-**17a**, 84308-07-6; (*Z*)-**17a**, 84308-08-7; (*E*)-**17b**, 96899-12-6; (*Z*)-**17b**, 96899-13-7; (*E*)-**17c**, 96899-14-8; (*Z*)-**17c**, 96899-15-9; (*E*)-**17d**, 96899-16-0; (*Z*)-**17d**, 96899-17-1; (*E*)-**18a**, 96899-18-2; (*Z*)-**18a**, 96899-19-3; (*E*)-**18b**, 96899-20-6; (*Z*)-**18b**, 96899-21-7; (*E*)-**19**, 84308-09-8; (*Z*)-**19**, 84308-10-1; (*E*)-**20a**, 86310-01-2; (*Z*)-**20a**, 62453-10-5; (*E*)-**20b**, 86310-02-3; (*Z*)-**20b**, 96899-22-8; (*E*)-**20c**, 96899-23-9; (*Z*)-**20c**, 96899-24-0; (*E*)-**20d**, 96899-25-1; (*Z*)-**20d**, 96899-26-2; **21**, 33944-94-4; (*E*)-**22a**, 86310-03-4; (*Z*)-**22a**, 96899-27-3; (*E*)-**22b**, 86310-04-5; (*Z*)-**22b**, 96899-28-4; (*E*)-**22c**, 96899-29-5; (*Z*)-**22c**, 96899-30-8; (*E*)-**22d**, 96899-31-9; (*Z*)-**22d**, 96899-32-0; **23**, 96899-33-1; (*E*)-**24a**, 87615-89-2; (*Z*)-**24a**, 84308-11-2; (*E*)-**24b**, 96899-34-2; (*Z*)-**24b**, 96899-35-3; (*E*)-**25**, 49784-51-2; (*Z*)-**25**, 49784-64-7; (*E*)-**26**, 96899-36-4; (*E*)-**27a**, 40595-76-4; (*E*)-**27b**, 96899-37-5; (*E*)-**27c**, 96899-38-6; (*Z*)-**27c**, 96899-39-7; **28**, 15904-85-5; (*E*)-**29a**, 96899-40-0; (*Z*)-**29a**, 96899-41-1; (*E*)-**29b**, 96899-42-2; (*Z*)-**29b**, 96899-43-3; **30**, 66716-63-0; **31**, 96899-44-4; (*E*)-**32**, 96899-45-5; (*Z*)-**32**, 96899-46-6; **33**, 96899-47-7; **34**, 96899-48-8; **35a**, 96899-49-9; **35b**, 96899-50-2; i, 96913-37-0; $(CH_3)_2CuLi$, 15681-48-8; $(PhSCuCH_3)Li$, 56831-21-1; $(MeOCMe_2C{\equiv}CCuCH_3)Li$, 79135-33-4; (PhSCuBu)Li, 53128-68-0; $(MeOCMe_2C{\equiv}CCuBu)Li$, 66777-74-0; (PhSCuBu-*sec*)Li, 53972-31-9; (PhSCuBu-*t*)Li, 50281-66-8; $(PhSCuC_3H_5)Li$, 84180-46-1; $(MeOCMe_2C{\equiv}CCuC_3H_5)Li$, 96898-97-4; $(PhSCuCH_2CH_2CH{=}CMe_2)Li$, 61136-35-4; BuCu, 34948-25-9; *t*-BuCu, 56583-96-1; $Ph_3P{\cdot}(CH_3)_2CuLi$, 96898-98-5; $n\text{-}Bu_3P{\cdot}(CH_3)_2CuLi$, 61817-79-6; $[(C_6H_{11})_2PCuCH_3]Li$, 88766-01-2; $[(CH_3)_2CuSCN]Li_2$, 91606-28-9; $[(CH_3)_2CuCN]Li_2$, 80473-70-7; $(CH_3CuCN)Li$, 41753-78-0; EtSH, 75-08-1; $CH_3SSO_2CH_3$, 2949-92-0; 2-formylcyclopentanone, 1192-54-7; (*E*)-2-(methylthiomethylene)cyclopentanone, 82753-83-1.

Supplementary Material Available: Atomic thermal parameters and structure factor tables for (*E*)-**15d** (11 pages). Ordering information is given on any current masthead page.

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Carbon–Oxygen Bond Cleavage Reactions by Electron Transfer. 2. Electrochemical Formation and Dimerization Reaction Pathways of Cyanodiphenyl Ether Radical Anions

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Abstract: The radical anions of 4-cyanodiphenyl ether (**1**) and 2-cyanodiphenyl ether (**2**) have been electrochemically generated and subsequently shown to dimerize in dry *N,N*-dimethylformamide (DMF). The radical anion of **1** undergoes irreversible dimerization ($k_2 = 1.1 \times 10^2$ M^{-1} s^{-1}) to form dimeric dianions, which result from coupling either at the 2 and 4 positions or at the 4 and 4 positions with respect to the cyano substituent. The 4–4 coupled dianion undergoes carbon–oxygen bond cleavage with loss of phenoxide ions ($k_1 = 3.8 \times 10^{-2}$ s^{-1}) to form 4,4′-dicyanobiphenyl (**3**). The 2–4 coupled dianion undergoes relatively rapid loss of one phenoxide ion to form an anion, which can be either further reduced to a radical dianion or oxidized in a two-electron process to 2,4′-dicyano-5-phenoxybiphenyl (**4**). The radical anion of **2** reversibly dimerizes ($k_f = 1.2 \times 10^3$ M^{-1} s^{-1}, $k_b = 9.5 \times 10^{-2}$ s^{-1}) to three possible coupled dimeric dianions. Although the 4–4 and 4–6 coupled products (respective to the cyano substituent) are apparently resistant to further reactions, the 2–4 coupled product undergoes loss of phenoxide ion to produce an anion which can be oxidized to 2′,4-dicyano-3-phenoxybiphenyl (**5**).

Introduction

Recent reports on the reductive carbon–oxygen bond cleavage of cyano-substituted anisole radical anions suggested decay by three major pathways, which are dependent on the electron-density distribution of the particular radical-anion isomer.[1] In the case of 2-cyanoanisole, dimerization of the radical anion results in the intermediacy of a dimeric dianion, which undergoes intramolecular electron transfer to produce 2-cyanophenoxide, methide ion, and 2-cyanoanisole. No dimeric-type products were observed either by cyclic voltammetry or analysis of the final products of electrolysis. In contrast to the 2-cyano isomer, the 4-cyanoanisole radical anion undergoes facile carbon–oxygen bond cleavage to form 4-cyanophenoxide and methyl radical.

There are no reports on the reductive electrochemical cleavage of carbon–oxygen bonds in diaryl ethers, including either diphenyl ether or substituted diphenyl ethers. In contrast, there are several reports on the reductive cleavage of diphenyl ether using chemical reductants.[2-10] Recent data by Woolsey and co-workers suggest

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