# 2-Hetero Substituted Silylated Ketene Acetals: Reagents for the Preparation of α-Functionalized Methyl Ketones from Carboxylic Acid Chlorides

Allan Wissner

*Metabolic Disease Research Section, Medical Research Division, Lederle Laboratories, American Cyanamid Company, Pearl River, New York 10965*

*Received March 30, 1979*

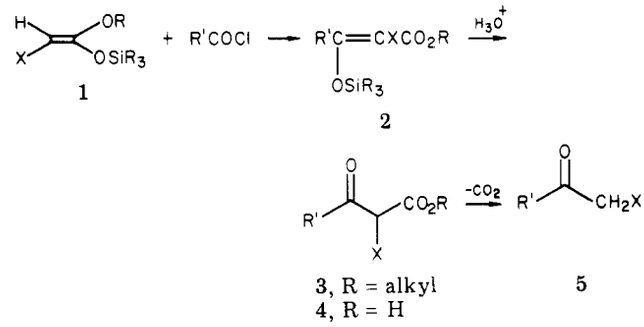
Silylated ketene acetals of structure $XCH{=}C(OR)OSi(CH_3)_3$ (X = $OCH_3$, $OSi(CH_3)_3$, $OC_6H_5$, or $SCH_3$; R = $CH_3$ or $Si(CH_3)_3$) have been prepared by silylation of appropriate ester enolates. The reaction of a carboxylic acid chloride (R'COCl) with 2 equiv of these reagents either under thermal or Lewis acid catalytic conditions followed by hydrolysis–decarboxylation of intermediates $R'(OSi(CH_3)_3)C{=}C(X)CO_2R$ gives α-functionalized methyl ketones ($R'COCH_2X$) in preparatively useful yields. Factors which would influence the choice of proper reaction conditions are discussed.

The conversion of a carboxylic acid chloride to an α-functionalized methyl ketone (eq 1) is an important and frequently encountered synthetic transformation. One of the most general methods by which this conversion is often accomplished is by the reaction of a carboxylic acid chloride with an excess of diazomethane followed by the reaction of the diazo ketone produced with various acidic reagents.[1] The toxicity and unpredictable stability of diazomethane is, however, a major disadvantage of this approach, particularly for large-scale preparations. Since we were faced with the necessity of converting a large quantity of a particular carboxylic acid chloride to a variety of α-functionalized methyl ketones under mild conditions, we sought a new method which would accomplish this transformation. We would now like to describe a series of reagents which will allow the preparation of compounds of structure **5** (X = OH, $OCH_3$, $OC_6H_5$, $SCH_3$) from carboxylic acid chlorides under mild conditions.[2]

$$RCOCl \rightarrow RCOCH_2X \quad (1)$$

The reaction of silylated ketene acetals **1** (R = alkyl; X = H or alkyl) with carboxylic acid chlorides either thermally[3] or in the presence of triethylamine[4] has been reported to furnish compounds of structure **2** which have been hydrolyzed to β-keto esters **3** (Scheme I). By analogy, it was anticipated that a silylated ketene acetal of structure **1** in which X is a heteroatom containing functionality (X = OR, SR, etc.) would undergo a similar sequence of reactions with a carboxylic acid chloride to furnish, after complete hydrolysis, a β-keto acid (**4**). Such a β-keto acid would be expected to decarboxylate readily to give the desired α-functionalized methyl ketone (**5**).

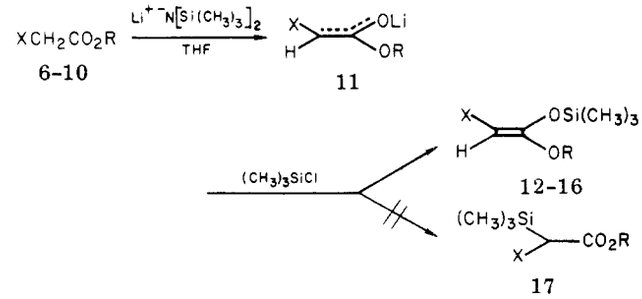
Scheme I




1 2 3, R = alkyl 4, R = H 5

## Results and Discussion

**Preparation of Functionalized Silylated Ketene Acetals.** We have prepared the silylated ketene acetals **12–16** shown in Table I by the addition of esters **6–10** to a tetrahydrofuran solution of lithio-1,1,1,3,3,3-hexamethyldisilazane[5] at −78 °C, followed by quenching of the resulting enolate **11** with chlorotrimethylsilane [$Me_3SiCl$].




We have observed little if any C-silylated products (**17**) in these preparations. The silylated esters **6–8** and **10** were prepared by the silylation of the corresponding carboxylic acids, using a 2:1 mixture of 1,1,1,3,3,3-hexamethyldisilazane [HMDS] and $Me_3SiCl$ in pyridine or pyridine–tetrahydrofuran mixtures.

The spectral data obtained for these functionalized silylated ketene acetals support the assigned structures. While the infrared spectra of those acetals containing an oxygen functionality at C2 (**12–15**) show an unusually high double bond stretching frequency (1703–1709 $cm^{-1}$) characteristic of such polyoxygenated olefins,[6] the sulfur-containing ketene acetal **16** absorbs at considerably lower frequency (1617 $cm^{-1}$). This dichotomy is also apparent in the $^1H$ and $^{13}C$ NMR spectra of these compounds. While the $^1H$ NMR spectra of the oxygen-substituted ketene acetals show a singlet for the olefinic proton in the region δ 5.2–5.8, the corresponding resonance for the sulfur-containing acetal **16** occurs at a considerably higher

(1) (a) M. Steiger and T. Reichstein, *Helv. Chim. Acta*, **20**, 1164 (1937); (b) W. Korytnyk and B. Lachmann, *J. Med. Chem.*, **14**, 641 (1971); (c) W. D. McPhee and E. Klingsberg, "Organic Syntheses", Collect. Vol. III, Wiley, New York, 1955; (d) G. R. Pettit, B. Green, and A. K. Das Gupta, *J. Org. Chem.*, **35**, 1381 (1970); (e) M. S. Newman and P. F. Beal, *J. Am. Chem. Soc.*, **72**, 5161 (1950); (f) P. Yates, *ibid.*, **74**, 5376 (1952); (g) J. L. E. Erickson, J. M. Dechary, and M. R. Kesling, *ibid.*, **73**, 5310 (1951); (h) T. Reichstein and W. Schindler, *Helv. Chim. Acta*, **23**, 669 (1940); (i) A. L. Wilds and C. H. Shunk, *J. Am. Chem. Soc.*, **70**, 2427 (1948).

(2) Part of the work described herein has been reported in a preliminary communication: A. Wissner, *Tetrahedron Lett.*, 2749 (1978).

(3) G. S. Burlachenko, U. V. Maltsev, Yu. I. Baukov, and I. F. Lutsenko, *Zh. Obshch. Khim.*, **43**, 1724 (1973).

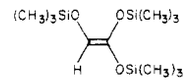
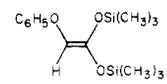
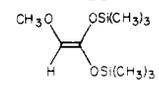
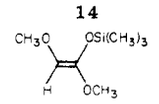
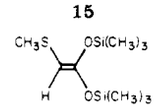
(4) M. W. Rathke and D. F. Sullivan, *Tetrahedron Lett.*, 1297 (1973).

(5) E. H. Amonoo-Neizer, R. A. Shaw, D. O. Skovlin, and B. C. Smith, *J. Chem. Soc.*, 2997 (1965).

(6) I. Ojima and S. Inaba, *Yuki Gosei Kagaku Kyokai Shi*, **36**, 610 (1978).

0022-3263/79/1944-4617$01.00/0 

Table I. Silylated Ketene Acetals Prepared

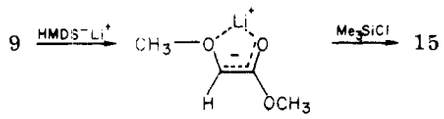
| ester | silylated ketene acetal | bp, °C (mm) | $\nu_{C=C}$, $cm^{-1}$ | % yield |
|---|---|---|---|---|
| $(CH_3)_3SiOCH_2CO_2Si(CH_3)_3$ (6) |  12 | 54-56 (0.1) | 1706 | 100 |
| $C_6H_5OCH_2CO_2Si(CH_3)_3$ (7) |  13 | 118-120 (1.2) | 1703 | 95 |
| $CH_3OCH_2CO_2Si(CH_3)_3$ (8) |  14 | 66-69 (6) | 1709 | 80 |
| $CH_3OCH_2CO_2CH_3$ (9) |  15 | 68-71 (35) | 1705 | 49[a] |
| $CH_3SCH_2CO_2Si(CH_3)_3$ (10) |  16 | 77-80 (1.0) | 1617 | 69 |

[a] The low yield in this case is due largely to difficulties encountered in purification.

field ($\delta$ 4.1). The $^{13}C$ absorption at C2 in **16** is at higher field ($\delta$ 76.1) then the corresponding absorptions in the oxygen analogues **12**–**15** ($\delta$ 114.4–106.5).

Insofar as both the nature of the ester group and the substituent at C2 play a role in determining the O-silylation–C-silylation ratio of ester enolates,[7] it is of interest that little if any C-silylation of the enolates **11** is observed.

The structure of **15** is of some interest. While O-silylation of the lithium enolate derived from **9** could, in principle, result in two configurational isomers, in fact the NMR spectral data obtained for **15** [$^1H$ NMR: $\delta_{Me_4Si}^{CDCl_3}$, 5.26 (s, 1 H, CH), 3.42 (s, 6 H, $OCH_3$), 0.19 (s, 9 H, $SiCH_3$); $^{13}C$ NMR $\delta$ 150.0 (C1), 112.5 (C2), 59.9, 55.5 ($OCH_3$), 0.03 (CSi)] clearly indicate that a single isomer was formed. It is tempting to speculate that **15** has the configuration



18

shown on the basis that enolate **18** can be expected to be stabilized by chelation of the lithium ion by both oxygen atoms. Trapping **18** with $Me_3SiCl$ would give **15**, having the methoxy and trimethylsilyloxy groups in a cis relationship.

We have experienced no difficulty in preparing reagent **12** on a multimolar scale. Furthermore, reagents **12**–**16** are stable to storage provided adequate precaution is taken to exclude moisture.

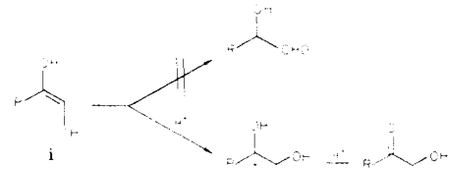
**Preparation of $\alpha$-Functionalized Methyl Ketones.** The reagents **12**–**16** have been found useful for the preparation of a variety of $\alpha$-functionalized methyl ketones. For example, when octanoyl chloride (**19**) and 2 equiv of reagent **12** are heated at 90 °C for 2 h in the absence of solvent, three products are obtained which have been identified as $Me_3SiCl$, **6**, and **21** (75% yield, Scheme II). Although the configuration about the double bond in **21** has not been determined, the $^{13}C$ NMR spectrum [$\delta_{Me_4Si}^{CDCl_3}$, 166.36 (C1), 154.99 (C3), 128.89 (C2), 33.17 (C4), 31.93 (C8), 29.41 (C6), 29.24 (C7), 27.93 (C5), 22.70 (C4), 14.11 (C10), 1.03, 0.09, -0.01 ($Si(CH_3)_3$)] clearly indicates that a single isomer was produced. Compound **21** presumably arises from a nucleophilic attack by reagent **12** on the acid chloride to furnish intermediate **20** which undergoes a trimethylsilyl transfer and loss of hydrogen chloride (not necessarily concerted). The hydrogen chloride liberated in this process consumes the second equivalent of the reagent to generate $Me_3SiCl$ and **6**. Treatment of **21** with dilute hydrochloric acid in tetrahydrofuran or dioxane results in an immediate exothermic hydrolysis (presumably to $\beta$-keto acid **22**) and decarboxylation to furnish the desired hydroxymethyl ketone **23** in 89% yield.[8]

In the preparation of these $\alpha$-functionalized methyl ketones, it is not necessary to isolate any of the intermediates; for example, direct hydrolysis–decarboxylation of the above reaction mixture gives **23** in 84% yield. We subsequently found that a number of these reactions could be efficiently catalyzed by Lewis acids; the reaction of octanoyl chloride (**19**) with reagent **12** in the presence of a catalytic amount of stannic chloride is exothermic and furnishes **23** in 90% yield after hydrolysis–decarboxylation.

The results obtained for the reaction of reagents **12**–**16** with a variety of carboxylic acid chlorides (**19** and **24**–**30**) are illustrated in Table II. Since it was readily apparent,

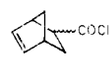
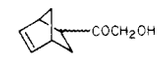
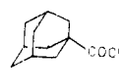
(7) (a) C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organomet. Chem.*, 59 (1972); (b) Y.-N. Kuo, F. Chen, C. Ainsworth, and J. J. Bloomfield, *Chem. Commun.*, 136 (1971); (c) M. W. Rathke and D. F. Sullivan, *Synth. Commun.*, **3**, 67 (1973); (d) R. P. Woodbury and M. W. Rathke, *J. Org. Chem.*, **43**, 881 (1978).

(8) Decarboxylation of $\beta$-keto acid **22** would give an ene diol of structure i which, in principle, could tautomerize to either an $\alpha$-hydroxyaldehyde or to the observed $\alpha$-hydroxy ketone. The absence of any $\alpha$-hydroxyaldehyde products in these reactions can presumably be accounted for by either an acid-catalyzed isomerization of any $\alpha$-hydroxyaldehyde produced to the corresponding $\alpha$-hydroxy ketone [K. Ogura and G. Tsuschihashi, *Tetrahedron Lett.*, 2681 (1972)] or, more likely, prefered protonation of i at C1.



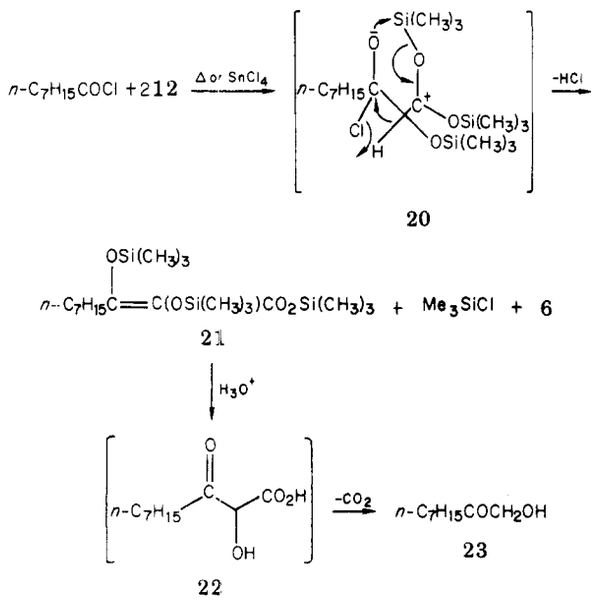
i

Table II. α-Functionalized Methyl Ketones Prepared

| entry no. | carboxylic acid chloride | silylated ketene acetal | conditions[a] | product(s) | % yield of products[b] |
|---|---|---|---|---|---|
| 1 | $n$-$C_7H_{15}COCl$ (19) | 12 | 95–100 °C, 4 h | $n$-$C_7H_{15}COCH_2OH$ (23) | 84 |
| 2 | 19 | 12 | $SnCl_4$, 1 h | 23 | 90 |
| 3 | 19 | 14 | $SnCl_4$, 2.5 h | $n$-$C_7H_{15}COCH_2OCH_3$ (31) | 81 |
| 4 | 19 | 15 | $SnCl_4$, 4 h | $n$-$C_7H_{15}COCH(OCH_3)CO_2CH_3$ (32) | 80 |
| 5 | 19 | 16 | 110 °C, 7 h | $n$-$C_7H_{15}COCH_2SCH_3$ (33) | 57 |
| | | | | $n$-$C_7H_{15}COCH_2SCOC_7H_{15}$-$n$ (34) | <15[c] |
| 6 | 19 | 16 | $C_6H_5Cl$, 5.5 h | 33 | 79 |
| | | | | 34 | <12[c] |
| 7 | $C_6H_5COCl$ (24) | 12 | 95 °C, 4 h | $C_6H_5COCH_2OH$ (35) | 62 |
| 8 | 24 | 13 | 100–120 °C, 4.25 h | $C_6H_5COCH_2OC_6H_5$ (36) | 75 |
| 9 | 24 | 13 | $SnCl_4$, 5 h | [d] | |
| 10 | 24 | 16 | 115 °C, 5 h | $C_6H_5COCH_2SCH_3$ (37) | 57 |
| | | | | $C_6H_5COCH_2SCOC_6H_5$ (38) | <21[c] |
| 11 | 24 | 16 | $C_6H_5Cl$, 5 h | 37 | 53 |
| | | | | 38 | <20[c] |
| 12 | 24 | 14 | $SnCl_4$, 24 h | $C_6H_5COCH_2OCH_3$ (39) | 79 |
| 13 | 24 | 14 | $SnCl_4$, 3 h | 39 | <50[c] |
| 14 | $C_6H_5CH_2COCl$ (25) | 12 | 95 °C, 4 h | $C_6H_5CH_2COCH_2OH$ (40) | 81 |
| 15 | 25 | 12 | $SnCl_4$, 3 h | 40 | 76 |
| 16 | 25 | 14 | $SnCl_4$, 1.5 h | $C_6H_5CH_2COCH_2OCH_3$ (41) | 88 |
| 17 | $n$-$C_5H_{11}COCl$ (26) | 13 | 110 °C, 3 h | $n$-$C_5H_{11}COCH_2OC_6H_5$ (42) | 73 |
| 18 | $Br(CH_2)_4COCl$ (27) | 12 | $SnCl_4$, 2.5 h | $Br(CH_2)_4COCH_2OH$ (43) | 79 |
| 19 | c-$C_6H_{11}$-$COCl$ (28) | 12 | 100 °C, 4 h | c-$C_6H_{11}$-$COCH_2OH$ (44) | 71 |
| 20 | 28 | 12 | $SnCl_4$, 5 h | 44 | 48 |
| 21 |  29 | 12 | 95 °C, 4.25 h |  45 | 69 |
| 22 |  30 | 12 | 95 °C, 4.5 h | [d] | |

[a] Reactions were conducted in the absence of solvent unless indicated. Reactions in chlorobenzene were conducted at reflux. The stannic chloride catalyzed reactions were allowed to exotherm without external cooling and then maintained at ambient temperature.[10] [b] Unless indicated, yields were obtained for distilled or recrystallized products. [c] Estimated yield based on the amount of crude product obtained. [d] No product obtained.

Scheme II



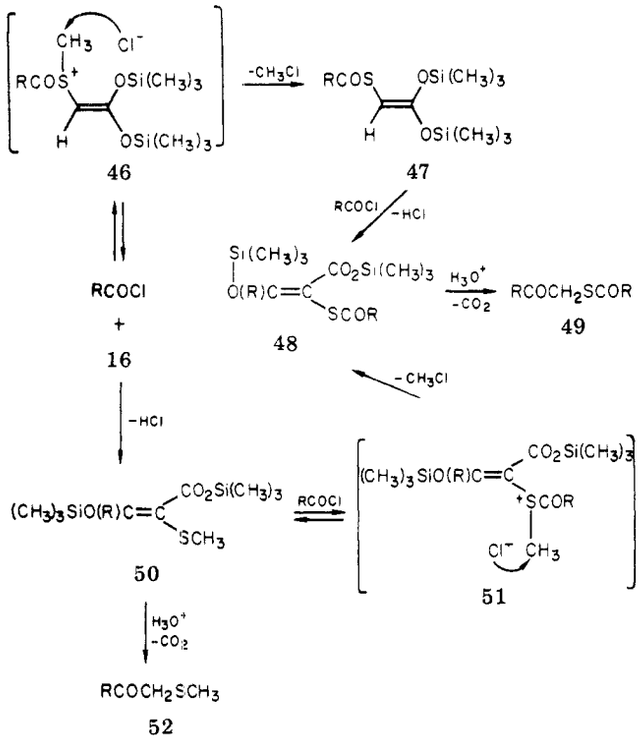

by monitoring several of these reactions by $^1H$ NMR spectroscopy, that the rate of reaction of these reagents with the liberated hydrogen chloride was at least as great as the rate of reaction with the acid chlorides, a reagent–acid chloride ratio of at least 2:1 was usually used.[9] These reactions were conducted using either the thermal or stannic chloride catalytic conditions. The thermal reactions were usually conducted in the absence of solvent with the exception of several examples which also were studied in refluxing chlorobenzene. The stannic chloride catalyzed reactions also were conducted in the absence of solvent; these reactions were allowed to exotherm without external cooling and then maintained at ambient temperature.[10] The results presented in Table II indicate that these reagents show promise for the synthesis of a wide variety of α-functionalized methyl ketones in preparatively useful yields. We have used these reagents to prepare hydroxymethyl (**23**, **35**, **40**, and **43–45**), methoxymethyl (**31**, **39**, and **41**), phenoxymethyl (**36** and **42**), and (methylthio)methyl (**33** and **37**) ketones. Furthermore, by incorporating both a trimethylsilyloxy and a methoxy group at C1 in reagent **15**, it is possible to stop at the β-keto ester stage as illustrated by the preparation of **32**.

In the course of our studies, we have made certain preliminary observations which might help influence the choice of proper reaction conditions. Both the thermal and catalytic reaction conditions appear to give similar results for less sterically hindered, nonconjugated acid chlorides (compare entries 1 and 2 and 14 and 15). However, for more hindered acid chlorides and aromatic acid chlorides, the thermal procedure was superior to the catalytic process (compare entries 8 and 9 and 19 and 20). In the reaction

(9) Preliminary experiments using an acid chloride–reagent ratio of 1:1, THF as a solvent, and triethylamine as a proton scavenger appear to be successful in some situations [R. E. Schaub, unpublished results].

(10) In view of the strongly exothermic nature of many of the $SnCl_4$-catalyzed reactions, large-scale preparations may require regulation of the reaction temperature either by external cooling or by controlled addition of the reactants.

Scheme III



of benzoyl chloride (24) with reagent 14, using the catalytic conditions, an improvement in yield was obtained by extending the reaction time (entries 12 and 13). The highly hindered acid chloride 30 failed to give any product under the standard thermal conditions (entry 22).

In the preparation of the (methylthio)methyl ketones 33 and 37, we observed the formation of side products 34 and 38, respectively. In the former case, the use of chlorobenzene as a solvent leads to an improvement in yield (entries 5 and 6), while in the latter case no improvement was observed (entries 10 and 11). There appears to be two mechanistic possibilities which would account for the formation of side products 34 and 38, as shown in Scheme III. Reagent 16 has two sites potentially susceptible to electrophilic attack; while attack at the C2 carbon atom followed by trimethylsilyl transfer and loss of hydrogen chloride would provide the normal product 50, hydrolysis–decarboxylation of which would give the desired ketone 52, attack at the sulfur atom followed by loss of methyl chloride could produce 47 as shown. The reaction of 47 with a second molecule of acid chloride might then give 48. Alternatively, 48 could be formed by an electrophilic attack by the acid chloride at the sulfur atom in 50. Hydrolysis–decarboxylation of 48 would result in the observed side product 49.

It is thus apparent from the preceding discussion that the methods desired herein can be used with advantage for the preparation of α-functionalized methyl ketones in preparatively useful yields under mild, nearly neutral conditions.[11] Although the silylated ketene acetals presently prepared have relatively simple heteroatom-containing functionality, there is no obvious reason why silylated ketene acetals containing more elaborate heteroatom groups could not be prepared (provided these groups are stable to enolate formation) and used for the synthesis of more complicated α-functionalized methyl ketones. Furthermore, it is worth pointing out that by the process of alkylation, hydrolysis, and decarboxylation of β-keto esters such as 32, it should be possible to prepare, in a regiospecific manner, nonterminal, unsymmetrical ketones containing the α-heteroatom functionality.

(11) It is possible to obtain 23 by simply exposing 21 to the laboratory atmosphere overnight.

## Experimental Section

**General.** All reaction solvents were dried over 4Å molecular sieves. Carboxylic acid chlorides were distilled before use. 1,1,1,3,3,3-Hexamethyldisilazane (HMDS) and chlorotrimethylsilane ($Me_3SiCl$) were used as supplied (Aldrich) without purification.

Large-scale distillations were conducted using a 30 × 2 cm Vigreux column. Unless indicated, small-scale distillations were accomplished with a short path distillation apparatus; molecular distillations were conducted with an Aldrich Kugelrohr apparatus.

$^1H$ and $^{13}C$ NMR spectra were recorded on a Varian Associates HA-100 or FT-80 spectrometer, using tetramethylsilane as a reference. IR spectra were obtained with a Nicolet-7000 spectrometer. Mass spectra were recorded with an AEI MS-9 mass spectrometer. Melting points were determined on a Melt-Temp apparatus and are uncorrected.

**Trimethylsilyl Trimethylsilyloxyacetate (6).** To a solution of 118 g (1.55 mol) of glycolic acid in 400 mL of pyridine was added under nitrogen with stirring 260 g (1.60 mol) of HMDS over a 30-min period during which time the reaction temperature reached 75 °C and a slurry formed. After the mixture was cooled to room temperature, 88 g (0.80 mol) of $Me_3SiCl$ was added dropwise. After 1 h, the mixture was filtered, dissolved in petroleum ether, and filtered again. The filtrate was concentrated and distilled twice (78–80 °C (12 mm)), giving 275 g (80%) of 6: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.16 (s, 2 H, $CH_2$), 0.30 (s, 9 H, $CO_2Si(CH_3)_3$), 0.14 (s, 9 H, $CH_2OSi(CH_3)_3$); MS calcd for $C_7H_{17}O_3Si_2$ (M − $CH_3$) 205.0716 (found 205.0708).

**Trimethylsilyl Phenoxyacetate (7).** To a solution of 75 g (0.49 mol) of phenoxyacetic acid in 70 mL of pyridine and 60 mL of THF was added with stirring 87.5 g (0.54 mol) of HMDS. After 10 min, 29.5 g (0.27 mol) of $Me_3SiCl$ was added dropwise. After the solution was stirred for 2 h, the solvent was removed, and the residue was dissolved in petroleum ether. The solution was filtered through Celite, and the solvent was removed. The residue was redissolved in petroleum ether, and the filtration process was repeated. Distillation (105–107 °C (2.7 mm)) gave 105.2 g (96%) of 7: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 6.99 (m, 5 H, $C_6H_5$), 4.63 (s, 2 H, $CH_2$), 0.37 (s, 9 H, $Si(CH_3)_3$).

Anal. Calcd for $C_{11}H_{16}O_3Si$: C, 58.90; H, 7.19. Found: C, 58.67; H, 7.28.

**Trimethylsilyl Methoxyacetate (8).** To a stirred solution of 87.0 g (0.97 mol) of methoxyacetic acid in 100 mL of THF and 50 mL of pyridine at 0 °C was added 155.9 g (0.97 mol) of HMDS followed by the dropwise addition of 52.5 g (0.48 mol) of $Me_3SiCl$. After the solution was stirred for 17 h, the mixture was diluted with petroleum ether and filtered through Celite. The solvent was removed, and the residue was distilled at aspirator pressure (54–55 °C) to give 125.3 g (80%) of 8: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 3.89 (s, 2 H, $CH_2$), 3.33 (s, 3 H, $OCH_3$), 0.23 (s, 9 H, $Si(CH_3)_3$).

Anal. Calcd for $C_6H_{14}O_3Si$: C, 44.41; H, 8.70. Found: C, 44.66; H, 8.77.

**Trimethylsilyl Methylthioacetate (10).** To a stirred solution of 164.5 g (1.55 mol) of methylthioacetic acid in 150 mL of pyridine and 200 mL of THF was added 187.6 g (1.16 mol) of HMDS followed by the dropwise addition of 50.5 g (0.46 mol) of $Me_3SiCl$. The solution was diluted with an equal volume of petroleum ether and filtered through Celite. The solvent was removed, and the residue was distilled (54–57 °C (1.5 mm)) to give 207.6 g (75%) of 10: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 3.02 (s, 2 H, $CH_2$), 2.04 (s, 3 H, $SCH_3$), 0.16 (s, 9 H, $Si(CH_3)_3$); IR (neat) 1718 $cm^{-1}$.

Anal. Calcd for $C_6H_{14}SO_2Si$: C, 40.41; H, 7.91; S, 17.94. Found: C, 41.12; H, 8.00; S, 17.25.

**General Procedure for the Preparation of Silylated Ketene Acetals: Tris(trimethylsilyloxy)ethylene (12).** To a stirred solution of 245 g (1.52 mol) of HMDS in 1.2 L of THF was added over 1.5 h under nitrogen, at 0 °C, 650 mL of 2.4 M *n*-butyllithium in hexane. The solution was then maintained at 45 °C for 30 min. The solution was cooled to −78 °C, and 275 g (1.25 mol) of 6 was added dropwise over a 30-min period. After

the solution was stirred an additional 30 min, 205 g (1.9 mol) of $Me_3SiCl$ was added dropwise. The solution was allowed to warm to room temperature. The solution was poured into 1 L of petroleum ether and filtered through Celite. The solvent was removed, and the residue was redissolved in petroleum ether. The filtration process was repeated. The solvent was removed, and the residue was distilled (54–56 °C (0.1 mm)) to give 366 g (100%) of **12**: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 5.44 (s, 1 H, CH), 0.18 (s, 9 H, $Si(CH_3)_3$), 0.26 (s, 9 H, $Si(CH_3)_3$), 0.22 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 145.07 (C1), 106.50 (C2), 0.74, 0.04, −0.39 (CSi); IR (neat) 1706 $cm^{-1}$.

Anal. Calcd for $C_{11}H_{26}O_3Si_3$: C, 45.15; H, 9.65. Found: C, 45.21; H, 9.74.

**2-Phenoxy-1,1-bis(trimethylsilyloxy)ethylene (13).** By using the above procedure, 90.0 g (0.40 mol) of **7** gave 112.8 g (95%) of **13** after distillation (118–120 °C (1.2 mm)): $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 7.18 (m, 5 H, $C_6H_5$), 5.81 (s, 1 H, CH), 0.42 (s, 9 H, $Si(CH_3)_3$), 0.36 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 147.5 (C1), 108.4 (C2), 158.8, 129.6, 121.5, 115.2 (aromatic), 0.74, 0.28 (CSi); IR (neat) 1703 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{24}O_3Si_2$: C, 56.71; H, 8.16. Found: C, 56.65; H, 8.31.

**2-Methoxy-1,1-bis(trimethylsilyloxy)ethylene (14).** By using the above procedure, 110 g (0.68 mol) of **8** gave 136.7 g (80%) of **14** after distillation (66–69 °C (6 mm)): $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 5.15 (s, 1 H, CH), 3.31 (s, 3 H, $OCH_3$), 0.12 (s, 9 H, $Si(CH_3)_3$), 0.09 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 144.5 (C1), 114.4 (C2), 59.7 (CO), 0.34, −0.17 (CSi); IR (neat) 1709 $cm^{-1}$.

Anal. Calcd for $C_9H_{22}O_3Si_2$: C, 46.11; H, 9.46. Found: C, 45.75; H, 9.38.

**1,2-Dimethoxy-1-(trimethylsilyloxy)ethylene (15).** By using the above procedure, 100 g (0.96 mol) of methyl methoxyacetate (**9**) gave 83 g (49%) of **15** after distillation (68–71 °C (35 mm)). The NMR spectrum of the forerun indicated that it consisted of a considerable amount of product **15** and HMDS: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 5.26 (s, 1 H, CH), 3.42 (s, 6 H, $OCH_3$), 0.19 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 150.0 (C1), 112.5 (C2), 59.9, 55.5 ($OCH_3$), 0.03 (CSi); IR (neat) 1705 $cm^{-1}$; MS calcd for $C_7H_{16}O_3Si$ 176.0869 (found 176.0877).

Anal. Calcd for $C_7H_{16}O_3Si$: C, 47.69; H, 9.15. Found: C, 47.03; H, 9.12.

**2-(Methylthio)-1,1-bis(trimethylsilyloxy)ethylene (16).** By using the above procedure, 178.3 g (1.0 mol) of **10** gave 173.5 g (69%) of **16** after distillation (77–80 °C (1.0 mm)): $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.10 (s, 1 H, CH), 2.00 (s, 3 H, $SCH_3$), 0.16 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 155.4 (C1), 76.1 (C2), 19.0 (CS), 0.40, −0.22 (CSi); IR (neat) 1617 $cm^{-1}$; MS, 250 ($M^+$) $m/e$.

Anal. Calcd for $C_9H_{22}SO_2Si_2$: C, 43.15; H, 8.85; S, 12.80. Found: C, 42.70; H, 8.81; S, 12.51.

**Trimethylsilyl 1,2-Bis(trimethylsilyloxy)-2-decenoate (21).** A mixture of 4.0 g (24.6 mmol) of octanoyl chloride (**19**) and 15.5 g (53.0 mmol) of **12** was heated at 90–95 °C for 2 h. At this time a vacuum was briefly applied and a distillate was collected in a trap maintained at −78 °C. The $^1H$ NMR spectrum of the distillate showed it to be $Me_3SiCl$.

The reaction mixture was fractionally distilled (Vigreux); early fractions consisted of **6**, **12**, and **19**. The major fraction (155–164 °C (3 mm)) consisted of 7.74 g (75%) of **21**: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 2.70 (t, 1 H, $CH_2$, $J$ = 7.3 Hz), 1.35 (m, 10 H, $-(CH_2)_5-$), 0.94 (m, 3 H, terminal $CH_3$), 0.38 (s, 9 H, $Si(CH_3)_3$), 0.28 (s, 9 H, $Si(CH_3)_3$), 0.22 (s, 9 H, $Si(CH_3)_3$); $^{13}C$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 166.36 (C1), 154.99 (C3), 128.89 (C2), 33.17 (C4), 31.93 (C8), 29.41 (C6), 29.24 (C7), 27.93 (C5), 22.70 (C9), 14.11 (C10), 1.03, 0.69, −0.01 (CSi); IR (neat) 1720, 1680 (sh), 1600 $cm^{-1}$; UV (hexane) $\lambda_{max}$ 225 nm (log $\epsilon$ 4.02); MS calcd for $C_{19}H_{42}O_4Si_3$ 418.2391 (found 418.2391).

**General Procedures for the Reaction of Silylated Ketene Acetals with Carboxylic Acid Chlorides. Method A. Thermal Reaction Conditions: 1-Hydroxy-2-nonanone (23).** A mixture of 4.0 g (24.6 mmol) of octanoyl chloride (**19**) and 15.5 g (53.0 mmol) of **12** was heated at 95–100 °C for 4 h. The mixture was allowed to cool, and a mixture of 25 mL of dioxane and 10 mL of 0.6 N HCl was slowly added; an exothermic, vigorous gas evolution ensued. The mixture was maintained at 85 °C for 30 min, cooled, saturated with NaCl, and extracted twice with ether. The ether solution was washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. The residue was distilled (83–85 °C (0.5 mm)), giving 3.28 g (84%) of **23** (see below for data).

**Method B. Stannic Chloride Catalyzed Conditions: 1-Hydroxy-2-nonanone (23).** To a stirred mixture of 4.0 g (24.6 mmol) of octanoyl chloride (**19**) and 15.5 g (53.0 mmol) of **12** was added three drops of $SnCl_4$. An exothermic reaction ensued over a 10-min period, reaching a final temperature of 60 °C. After 1 h, the mixture was slowly poured into a mixture of 25 mL of dioxane and 10 mL of 0.6 N HCl; a rapid gas evolution and exotherm ensued. The mixture was maintained at 90 °C for 10 min, saturated with NaCl, and extracted with ether. The ether solution was washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. Distillation (83–85 °C (0.3 mm)) gave 3.51 g (90%) of **23**: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.25 (s, 2 H, $CH_2OH$), 3.88 (bs, 1 H, OH), 2.41 (t, 2 H, $CH_2CO$, $J$ = 7.0 Hz), 1.82–1.15 (m, 10 H, $-(CH_2)_5-$), 0.88 (m, 3 H, terminal $CH_3$); IR (neat) 3300, 1725 $cm^{-1}$; MS 158 ($M^+$) $m/e$.

Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 68.20; H, 12.14.

**1-Methoxy-2-nonanone (31).** This compound was prepared (method B) from 2.0 g (12.2 mmol) of octanoyl chloride (**19**), 5.77 g (24.6 mmol) of **14**, and 4 drops of $SnCl_4$. After a 2.5-h reaction time and molecular distillation (bath temperature = 100–140 °C (20 mm)), 1.70 g (81%) of **31** was obtained: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.02 (s, 2 H, $OCH_2$), 3.42 (s, 3 H, $OCH_3$), 2.44 (t, 2 H, $CH_2CO$), 1.58, 1.30 (m, 10 H, $-(CH_2)_5-$), 0.88 (m, 3 H, terminal $CH_3$); IR (neat) 1724 $cm^{-1}$.

Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.34; H, 12.08.

**α-Hydroxyacetophenone (35).** This compound was prepared (method A) from 3.93 g (28.0 mmol) of benzoyl chloride (**24**) and 17.0 g (58.1 mmol) of **12** at 95 °C for 4 h. Workup and recrystallization from hexane gave 2.35 g (62%) of **35**, mp 81–84 °C (lit.[1e] mp 85–86 °C). The acetate of this compound was identical with an authentic sample by $^1H$ NMR and TLC.

**α-Phenoxyacetophenone (36).** This compound was prepared (method A) from 3.5 g (24.9 mmol) of **24** and 14.8 g (49.8 mmol) of **13** by heating the mixture at 100–120 °C for 4.25 h. Workup and recrystallization from hexane gave 3.95 g (75%) of **36**: mp 67–68 °C (lit.[1f] mp 73–73.5 °C); $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 8.07–6.92 (m, 10 H, $C_6H_5$), 5.28 (s, 2 H, $CH_2$); IR (KBr) 1709 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.23; H, 5.70. Found: C, 79.11; H, 5.54.

An attempt to prepare **36** by method B (identical quantities of **24** and **13**, 6 drops of $SnCl_4$, 5 h of reaction time) gave no detectable product.

**α-Methoxyacetophenone (39).** This compound was prepared (method B) from 2.0 g (14.2 mmol) of benzoyl chloride (**24**), 6.67 g (28.4 mmol) of **14** and 3 drops of $SnCl_4$. After 24 h of reaction time, workup and molecular distillation gave 1.69 g (79%) of **39**. The $^1H$ NMR and IR spectra of this material were identical with those of an authentic sample (Aldrich).

This reaction was repeated using 3-h reaction time. From the amount and quality of the crude product, a yield of **39** of less than 50% can be estimated.

**1-Hydroxy-3-phenyl-2-propanone (40).** This compound was prepared (method A) from 3.0 g (19.0 mmol) of **25** and 17.0 g (58.2 mmol) of **12** by heating the mixture at 95 °C for 4 h. Workup and recrystallization from hexane gave 2.25 g (81%) of **40**.

Using method B, 2.0 g (12.9 mmol) of **25**, 8.2 g (28.0 mmol) of **12**, and 2 drops of $SnCl_4$ gave 1.47 g (76%) of **40**: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 7.25 (m, 5 H, $C_6H_5$), 4.26 (s, 2 H, $CH_2O$), 3.69 (s, 2 H, $CH_2Co$), 3.00 (bs, 1 H, OH); IR (KBr) 1722 $cm^{-1}$.

Anal. Calcd for $C_9H_{10}O_2$: C, 71.97; H, 6.71. Found: C, 72.15; H, 6.49.

**1-Methoxy-3-phenyl-2-propanone (41).** This compound was prepared (method B) from 2.0 g (12.9 mmol) of **25**, 6.0 g (25.8 mmol) of **14**, and 1 drop of $SnCl_4$. After a 1.5-h reaction time, workup, and molecular distillation (bath temperature 100 °C (1 mm)), 1.87 g (88%) of **41** was obtained: $^1H$ NMR ($CDCl_3$) $\delta_{Me_4Si}$ 7.23 (m, 5 H, $C_6H_5$), 4.00 (s, 2 H, $CH_2O$), 3.71 (s, 2 H, $CH_2CO$), 3.34 (s, 3 H, $OCH_3$).

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.42; H, 7.63.

**1-Phenoxy-2-heptanone (42).** This compound was prepared (method A) from 4.0 g (29.7 mmol) of **26** and 17.6 g (59.4 mmol)

of **13** by heating the mixture at 110 °C for 3 h. Workup and distillation (119–121 °C (0.3 mm)) gave 4.46 g (73%) of **42**: $^1$H NMR ($CDCl_3$) $\delta Me_4Si$ 7.40–6.70 (m, 5 H, $C_6H_5$), 4.51 (s, 2 H, $CH_2O$), 2.56 (t, 2 H, $CH_2CO$), 1.85–1.05 (m, 6 H, $-(CH_2)_3-$), 0.90 (m, 3 H, terminal $CH_3$); MS calcd for $C_{13}H_{18}O_2$ 206.1307 (found 206.1309).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 74.79; H, 8.86.

**6-Bromo-1-hydroxy-2-hexanone (43).** This compound was prepared (method B) from 87.0 g (0.44 mol) of **27**, 191.4 g (0.65 mol) of **12**, and 15 drops of $SnCl_4$. After a 2.5-h reaction time, workup and recrystallization from petroleum ether gave 64.7 g (79%) of **43**: mp 40–42 °C; $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.28 (s, 2 H, $OCH_2$), 3.42 (t, 2 H, $CH_2Br$), 3.10 (bs, 1 H, OH), 2.43 (t, 2 H, $CH_2CO$), 1.80 (m, 4 H, $CH_2CH_2$).

Anal. Calcd for $C_6H_{11}O_2Br$: C, 36.94; H, 5.69. Found: C, 37.29; H, 5.92.

**Cyclohexyl Hydroxymethyl Ketone (44).** This compound was prepared (method A) from 3.0 g (20.4 mmol) of **28** and 12.6 g (42.9 mmol) of **12** by heating the mixture at 100 °C for 4 h. Workup and molecular distillation (bath temperature = 60–70 °C (0.5 mm)) gave 2.05 g (71%) of **44**.

This compound was also prepared by method B, using 1.0 g (6.8 mmol) of **28**, 3.98 g (13.6 mmol) of **12**, and 2 drops of $SnCl_4$ and a 5-h reaction time, to give 0.46 g (48%) of **44**: $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.29 (s, 2 H, $CH_2O$), 3.25 (bs, 1 H, OH), 2.36 (m, 1 H, CHCO), 2.00–1.05 (m, 10 H, $-(CH_2)_5-$); IR (neat) 3420, 1710 $cm^{-1}$.

Anal. Calcd for $C_8H_{14}O_6$: C, 67.58; H, 9.92. Found: C, 67.19; H, 9.97.

**5-Norobornen-2-yl Hydroxymethyl Ketone (45).** This compound was prepared (method A) from 5.0 g (32.0 mmol) of **29** (mixture of isomers) and 20.1 g (68.6 mmol) of **12** by heating the mixture at 95 °C for 4.25 h. Workup and distillation (84–85 °C (0.2 mm)) gave 3.36 g (69%) of **45** as a mixture of isomers: $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 6.18, 5.90 (m, 2 H, olefinic), 4.30, 4.38 (q's, 2 H, $COCH_2$, $J$'s = 16.5 Hz), 3.40–2.65 (m's, 3 H, allylic, CHCO), 3.00 (b s, 1 H, OH), 1.44 (m, 4 H, $CH_2$'s); IR (neat) 3410, 1710 $cm^{-1}$; MS calcd for $C_{13}H_{18}O_2$ 152.0837 (found 152.0832).

**Methyl 2-Methoxy-3-oxodecanoate (32).** This compound was prepared (method B) from 6.0 g (36.9 mmol) of **19**, 13.01 g (73.8 mmol) of **15**, and 6 drops of $SnCl_4$. After a 4-h reaction time, workup and distillation (123–126 °C (2.5 mm)) gave 6.8 g (80%) of **32**: $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 4.27 (s, 1 H, CHO), 3.77 (s, 3 H, $OCH_3$), 3.43 (s, 3 H, $OCH_3$), 2.58 (t, 2 H, $CH_2CO$), 1.24 (m, 10 H, $-(CH_2)_5-$), 0.84 (m, 3 H, terminal $CH_3$); IR (neat) 1754, 1724 $cm^{-1}$; MS calcd for $C_{12}H_{22}O_4$ 230.1518 (found 230.1526).

Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.71; H, 9.73.

**1-(Methylthio)-2-nonanone (33) and *S*-2-Oxononyl Thiooctanoate (34).** A mixture of 3.0 g (18.4 mmol) of octanoyl chloride (**19**) and 9.24 g (36.9 mmol) of **16** was heated at 110 °C for 7 h. Workup according to method A gave after molecular distillation (bath temperature = 90–100 °C (0.1 mm)) 1.93 g (56%) of **33**. The $^1$H NMR spectrum of the pot residue (0.42 g) indicated that it consisted largely of **34** (15%); an analytical sample was obtained by recrystallization from petroleum ether at −78 °C.

The above reaction was repeated by refluxing the reactants in 50 mL of chlorobenzene for 5.5 h. The chlorobenzene was removed at reduced pressure, and the residue was worked up as before, giving 2.75 g (79%) of **33** and 0.32 g (12%) of crude **34**. For **33**: $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 3.20 (s, 2 H, $CH_2S$), 2.63 (t, 2 H, $CH_2CO$), 2.08 (s, 3 H, $CH_3S$), 1.61, 1.32 (m, 10 H, $-(CH_2)_5-$), 0.89 (m, 3 H, terminal $CH_3$); IR (neat) 1715 $cm^{-1}$; MS 188 ($M^+$) $m/e$.

Anal. Calcd for $C_{10}H_{20}SO$: C, 63.78; H, 10.70. Found: C, 63.66; H, 11.09.

For **34**: mp 39–40 °C; $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 3.73 (s, 2 H, $CH_2S$), 2.52 (m, 4 H, $CH_2CO$), 1.80–1.20 (m, 20 H, $-(CH_2)_5-$), 0.94 (m, 6 H, terminal $CH_3$'s); IR (KBr) 1718, 1694 $cm^{-1}$; MS 300 ($M^+$) $m/e$.

Anal. Calcd for $C_{17}H_{32}O_2S$: C, 67.95; H, 10.73; S, 10.67. Found: C, 67.55; H, 10.97; S, 10.34.

**α-(Methylthio)acetophenone (37) and *S*-Benzoylmethyl Thiobenzoate (38).** A mixture of 3.5 g (24.9 mmol) of benzoyl chloride (**24**) and 12.5 g (49.8 mmol) of **16** was heated under argon at 115 °C for 5 h. Workup according to method A gave after molecular distillation (bath temperature = 120–125 °C (1.2 mm)) 2.34 g (57%) of **37**. The TLC and $^1$H NMR spectrum of the pot residue (0.66 g) indicated that it consists mostly of **38** (21%); an analytical sample was obtained by recrystallization from hexane–ether 10:1 at −78 °C.

This reaction was repeated by refluxing the reactants in 50 mL of chlorobenzene and working up the reaction mixture as before; no improvement in the yield of **37** was obtained. For **37**: $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 8.25–7.35 (m, 5 H, $C_6H_5$), 3.68 (s, 2 H, $CH_2S$), 2.10 (s, 3 H, $CH_3S$); IR (neat) 1675 $cm^{-1}$; MS 166 ($M^+$) $m/e$.

Anal. Calcd for $C_9H_{10}OS$: C, 65.03; H, 6.06. Found: C, 64.64; H, 6.07.

For **38**: mp 79–80 °C; $^1$H NMR ($CDCl_3$) $\delta_{Me_4Si}$ 8.15–7.30 (m, 10 H, aromatic), 4.61 (s, 2 H, $CH_2S$); IR (KBr) 1699, 1663 $cm^{-1}$; MS 256 ($M^+$) $m/e$.

Anal. Calcd for $C_{15}H_{12}O_2S$: C, 70.29; H, 4.72; S, 12.51. Found: C, 70.26; H, 4.99; S, 12.46.

**Acknowledgment.** We wish to thank Mr. L. Brancone and staff for microanalyses, M. G. Morton, Dr. R. T. Hargreaves, Dr. G. J. Jordan, and staff for spectral data, and Drs. C. V. Grudzinskas and M. B. Floyd for helpful discussions.

**Registry No.** **6**, 33581-77-0; **7**, 21273-08-5; **8**, 63591-12-8; **9**, 6290-49-9; **10**, 71616-95-0; **12**, 69097-20-7; **13**, 71616-96-1; **14**, 71616-97-2; **15**, 71616-98-3; **16**, 71616-99-4; **19**, 111-64-8; **21**, 71617-00-0; **23**, 1072-08-8; **24**, 98-88-4; **25**, 103-80-0; **26**, 142-61-0; **27**, 4509-90-4; **28**, 2719-27-9; *endo*-**29**, 37750-50-8; *exo*-**29**, 34733-86-3; **31**, 925-50-8; **32**, 71617-01-1; **33**, 71617-02-2; **34**, 71617-03-3; **35**, 582-24-1; **36**, 721-04-0; **37**, 5398-93-6; **38**, 49742-23-6; **39**, 4079-52-1; **40**, 4982-08-5; **41**, 29417-89-8; **42**, 71617-04-4; **43**, 69097-19-4; **44**, 6004-53-1; *endo*-**45**, 52747-94-1; *exo*-**45**, 52747-95-2; methoxyacetic acid, 625-45-6; methylthioacetic acid, 2444-37-3; glycolic acid, 79-14-1; HMDS, 1450-14-2; $Me_3SiCl$, 75-77-4; phenoxyacetic acid, 122-59-8.