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New Methods for Stereoselective Synthesis of α-Alkylidene-γ-butyrolactones Using Monoanion of *O*-Ethyl *S*-(Tetrahydro-2-oxo-3-furanyl) Thiocarbonate and Dianion of α-Mercapto-γ-butyrolactone

Kazuhiko Tanaka,* Hideki Uneme, Nobuyuki Yamagishi,
Rikuhei Tanikaga, and Aritsune Kaji
Department of Chemistry, Faculty of Science, Kyoto University, Sakyo-ku, Kyoto 606

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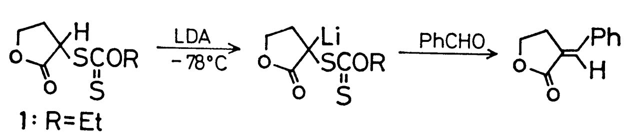
The lithium enolates of *O*-ethyl *S*-(tetrahydro-2-oxo-3-furanyl) dithiocarbonate and thiocarbonate were found to be efficient reagents for the stereoselective synthesis of α-alkylidene-γ-butyrolactones from carbonyl compounds. The dianion of α-mercapto-γ-butyrolactone was successfully generated by treatment of α-mercapto-γ-butyrolactone with 2.2 equivalents of lithium diisopropylamide in the presence of *N,N,N′,N′*-tetramethylethylenediamine at −78°C in THF. The dianion thus formed has been utilized for the efficient and stereoselective synthesis of α-alkylidene-γ-butyrolactones from carbonyl compounds.

Much attention has been focused on the synthesis of α-methylene-γ-butyrolactone (dihydro-3-methylene-2(3*H*)-furanone) and α-alkylidene-γ-butyrolactones (3-alkylidenedihydro-2(3*H*)-furanone) since these compounds serve as useful intermediates in organic synthesis[1] and constitute the biologically active natural products.[2] Since carbonyl compounds such as aldehydes and ketones are readily available in organic synthesis, the direct procedure for the preparation of these unsaturated lactones from carbonyl compounds is very attractive. Several methods have been reported for the direct introduction of an alkylidene group α to a γ-butyrolactone. These have included (1) the base-catalyzed condensation of γ-butyrolactone with aldehydes[3] and (2) the reaction of aldehydes with the anion of α-triphenylphosphoranylidene-γ-butyrolactone,[4] the anion of diethyl (tetrahydro-2-oxo-3-furanyl)phosphonate,[5] or the anion of α-trimethylsilyl-γ-butyrolactone.[6] However, there has been no general method for the stereoselective introduction of an alkylidene moiety onto the α-position of γ-butyrolactone.

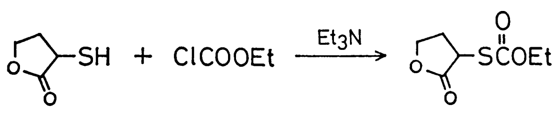
We have reported in the preliminary communications[7,8] that lithium enolates of *O*-ethyl *S*-(tetrahydro-2-oxo-3-furanyl) dithiocarbonate and the corresponding thiocarbonate as well as the dianion of α-mercapto-γ-butyrolactone are useful and convenient reagents for the direct synthesis of α-alkylidene-γ-butyrolactones with high stereoselectivity. This report will provide, in greater detail, the scope and limitations of these useful and stereoselective α-ylidenation of γ-butyrolactone.

Results and Discussion

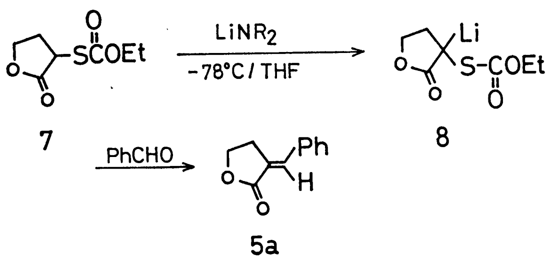
Lithium Enolates of O-*Ethyl* S-*(Tetrahydro-2-oxo-3-furanyl) Dithiocarbonate and Thiocarbonate.* Treatment of *O*-ethyl *S*-(tetrahydro-2-oxo-3-furanyl) dithiocarbonate (**1**)[9] with lithium diisopropylamide (LDA) at −78 °C in THF produced the yellow solution of lithium enolate **4**, which reacted with benzaldehyde to afford exclusively (*E*)-α-benzylidene-γ-butyrolactone (**5a**)[5] in 60% isolated yield. The starting material **1** can easily be prepared by the addition of α-bromo-γ-butyrolactone to potassium *O*-ethyl dithiocarbonate in ethanol. Attempts to purify the dithiocarbonate **1** by distillation, however, failed due to decomposition. This material can be purified by column chromatography on silica gel using benzene as eluent, but the procedure is unsuitable for the large scale preparation of **1**. Attempts to transform the dithiocarbonate **1** into the volatile liquid or the readily crystallizable material by preparing *O*-methyl *S*-(tetrahydro-2-oxo-3-furanyl) dithiocarbonate (**2**) or *O*-isopropyl analogue **3** were also fruitless. We have found that a monothiocarbonate (**7**), readily prepared from α-mercapto-γ-butyrolactone (**6**)[10] and ethyl chloroformate in high yield, can be easily purified by distillation. Reaction of **7** with lithium amide afforded the enolate **8** which smoothly reacted with benzaldehyde to give exclusively (*E*)-**5a**. Among the various lithium amides examined, lithium diethylamide is the most efficient base for converting thiocarbonate **7** into the enolate **8** as shown in Table 1. To show the generality of this method, a series of carbonyl compounds was utilized for α-ylidenation of γ-butyrolactone. In all cases examined, (*E*)-isomers were obtained predominantly. The *E*/*Z* ratio of a product **5** was determined by NMR and GLC analysis. For example, the ^{1}H-NMR spectrum of **5b** shows the vinyl proton β to the carbonyl



1: R=Et
2: R=Me
3: R=i-Pr
4: R=Et
5a



6
7 (91%)



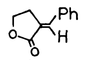
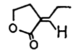
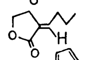
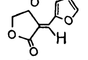
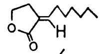
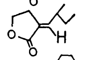
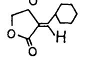
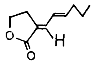
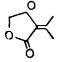
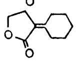
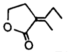
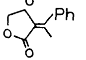
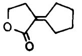
7
8
5a

TABLE 1. EFFECT OF LITHIUM AMIDE IN THE REACTION OF **7** WITH BENZALDEHYDE

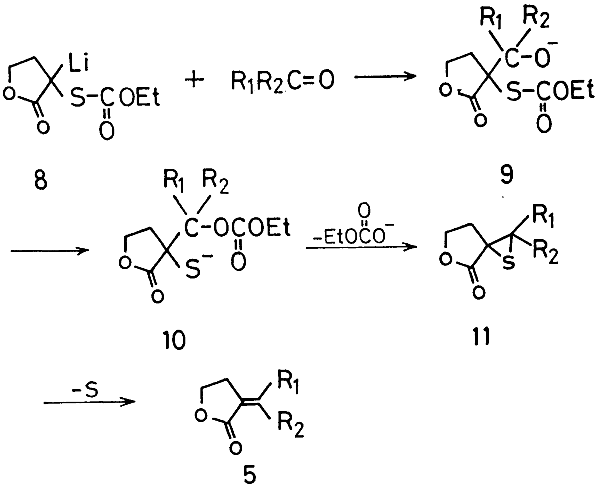
Lithium amide	% Yield of **5a**
$(i\text{-Pr})_2NLi$	53
$(i\text{-Pr})_2NLi$-TMEDA	54
$(Me_3Si)_2NLi$	39
Et_2NLi	84

at δ 6.48 for *E*-isomer and at δ 6.00 for *Z*-isomer, respectively. Integration of the vinyl proton gave a 93: 7 mixture of *E*-**5b** and *Z*-**5b**, being identical with the ratio obtained by GLC analysis (*E*/*Z*=94/6). The reaction appears to follow the pathway outlined in Scheme 1. The lithium reagent **8** attacks at the carbonyl carbon leading to **10** with transfer of the ethoxycarbonyl group from sulfur to oxygen. The intramolecular displacement affords a thiirane **11** which loses sulfur to give α-alkylidene-γ-butyrolactone (**5**). The extrusion of sulfur from thiiranes having electron-attracting substituents such as alkoxycarbonyl or cyano groups is a well-recognized process.[11,12]

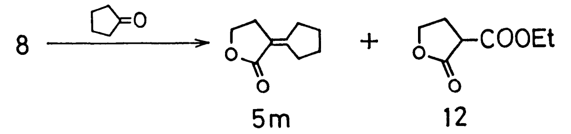
TABLE 2. SYNTHESIS OF α-ALKYLIDENE-γ-BUTYROLACTONES FROM *O*-ETHYL *S*-(TETRAHYDRO-2-OXO-3-FURANYL) THIOCARBONATE (**7**) AND CARBONYL COMPOUNDS

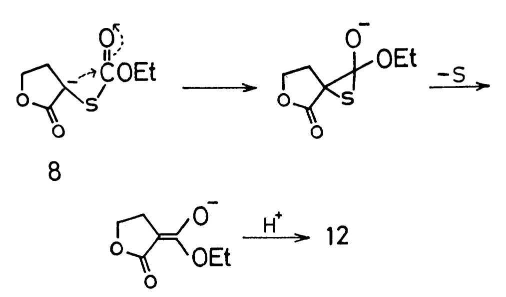
Carbonyl compound	(mmol)	Product (5)		Yield %	E/Z ratio
Benzaldehyde	25		(5a)	84	100/0
Propanal	26		(5b)	78	94/6
Butanal	25		(5c)	76	95/5
2-Furancarbaldehyde	25		(5d)	75	100/0
Heptanal	25		(5e)	83	94/6
2-Methylbutanal	26		(5f)	93	85/15
Cyclohexanecabaldehyde	25		(5g)	82	92/8
(E)-2-Hexenal	25		(5h)	76	91/9
Acetone	26		(5i)	75	
Cyclohexanone	25		(5j)	65	
2-Butanone	25		(5k)	59	48/52
Acetophenone	25		(5l)	22	100/0
Cyclopentanone	25		(5m)	16	

Stability of Lithium Enolate 8. In the case of cyclopentanone, we obtained 39% of α-ethoxycarbonyl-γ-butyrolactone (**12**)[13] in addition to 16% of α-cyclopentylidene-γ-butyrolactone (**5m**). This result suggests that the self-rearrangement of lithium enolate **8** takes place competitively. In order to examine the stability of lithium reagent **8**, the thiocarbonate **7** was treated with 1.1 equiv of lithium diethylamide in THF at −78 °C, allowed to reach room temperature, and then quenched with saturated aqueous ammonium chloride solution. Upon workup, the lactone **12** was isolated in 45% yield. This transformation appears to involve the formation of a thiirane by intramolecular cyclization, followed by expulsion of sulfur.

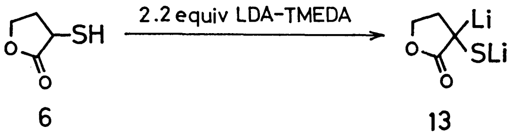


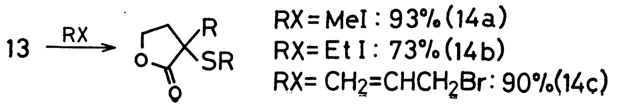
Scheme 1.



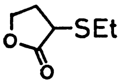


Dianion of α-Mercapto-γ-butyrolactone. The dianion of α-mercapto-γ-butyrolactone (**6**) is readily produced under mild conditions. Thus, treatment of **6** with 2.2 equiv of LDA in the presence of 2.2 equiv of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) in THF at −78 °C generated the dianion **13**, which afforded the dialkylated products (**14**) in high yields upon quenching





with excess of alkyl halides. The yield of the dialkylated compound (**14b**), however, decreased to 73% when ethyl iodide was used, providing a significant amount of the mono-alkylated derivatives, α-ethylthio-γ-butyrolactone (**15**) (22%). The dimethylated product **14a** can be converted into α-methylene-γ-butyrolactone (Tulipalin A, **17**) by the reported procedure.[14)] Thus, oxidation of **15a** and dehydrosulfenylation of **16** afforded Tulipalin A (**17**) and **18** in a ratio of 15: 85. The dianion **13** is highly reactive toward carbonyl compounds. Thus, treatment of **13** with carbonyl compounds at −78 °C and subsequent treatment of the reaction mixture with ethyl chloroformate gave predominantly (*E*)-α-alkylidene-γ-butyrolactones (**5**) in good yields. The scope of this experimentally simple synthesis of **5** is illustrated in Table 3. This reaction can be applied to a variety of aliphatic, aromatic, and heteroaromatic aldehydes, as well as α,β-unsaturated aldehydes, and afforded the desired products in moderate to good yields. However, the reaction of the dianion **13** with gaseous formaldehyde gave a disappointing yield of 7% for α-methylene-γ-butyrolactone (**5n**), probably due to polymerization of formaldehyde.



15

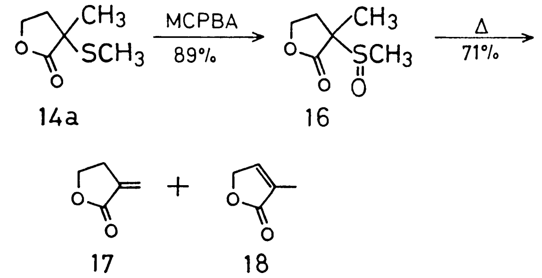
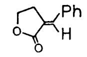
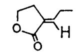
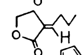
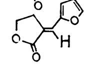
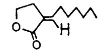
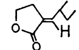
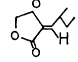
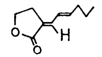
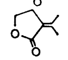
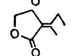
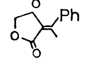
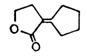
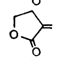
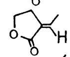
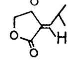
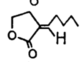
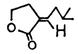
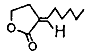
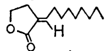
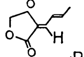
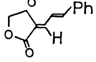
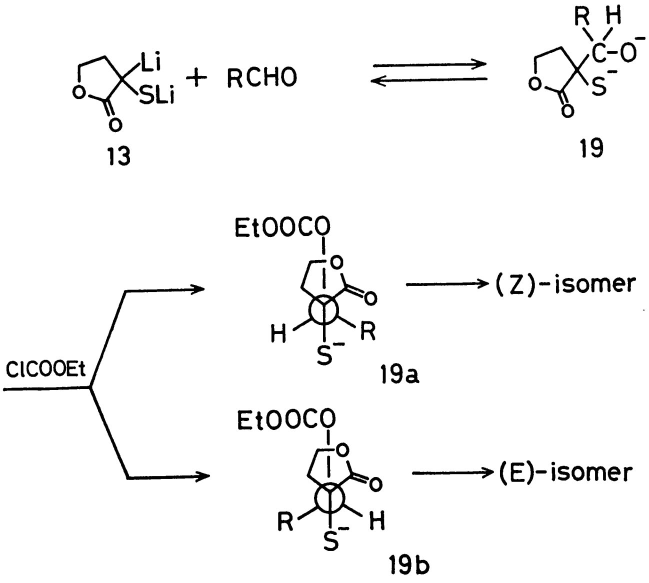


TABLE 3. SYNTHESIS OF α-ALKYLIDENE-γ-BUTYROLACTONES FROM DIANION (**13**) AND CARBONYL COMPOUNDS

Carbonyl compound	(mmol)	Product (5)		Yield %	E/Z ratio
Benzaldehyde	40		(5a)	54	100/0
Propanal	22		(5b)	36	92/8
Butanal	25		(5c)	61	97/3
2-Furancarbaldehyde	40		(5d)	57	100/0
Heptanal	30		(5e)	67	92/8
2-Methylbutanal	40		(5f)	51	93/7
2-Methylbutanal	25		(5f)	43	96/4[a)]
(E)-2-Hexenal	40		(5h)	45	78/22
Acetone	50		(5i)	50	
2-Butanone	50		(5k)	49	50/50
Acetophenone	50		(5l)	40	100/0
Cyclopentanone	25		(5m)	43	
Formaldehyde	30		(5n)	7	
Acetaldehyde	25		(5o)	30	92/8
2-Methylpropanal	25		(5p)	61	95/5
Pentanal	40		(5q)	69	95/5
3-Methylbutanal	30		(5r)	64	95/5
Hexanal	25		(5s)	64	97/3
Nonanal	25		(5t)	69	94/6
(E)-2-Butenal	40		(5u)	40	88/12
(E)-3-Phenyl-3-propenal	40		(5v)	38	b

a) Lithium diethylamide was used as a base. b) Not determined.

As can be seen from the data listed in Tables 2 and 3, the predominant geometry of the α-alkylidene unsaturation in **5** is *E* configuration. Such a result can be rationalized by considering the conformations of two possible stereoisomeric precursors (**19a** and **19b**) leading to **5** as shown in Scheme 2. In both cases, if the conformation, in which the OCO_2Et and S^- groups are anti-periplanar, is favorable one for the subsequent intramolecular attack of S^- group and elimination of the $^-OCO_2Et$ species, the orientation of R group is represented as **19a** and **19b**, respectively. The equilibrium between the stereoisomers **19a** and **19b**, if present with or without the participation of the *S*-ethoxycarbonylated derivative such as **9**, would surely favor **19b**, since the steric interaction between a bulky R group and a lactone carbonyl is minimized in **19b**. On the other hand, the stereoisomer **19a**, in which the alkyl and carbonyl group are *gauche*, would exhibit severe

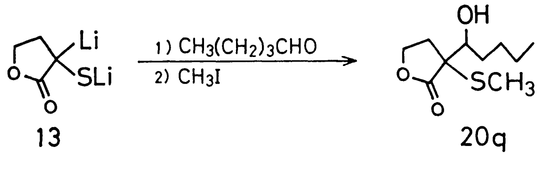


Scheme 2.

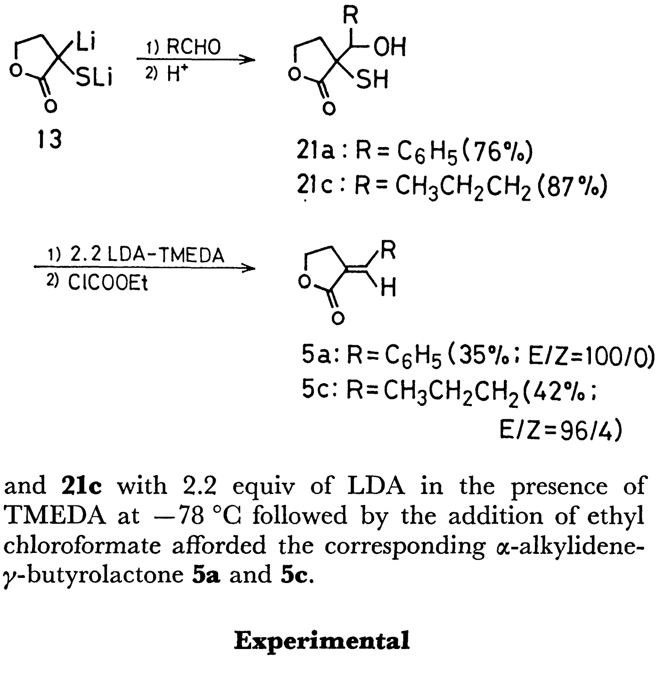
interactions. Thus, the *E*-isomer of α-alkylidene-γ-butyrolactone predominates.

In the case of the reaction of the carbanion **8** with carbonyl compounds, the predominant formation of the *E*-isomer is also explained by the same argument.

Evidence for the adduct **19** rests on quenching the reaction mixture of **13** and pentanal at −78 °C with methyl iodide and isolating the lactone **20q** in 84% yield. The ^{1}H-NMR spectrum of **20q** shows a doublet at δ 2.10 which indicates a mixture of diastereoisomers. An attempt to determine the ratio of this mixture by gas chromatography, however, failed due to decomposition.



When the reaction mixture of **13** and an aldehyde was quenched with saturated aqueous ammonium chloride solution at −78 °C, the adduct **21** was obtained in good yield as shown below. Reaction of adduct **21a** and **21c** with 2.2 equiv of LDA in the presence of TMEDA at −78 °C followed by the addition of ethyl chloroformate afforded the corresponding α-alkylidene-γ-butyrolactone **5a** and **5c**.



Experimental

General. Melting points were determined with a Yanagimoto melting point apparatus and are uncorrected. Boiling points were determined during distillation and are uncorrected. Nuclear magnetic resonance spectra were determined on a JEOL Model PS-100 spectrometer. Chemical shifts are given in δ units, part per million relative to tetramethylsilane as internal standard. Infrared spectra were determined on a Hitachi Model 215 spectrophotometer. Gas chromatograms were obtained using a Varian Aerograph Model 920 instrument with a 0.15 cm × 120 cm glass column (20% Silicone DC-550 on Celite 545). Mass spectra were determined on a Hitachi Model M-52 mass spectrometer. Tetrahydrofuran (THF) was dried by distillation from calcium hydride and by subsequent distillation from lithium aluminum hydride under a nitrogen atmosphere. Diisopropylamine, diethylamine, and *N,N,N',N'*-tetramethylethylenediamine were distilled from calcium hydride and stored over molecular sieves. All reactions were performed under a nitrogen atmosphere. The glassware was dried by flaming in a nitrogen stream.

Preparation of O-*Ethyl* S-*(Tetrahydro-2-oxo-3-furanyl) Dithiocarbonate (1).* To an ethanol solution of freshly prepared potassium *O*-ethyl dithiocarbonate (0.167 mol) was added a solution of 25 g (0.152 mol) of α-bromo-γ-butyrolactone in 100 ml of ethanol at 0 °C. After the reaction mixture was stirred for 7 h at room temperature, the ethanol was removed under reduced pressure, the residue was extracted with ether three times, washed, and dried (anhydrous Na_2SO_4), and evapoarated to give **1** as a viscous yellow oil which was unstable toward distillation. The crude product was chromatographed twice on silica gel using benzene as eluent to give an analytical sample of dithiocarbonate **1**: ^{1}H-NMR(CCl_4) δ 4.60 (q, J=7 Hz, 2H, CH_2O), 4.30 (m, 3H, CH_2 and CH), 2.00—3.00 (m, 2H, CH_2), 1.40 (t, J=7 Hz, 3H, CH_3). IR (neat); 2990, 1775, 1220, 1040 cm^{-1}. Found: C, 40.63; H, 5.03%. Calcd for $C_7H_{10}O_3S_2$: C, 40.76; H, 4.89%.

*Synthesis of α-Benzylidene-γ-butyrolactone Using Lithium Enolate **4**.* To a solution of diisopropylamine (3.4 ml, 20 mmol) in 40 ml of THF at −78 °C was added butyllithium (20 mmol, 14 ml, 1.43 mol dm^{-3} in hexane) over 5 min. After the resulting pale yellow solution was stirred at −78 °C for 20 min, a solution of 4.13 g (20 mmol) of *O*-ethyl *S*-(tetrahydro-2-oxo-3-furanyl) dithiocarbonate (**1**) in 5 ml of THF was added over 6 min. After 30 min, a solution of 2.33 g (20 mmol) of benzaldehyde in 3 ml of THF was added over 2 min. The reaction mixture was stirred at −78 °C for 2 h and at room temperature for 1 h before quenching with saturated aqueous ammonium chloride solution (10 ml) and 0.6 mol dm^{-3} hydrochloric acid (100 ml). The resulting mixture was extracted four times with 50 ml portions of ether. The combined organic extracts were washed three times with saturated aqueous sodium chloride solution, dried (Na_2SO_4), and concentrated. Silica gel chromatography (benzene) gave 2.10 g (60%) of α-benzylidene-γ-butyrolactone, mp 117.5—118.5 °C. The product was identified by comparison of ^{1}H-NMR spectrum with the corresponding data from independently synthesized material.[8)]

Preparation of O-*Ethyl* S-*(Tetrahydro-2-oxo-3-furanyl) Thiocarbonate (7).* To a mixture of 13 g (0.11 mol) of α-mercapto-γ-butyrolactone[10)] (**6**) and 11.9 g (0.11 mol) of ethyl chloroformate in 80 ml of dry benzene at 0 °C was added a solution of 11.1 g (0.11 mol) of dry triethylamine in 20 ml of dry benzene. When addition was complete, the ice-bath was removed, and reaction mixture was stirred at room temperature for 2 h. Product isolation gave an oil that was distilled twice (bp 122 °C/0.6 Torr) (1 Torr=133.322 Pa), afforded 19 g (91%) of **7**: ^{1}H-NMR(CCl_4) δ 4.30 (q, J=7 Hz, 2H, CH_2), 4.20 (m, 2H, CH_2O), 4.00 (t, J=9 Hz, 1H, CH), 2.80 (m, 1H), 2.42 (m, 1H), 1.36 (t, J=7 Hz, 3H, CH_3). IR (neat); 2990, 1790, 1727, 1160, 1010 cm^{-1}. Found: C, 44.07; H, 5.45%. Calcd for $C_7H_{10}O_4S$: C, 44.20; H, 5.30%.

Reaction of Lithium Enolate of 7 with Carbonyl Compounds.
General Procedure: Lithium diethylamide (22 mmol) was prepared as usual in 40 ml of THF at −78 °C. After 20 min, a solution of 3.80 g (20 mmol) of *O*-ethyl *S*-(tetrahydro-2-oxo-3-furanyl) thiocarbonate (**7**) in 5 ml of THF was added over a period of 3 min. After stirring at −78 °C for 1 h, a solution of a carbonyl compound (25 mmol) in 3 ml of THF was added. The reaction mixture was stirred at −78 °C for 2 h and then at room temperature for 1 h. The reaction mixture was poured into a separatory funnel containing 100 ml of 0.6 mol dm^{-3} hydrochloric acid and extracted four times with 50 ml portions of ether. The extracts were washed

with saturated sodium chloride solution, dried (Na_2SO_4), and evaporated. The crude product was purified by distillation and/or column chromatography over silica gel.

Decomposition of Lithium Enolate 8. The lithium enolate **8** was generated as usual from 3.80 g (20 mmol) of **7** and 22 mmol of lithium diethylamide in 40 ml of THF. After stirring at −78 °C for 1 h, the cooling bath was removed, and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched by adding 10 ml of saturated aqueous ammonium chloride solution. Product isolation gave 1.42 g (45%) of α-ethoxycarbonyl-γ-butyrolactone (**12**): bp 105—110 °C/1.5 Torr (lit,[13] bp 175 °C/25 Torr); ^{1}H-NMR(CCl_4) δ 4.0—4.5 (m, 4H, CH_2 and CH_2O), 3.47 (t, J=9 Hz, 1H, CH), 2.4—2.7 (m, 2H, CH_2), 1.32 (t, J=7 Hz, 3H, CH_3); IR(neat); 1770(COO), 1730(COO) cm^{-1}; MS(20 eV) *m/e* (relative intensity) 158 (M^+, 2), 86 (100). Found: C, 52.97; H, 6.54%. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37%.

Generation of Dianion of α-Mercapto-γ-butyrolactone (6) and Dialkylation. In a nitrogen atmosphere, 44 mmol of butyllithium was added to a solution of 4.5 g (44 mmol) of diisopropylamine and 5.1 g (44 mmol) of TMEDA in 40 ml of THF at −78 °C. After stirring at −78 °C for 20 min, a solution of 2.4 g (20 mmol) of α-mercapto-γ-butyrolactone (**6**) in 7 ml of THF was added slowly with a syringe. After stirring for 1 h at −78 °C, 11.4 g (80 mmol) of methyl iodide was added. The reaction mixture was stirred for 30 min and then at room temperature for 1 h. To this was added 10 ml of saturated aqueous ammonium chloride solution, and the mixture was poured into 0.6 mol dm^{-3} hydrochloric acid (100 ml) and extracted four times with ether. The ether extracts were washed twice with saturated aqueous sodium chloride solution, dried (Na_2SO_4), and concentrated. The residue was distilled to give 2.7 g (93%) of α-methyl-α-methylthio-γ-butyrolactone (**14a**)[14]: bp 80—81 °C/2.5 Torr; ^{1}H-NMR (CCl_4) δ 4.24 (m, 2H, CH_2O), 2.0—2.5 (m, 2H, CH_2), 2.13 (s, 3H, SCH_3), 1.51 (s, 3H, CH_3). IR (neat); 1760 (COO) cm^{-1}. Similar procedures to the above were used for diethylation and diallylation.

α-Ethyl-α-ethylthio-γ-butyrolactone (14b): Bp 77—80 °C/0.75 Torr; ^{1}H-NMR(CCl_4) δ 4.2—4.5 (m, 2H, CH_2O), 1.5—2.8 (m, 6H, $3CH_2$), 1.23 (t, J=7 Hz, 3H, CH_3), 1.02 (t, J=7 Hz, 3H, CH_3); MS(20 eV) *m/e* (relative intensity) 174 (M^+, 6), 114 (100). IR (neat); 1760 (COO) cm^{-1}. Found: C, 55.43; H, 8.45%. Calcd for $C_8H_{14}O_2S$: C, 55.14; H, 8.10%.

α-Ethylthio-γ-butyrolactone (15): ^{1}H-NMR (CCl_4) δ 4.2—4.5 (m, 2H, CH_2O), 3.3—3.5 (m, 1H, CH), 1.9—3.0 (m, 4H, $2CH_2$), 1.30 (t, J=7 Hz, 3H, CH_3). IR (neat); 1765 (COO) cm^{-1}. MS (20 eV) *m/e* (relative intensity) 146 (M^+, 26), 86 (100).

α-(2-Propenyl)-α-(2-propenylthio)-γ-butyrolactone (14c): Bp 93—95 °C/0.75 Torr; ^{1}H-NMR (CCl_4) δ 5.5—6.0 (m, 2H, 2CH=C), 4.9—5.4 (m, 4H, $2CH_2$=C), 4.0—4.5 (m, 2H, CH_2O), 3.1—3.5 (m, 2H, SCH_2), 2.55 (d, J=7 Hz, 2H, CH_2), 1.9—2.5 (m, 2H, β-CH_2). MS (20 eV) *m/e* (relative intensity) 198 (M^+, 2), 126 (100). IR (neat); 1760 (COO), 1640 (C=C) cm^{-1}. Found: C, 60.46; H, 7.32%. Calcd for $C_{10}H_{14}O_2S$: C, 60.58; H, 7.12%.

Preparation of α-Alkylidene-γ-butyrolactones from Dianion 13 and Carbonyl Compounds. The example of benzaldehyde is given here as a typical experiment. To a magnetically stirred solution of the dianion **13** prepared from 44 mmol of LDA and 44 mmol of TMEDA in 40 ml of THF at −78 °C was added a solution of benzaldehyde (40 mmol) in 3 ml of THF. Stirring was continued at −78 °C for 2 h and then a solution of ethyl chloroformate (2.2 g, 20 mmol) in dry THF (5 ml) was added dropwise at −78 °C. The reaction mixture was stirred at −78 °C for 30 min and the cooling bath was removed. After 1 h the reaction mixture was quenched with saturated aqueous ammonium chloride solution (10 ml) and extracted with ether (4×50 ml). The combined ether extracts were washed with brine, saturated $NaHCO_3$ solution, and brine. The dried (Na_2SO_4) solvent were removed and the residue was purified by column chromatography (silica gel, chloroform) to afford pure **5a** (1.89 g, 54%) as colorless crystals.

Physical Properties of α-Alkylidene-γ-butyrolactones. The analytical samples were obtained by silica gel chromatography and/or distillation.

(E)-α-Benzylidene-γ-butyrolactone (5a): Recrystallization from ethanol–acetone afforded an analytical sample of **5a**. Mp 117.5—118.5 °C (lit,[5] mp 118.5 °C). ^{1}H-NMR ($CDCl_3$) δ 7.2—7.6 (m, 6H, aromatic and CH=C), 4.46 (t, J=6.8 Hz, 2H, CH_2O), 3.25 (dt, J=6.8, 3 Hz, 2H, CH_2); ^{1}H-NMR (C_6D_6) δ 7.59 (t, J=3 Hz, 1H, CH=C), 7.12 (s, 5H, aromatic), 3.65 (t, J=6.5 Hz, 2H, CH_2O), 2.28 (dt, J=6.5, 3 Hz, 2H, CH_2). IR (KBr pellet); 1740 (COO), 1650 (C=C) cm^{-1}. MS (20 eV) *m/e* 174 (M^+). Found: C, 75.55; H, 5.78%. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79%.

α-Propylidene-γ-butyrolactone (5b): Bp 70—75 °C/0.6 Torr. (lit,[5] bp 60 °C/0.5 Torr). The *E*- and *Z*-isomers of **5b** were separated by gas chromatography. *E*-Isomer: ^{1}H-NMR (CCl_4) δ 6.48 (m, 1H, CH=C), 4.22 (t, J=7 Hz, 2H, CH_2O), 2.80 (m, 2H, CH_2), 2.20 (m, 2H, CH_2), 1.10 (t, J=7 Hz, 3H, CH_3). MS (20 eV) *m/e* 126 (M^+). IR (neat); 1750 (COO), 1680 (C=C) cm^{-1}. *Z*-Isomer: ^{1}H-NMR (CCl_4) δ 6.0 (m, 1H, CH=C), 4.2 (t, J=7 Hz, 2H, CH_2O), 2.8 (m, 4H, $2CH_2$), 1.0 (t, J=7 Hz, 3H, CH_3). MS (20 eV) *m/e* 126 (M^+). IR (neat); 1750 (COO), 1670 (C=C) cm^{-1}.

α-Butylidene-γ-butyrolactone (5c):[15] Bp 88—94 °C/0.8 Torr. ^{1}H-NMR (CCl_4) δ 6.12 (m, 0.05H, CH=C for *Z*-isomer), 6.53 (m, 0.95H, CH=C for *E*-isomer), 4.27 (t, J=7 Hz, 2H, CH_2O), 2.84 (m, 2H, CH_2), 2.18 (m, 2H, CH_2), 1.2—1.7 (m, 2H, CH_2), 0.98 (t, J=7 Hz, 3H, CH_3). MS (20 eV) *m/e* 140 (M^+). IR (neat); 1755 (COO), 1680 (C=C) cm^{-1}. Found: C, 68.18; H, 8.57%. Calcd for $C_8H_{12}O_2$: C, 68.53; H, 8.63%.

α-(2-Furylmethylene)-γ-butyrolactone (5d): Mp 94—95 °C (lit,[4a] mp 91—92 °C). ^{1}H-NMR ($CDCl_3$) δ 7.54 (m, 1H, furan), 7.30 (m, 1H, CH=C), 6.6 (m, 2H, furan), 4.42 (t, J=7 Hz, 2H, CH_2O), 3.26 (m, 2H, CH_2). MS (20 eV) *m/e* 164 (M^+). IR (KBr pellet); 1730 (COO), 1645 (C=C) cm^{-1}. Found: C, 66.07; H, 5.10%. Calcd for $C_9H_8O_3$: C, 65.85; H, 4.91%.

α-Heptylidene-γ-butyrolactone (5e): Bp 108—112 °C/0.4 Torr. ^{1}H-NMR (CCl_4) δ 6.52 (m, 1H, CH=C), 4.26 (t, J=7 Hz, 2H, CH_2O), 2.83 (m, 2H, CH_2), 2.18 (m, 2H, CH_2), 1.2—1.6 (m, 8H, $4CH_2$), 0.09 (m, 3H, CH_3). MS (20 eV) *m/e* 182 (M^+). IR (neat); 1760 (COO), 1680 (C=C) cm^{-1}. Found: C, 72.31; H, 9.65%. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95%.

α-(2-Methylbutylidene)-γ-butyrolactone (5f): Bp 80—85 °C/0.6 Torr. ^{1}H-NMR (CCl_4) δ 6.25 (m, 1H, CH=C for *E*-isomer), 5.8 (m, CH=C for *Z*-isomer), 4.2 (t, J=7 Hz, 2H, CH_2O), 2.80 (m, 2H, CH_2), 2.2 (m, 1H, CH), 1.1—1.6 (m, 2H, CH_2), 0.7—1.1 (m, 6H, $2CH_3$). IR (neat); 1760 (COO), 1680 (C=C) cm^{-1}. Found: C, 70.18; H, 9.25%. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15%.

α-(Cyclohexylmethylene)-γ-butyrolactone (5g): Bp 110—111 °C/0.5 Torr. ^{1}H-NMR (CCl_4) δ 6.33 (dt, J=9.5, 2.7 Hz, 1H, CH=C), 4.25 (t, J=7 Hz, 2H, CH_2), 2.86 (dt, J=7, 2.7 Hz, 2H, CH_2), 2.20 (m, 1H), 0.7—1.9 (m, 10H). MS (20 eV) *m/e* 180 (M^+). IR (neat); 1760 (COO), 1680 (C=C) cm^{-1}.

α-[(E)-2-Hexenylidene]-γ-butyrolactone (5h): Bp 113—115 °C/0.8 Torr. The *E*- and *Z*-isomers of **5h** were separated by silica gel chromatography using benzene as eluent. *E*-Isomer: ^{1}H-NMR (CCl_4) δ 6.9 (m, 1H, CH=C), 5.9—6.3 (m, 2H, CH=C), 4.03 (t, $J=7$ Hz, 2H, CH_2O), 2.93 (m, 2H, CH_2), 2.20 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 0.96 (t, $J=7$ Hz, 3H, CH_3). MS (20 eV) *m/e* 166 (M^+). IR (neat); 1750 (COO), 1650 (C=C) cm^{-1}. *Z*-Isomer: ^{1}H-NMR (CCl_4) δ 7.2—7.6 (m, 1H, CH=C), 6.45 (m, 1H, CH=C), 5.78 (m, 1H, CH=C), 4.24 (t, $J=7$ Hz, 2H, CH_2O), 2.92 (m, 2H, CH_2), 2.19 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 0.94 (t, $J=7$ Hz, 3H, CH_3). MS (20 eV) *m/e* 166 (M^+). IR (neat); 1740 (COO), 1650 (C=C) cm^{-1}.

α-(1-Methylethylidene)-γ-butyrolactone (5i): Bp 70—73 °C/0.7 Torr. ^{1}H-NMR (CCl_4) δ 4.06 (t, $J=7$ Hz, 2H, CH_2), 2.78 (m, 2H, CH_2), 2.06 (t, $J=2$ Hz, 3H, CH_3), 1.80 (t, $J=1.5$ Hz, 3H, CH_3). MS (20 eV) *m/e* 126 (M^+). IR (neat); 1740 (COO), 1660 (C=C) cm^{-1}. Found: C, 66.57; H, 8.21%. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99%.

α-Cyclohexylidene-γ-butyrolactone (5j): Bp 115—120 °C/2.5 Torr (lit,[5] bp 106 °C/0.5 Torr). ^{1}H-NMR (CCl_4) δ 4.18 (t, $J=7$ Hz, 2H, CH_2O), 2.86 (m, 4H, $2CH_2$), 2.22 (m, 2H, CH_2), 1.64 (m, 6H, $3CH_2$). MS (20 eV) *m/e* 166 (M^+). IR (neat); 1745 (COO), 1660 (C=O) cm^{-1}.

α-(1-Methylpropylidene)-γ-butyrolactone (5k): Bp 70—75 °C/0.7 Torr. ^{1}H-NMR (CCl_4) δ 4.08 (t, $J=7$ Hz, 2H, CH_2), 2.0—3.0 (m, 4H, $2CH_2$), 1.8—2.2 (m, 3H, CH_3), 0.9—1.4 (m, 3H, CH_3). MS (20 eV) *m/e* 140 (M^+). IR (neat); 1740 (COO), 1660 (C=C) cm^{-1}. Found: C, 68.31; H, 8.82% Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63%.

α-(1-Phenylethylidene)-γ-butyrolactone (5l): Bp 120 °C/0.2 Torr; mp 75—78 °C. ^{1}H-NMR ($CDCl_3$) δ 7.1—7.5 (m, 5H, aromatic), 4.22 (t, $J=7$ Hz, 2H, CH_2O), 2.88 (m, 2H, CH_2), 2.57 (t, $J=2.4$ Hz, 3H, CH_3). MS (20 eV) *m/e* 188 (M^+). IR (KBr pellet); 1735 (COO), 1665 (C=C) cm^{-1}. Found: C, 76.56; H, 6.47%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43%.

α-Cyclopentylidene-γ-butyrolactone (5m): Bp 110—135 °C/1.1—1.3 Torr. ^{1}H-NMR (CCl_4) δ 4.15 (t, $J=7.6$ Hz, 2H, CH_2O), 2.70 (m, 4H, $2CH_2$), 2.26 (m, 2H, CH_2), 1.70 (m, 4H, $2CH_2$). IR (neat); 1730 (COO), 1680 (C=C) cm^{-1}.

α-Methylene-γ-butyrolactone (5n): Bp 60 °C/4 Torr (lit,[4c] bp 50—53 °C/0.45 Torr). ^{1}H-NMR (CCl_4) δ 6.14 (t, $J=3$ Hz, 1H, CH=C), 5.62 (t, $J=3$ Hz, 1H, CH=C), 4.32 (t, $J=7$ Hz, 2H, CH_2O), 2.92 (m, 2H, CH_2). IR (neat); 1760 (COO), 1665 (C=C) cm^{-1}.

α-Ethylidene-γ-butyrolactone (5o)[15]: Bp 85—86 °C/2.5 Torr. ^{1}H-NMR (CCl_4) δ 6.64 (m, 0.92H, CH=C), 6.27 (m, 0.08H, CH=C), 4.30 (t, $J=7$ Hz, 2H, CH_2O), 2.86 (m, 2H, CH_2), 1.85 (dt, $J=2$, 7 Hz, 3H, CH_3). MS (20 eV) *m/e* 112 (M^+). IR (neat); 1750 (COO), 1680 (C=C) cm^{-1}. Found: C, 63.96; H, 7.47%. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19%.

α-(2-Methylpropylidene)-γ-butyrolactone (5p): Bp 83—84 °C/1.0—1.1 Torr. ^{1}H-NMR (CCl_4) δ 6.34 (dt, $J=2$, 10 Hz, 0.95 H, CH=C for *E*-isomer), 5.94 (m, 0.05H, CH=C for *Z*-isomer), 4.27 (t, $J=7$ Hz, 2H, CH_2O), 2.87 (dt, $J=2$, 7 Hz, 2H, CH_2), 2.3—2.7 (m, 1H, CH), 0.8—1.2 (d, $J=7$ Hz, 6H, $2CH_3$). MS (20 eV) *m/e* 140 (M^+). IR (neat); 1750 (COO), 1680 (C=C) cm^{-1}.

α-Pentylidene-γ-butyrolactone (5q): Bp 83—85 °C/0.35 Torr. ^{1}H-NMR (CCl_4) δ 6.47 (m, 0.95H, CH=C for *E*-isomer), 6.08 (m, 0.05H, CH=C for *Z*-isomer), 4.24 (t, $J=7$ Hz, 2H, CH_2O), 2.82 (m, 2H, CH_2), 1.9—2.3 (m, 2H, CH_2), 1.1—1.6 (m, 4H, $2CH_2$), 0.95 (m, 3H, CH_3). MS (20 eV) *m/e* 154 (M^+). IR (neat); 1750 (COO), 1680 (C=C) cm^{-1}. Found: C, 69.80; H, 9.03%. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15%.

α-(3-Methylbutylidene)-γ-butyrolactone (5r): Bp 93—94 °C/0.8 Torr. ^{1}H-NMR (CCl_4) δ 6.64 (m, 0.95H, CH=C for *E*-isomer), 6.10 (m, 0.05H, CH=C for *Z*-isomer), 4.30 (t, $J=7$ Hz, 2H, CH_2O), 2.83 (m, 2H, CH_2), 2.07 (m, 2H, CH_2), 1.6—2.0 (m, 1H, CH), 0.93 (d, $J=6.5$ Hz, 6H, $3CH_2$). MS (20 eV) *m/e* 154 (M^+). IR (neat); 1760 (COO), 1680 (C=C) cm^{-1}. Found: C, 70.43; H, 9.19%. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15%.

α-Hexylidene-γ-butyrolactone (5s): Bp 115—117 °C/1.1 Torr. ^{1}H-NMR (CCl_4) δ 6.46 (m, 0.96H, CH=C for *E*-isomer), 6.10 (m, 0.04H, CH=C for *Z*-isomer), 4.23 (t, $J=7$ Hz, 2H, CH_2O), 2.83 (m, 2H, CH_2), 1.9—2.3 (m, 2H, CH_2), 1.1—1.7 (m, 6H, $3CH_2$), 0.90 (m, 3H, CH_3). MS (20 eV) *m/e* 168 (M^+). IR (neat); 1750 (COO), 1680 (C=C) cm^{-1}. Found: C, 71.44; H, 9.55%. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59%.

α-Nonylidene-γ-butyrolactone (5t): Bp 140—149 °C/1.5 Torr. ^{1}H-NMR (CCl_4) δ 6.46 (m, 0.95H, CH=C for *E*-isomer,) 6.08 (m, 0.05H, CH=C for *Z*-isomer), 4.22 (t, $J=7$ Hz, 2H, CH_2O), 2.91 (m, 2H, CH_2), 1.9—2.3 (m, 2H, CH_2), 1.1—1.7 (m, 12H, $6CH_2$), 0.87 (m, 3H, CH_3). MS (20 eV) *m/e* 210 (M^+). IR (neat); 1760 (COO), 1685 (C=C) cm^{-1}. Found: C, 74.06; H, 10.65%. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%.

α-[(E)-2-Butenylidene]-γ-butyrolactone (5u): Bp 100—106 °C/1.2—1.3 Torr. ^{1}H-NMR (CCl_4) δ 6.7—7.3 (m, 1H, CH=C), 5.7—6.2 (m, 2H, CH=C), 4.27 (m, 2H, CH_2O), 2.91 (m, 2H, CH_2), 1.90 (m, 3H, CH_3). MS (20 eV) *m/e* 138 (M^+). IR (neat); 1740 (COO), 1650 (C=C) cm^{-1}.

α-(3-Phenyl-2-propenylidene)-γ-butyrolactone (5v): Mp 135—136 °C (lit,[5] mp 135—136 °C). ^{1}H-NMR ($CDCl_3$) δ 7.1—7.7 (m, 6H, aromatic and CH=C), 6.6—7.0 (m, 2H, CH=C), 4.43 (t, $J=7$ Hz, 2H, CH_2O), 3.08 (dt, $J=7$, 2 Hz, 2H, CH_2). MS (20 eV) *m/e* 200 (M^+). IR (neat); 1740 (COO), 1640 (C=C) cm^{-1}. Found: C, 77.81; H, 5.97%. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%.

Preparation of α-(1-Hydroxypentyl)-α-methylthio-γ-butyrolactone (20q): Into a solution of 22 mmol of the dianion **13** of α-mercapto-γ-butyrolactone (generated from 44 mmol of LDA and 44 mmol of TMEDA) in 40 ml of THF, was added at −78 °C 2.1 g (25 mmol) of pentanal. After 1 h at −78 °C, a solution of 3.1 g (22 mmol) of methyl iodide in 3 ml of THF was added with a syringe over a 3-min period. The resulting solution was stirred at −78 °C for 30 min and at room temperature for 1 h. The usual workup and distillation gave 3.65 g (84%) of **20q**: bp 125—132 °C/1.0—1.1 Torr. ^{1}H-NMR (CCl_4) δ 4.22 (m, 2H, CH_2O), 3.78 (m, 1H, CH), 3.45 (brs, 1H, OH), 2.2—2.9 (m, 2H, CH_2), 2.06 and 2.14 (s, 3H, SCH_3), 1.0—2.0 (m, 6H, $3CH_2$), 0.9 (m, 3H, CH_3). IR (neat); 3520 (OH), 1750 (COO) cm^{-1}.

α-(α-Hydroxybenzyl)-α-mercapto-γ-butyrolactone (21a): The dianion of 4.2 g (44 mmol) of **6** was generated with 88 mmol of LDA and 88 mmol of TMEDA in 80 ml of THF at −78 °C. A solution of benzaldehyde (4.2 g, 40 mmol)in dry THF (40 ml) was added dropwise and the reaction mixture was stirred at −78 °C for 2 h. The cooling bath was removed and the reaction mixture was quenched with 20 min of saturated aqueous ammonium chloride solution, diluted with chloroform (40 ml). The product was extracted with chloroform (4×50 ml), and the combined chloroform solution was washed with brine and dried (Na_2SO_4). The residue obtained after evaporation was chromagraphed on a silica gel column using benzene as eluent to afford pure **21a** (3.14 g, 76%): mp 125—125.5 °C. ^{1}H-NMR ($CDCl_3$) δ 7.34 (m, 5H, aromatic), 4.97 (s, 1H, CH), 3.98—4.5 (m, 3H, CH_2 and OH), 1.6—2.8 (m, 3H, CH_2 and SH). IR (KBr pellet) 3535 (OH), 2550 (SH), 1740 (C=O) cm^{-1}. Found: C, 58.93; H, 5.32%. Calcd for $C_{11}H_{12}O_3S$: C, 58.91; H, 5.40%.

α-(1-Hydroxybutyl)-α-mercapto-γ-butyrolactone (21c): A similar reaction utilizing 44 mmol of the dianion **13** and 3.60 g (50 mmol) of butanal gave 6.63 g (87%) of **21c**: bp 128—131 °C/

2.0 Torr. ^{1}H-NMR (CCl_4) δ 4.1—4.6 (m, 2H, CH_2O), 3.4—4.0 (m, 1H, OH), 1.1—3.0 (m, 8H), 0.97 (m, 3H, CH_3). IR (neat) 3520 (OH), 2555 (SH), 1755 (COO) cm^{-1}.

*Preparation of (*E*)-α-Benzylidene-γ-butyrolactone (5a) from α-(α-Hydroxybenzyl)-α-mercapto-γ-butyrolactcne (21a)*: Into a solution of 20.5 mmol of LDA in 19 ml of THF and 2.8 ml (20.5 mmol) of TMEDA, 2.09 g (9.30 mmol) of **21a** in 6 ml of THF was added at −78 °C. After stirring at −78 °C for 30 min, ethyl chloroformate (9.3 mmol) in 3 ml of THF was added. After stirring at −78 °C for 30 min and then at room temperature for 1 h, the usual workup and chromatographic isolation yielded 0.57 g (35%) of **5a**, which was identical by spectroscopic comparison with an authentic sample.

α-Butylidene-γ-butyrolactone (5c): A similar reaction utilizing 21.1 mmol of LDA, 2.9 ml of TMEDA, 1.82 g (9.57 mmol) of **21c**, and 9.6 ml of ethyl chloroformate gave 0.56 g (42%) of **5c**.

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