Addition of a solution of ketone **6** in 2:1 ether–THF to methylmagnesium iodide in ether at 0–25 °C gave alcohol **7** ($[\alpha]^{24}_{\mathrm{D}}$ -133.3° ($CHCl_3$, *c* 4.25)) as a single stereoisomer (^{13}C NMR[10]) in 92–100% yield. Protection of the hydroxyl group in **7** was effected by treatment with NaH in THF followed by the addition of methyl iodide; methyl ether **8** ($[\alpha]^{24}_{\mathrm{D}}$ -68.5° ($CHCl_3$, *c* 21.5)) was thus obtained in 87–98% yield. ^{13}C NMR confirmed **8** to be a single stereoisomer.

Hydrolysis of **8** to atrolactic aldehyde methyl ether **9** required somewhat more carefully controlled conditions than in the previous study,[1] since extended reaction times led to decomposition. However, treatment of **8** with methyl iodide and calcium carbonate in 80% aqueous acetonitrile[1] at reflux for 4–5 h gave aldehyde **9** in fair yield (62–65%). Oxidation of **9** with Jones reagent[1] gave atrolactic acid methyl ether **1** $[\alpha]^{25}_{\mathrm{D}}$ + 37.6° (CH_3OH, *c* = 8.8), whose ee was determined after conversion to the methyl ester by diazomethane[1] to be 97 ± 2% by proton NMR spectroscopy using the chiral shift reagent Eu(hfbc)$_3$.[11]

The present method is competitive with that recently reported by Mukaiyama et al.[12] which yields **1** in about 95% ee.

Acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No. 1, 24190-10-1; *exo*-**3**, 71242-58-5; *endo*-**3**, 71242-59-6; **4**, 71215-16-2; **5** isomer 1, 71215-17-3; **5** isomer 2, 71242-60-9; **6**, 71215-18-4; **7**, 71215-19-5; **8**, 71215-20-8; **9**, 66221-50-9; (+)-10-camphorsulfonic acid, 3144-16-9; (+)-10-camphorsulfonyl chloride, 21286-54-4.

---

(10) A mixture of the two diasteromers was produced, for NMR comparison, by reaction of the lithium derivative of **4** with acetophenone.

(11) Goering, H. L.; Eikenberry, J. N.; Koermer, G. S.; Lattimer, C. J. *J. Am. Chem. Soc.* **1974**, *96*, 1493.

(12) Mukaiyama, T.; Sakito, Y.; Asani, M. *Chem. Lett.* **1978**, 1253.

Ernest L. Eliel,* William J. Frazee
W. R. Kenan, Jr., Laboratories
Department of Chemistry
University of North Carolina
Chapel Hill, North Carolina 27514

Received June 19, 1979

Ketene Bis(phenylthio)acetals. Easily Prepared Intermediates for the Conversion of Acids and Esters to α-Alkylidene Ketones and Sulfur-Substituted Dienes

Summary: Treatment of acids or esters with Al(SPh)$_3$ produces ketene bis(phenylthio)acetals which, by independent manipulation of the phenylthio groups, are capable of a varity of transformations.

Sir: Aluminum thiophenoxide (**1**), which at 25 °C converts carboxylic esters into thioesters,[1] has now been found to react at the temperatures of refluxing benzene and xylene with carboxylic esters and acids, respectively, to produce in the case of unconjugated substrates (**2**) simple ketene bis(phenylthio)acetals (**3**) and in the case of α,β-unsaturated esters (**4**) 1,1,3-tris(phenylthio)-1-alkenes (**5**; eq 1 and 2). The yields in the nonconjugated cases are excellent

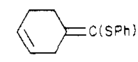
$$\underset{\mathbf{1}}{\mathrm{Al(SPh)_3}} + \underset{\mathbf{2}}{\mathrm{R^1R^2CHCO_2R}} \rightarrow \underset{\mathbf{3}}{\mathrm{R^1R^2C{=}C(SPh)_2}} \qquad (1)$$

$$\mathrm{R = H\ or\ CH_3}$$

$$\mathbf{1} + \underset{\mathbf{4}}{\mathrm{R^3R^4C{=}CHCO_2R}} \rightarrow \underset{\mathbf{5}}{\mathrm{R^3R^4C(SPh)CH{=}C(SPh)_2}} \qquad (2)$$

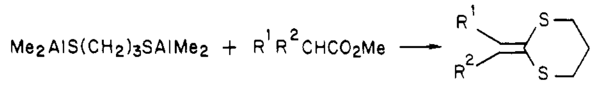
except when a carboxylic acid in which there is no branching at the α- or β-positions is used (Table I);[2] in these cases, an important byproduct is a 1,1,1-tris(phenylthio)alkane, and a modification of this procedure can be used to prepare tris(phenylthio)orthoacetate, a precursor of the useful ketene bis(phenylthio)acetal (**3**, $R^1 = R^2 = H$).[3] The yields are somewhat lower for conjugated esters.[4]

Table I. Ketene Bis(phenylthio)acetals from the Reaction of Aluminum Thiophenoxide with Acids (A) and Methyl Esters (E)

product	from	refluxing solvent	time, h[a]	yields, %
$MeCH{=}C(SPh)_2$	A	xylene	17	56[b]
$EtCH{=}C(SPh)_2$	A	xylene	17	65[b]
$Me_2CHCH{=}C(SPh)_2$	A	xylene	12	98[c]
c-C_6H_{11}-$CH{=}C(SPh)_2$	A	xylene	17	97[c]
$Me_2C{=}C(SPh)_2$	A	xylene	17	96[c]
$Me_2C{=}C(SPh)_2$	E	benzene	4	89[b]
c-$C_6H_{10}{=}C(SPh)_2$	A	xylene	17	100[c]
c-$C_6H_{10}{=}C(SPh)_2$	E	benzene	4	96[c]
	A	xylene	17	97[c]
	E	benzene	4	100[c]
$MeCH(SPh)CH{=}C(SPh)_2$	E[d]	benzene	17	70[b]
$PhCH(SPh)CH{=}C(SPh)_2$	E[e]	benzene	17	70[b]
$Me_2C(SPh)CH{=}C(SPh)_2$	E[f]	benzene	17	85[c]

[a] At reflux. [b] After silica chromatography. [c] Obtained spectroscopically pure directly from reaction. [d] Methyl crotonate. [e] Methyl cinnamate. [f] Methyl 3-methyl-2-butenoate.

Corey and Kozikowski[5] have reported a somewhat analogous transformation to that in eq 1; they showed that alkylidenedithianes (**7**) are produced by reaction of esters (**2**) with **6** (eq 3). Although most discussions[5-7] of the uses



(3)

6 **2**, R = Me **7**

of simple ketene thioacetals as synthetic intermediates have focused on alkylidenedithianes produced by eq 3 or by Peterson or Wittig type olefinations,[6,8,9] we are convinced that the synthetic utility of ketene thioacetals is

---

(1) T. Cohen and R. E. Gapinski, *Tetrahedron Lett.*, 4319 (1978).

(2) New compounds were characterized by ^{1}H NMR, IR, and mass spectroscopy and by their exact masses, as determined by high-resolution mass spectroscopy.

(3) (a) T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, Jr., *J. Org. Chem.*, **40**, 812 (1975); (b) T. Cohen, R. B. Weisenfeld, and R. E. Gapinski, submitted for publication.

(4) Unsaturated acids (**4**, R = H) could also be converted to **5**, but the yields (~50%) were less satisfactory.

(5) E. J. Corey and A. P. Kozikowski, *Tetrahedron Lett.*, 925 (1975).

(6) For an excellent review, see: B.-T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).

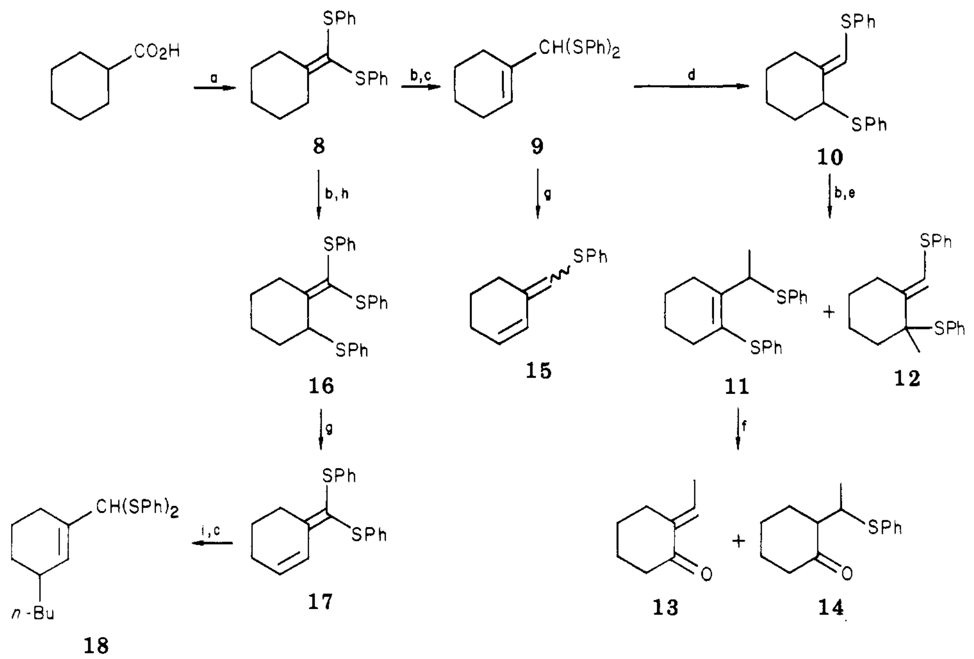
(7) N. H. Anderson, P. F. Duffy, A. D. Denniston, and D. B. Grotjahn, *Tetrahedron Lett.*, 4315 (1978); N. H. Anderson, Y. Yamamoto, and A. D. Denniston, *ibid.*, 4547 (1975).

(8) B.-T. Gröbel and D. Seebach, *Chem. Ber.*, **110**, 852 (1977).

(9) M. Mikolajczyk, S. Grzejszczak, A. Zatorski, B. Mlotkowska, H. Gross, and B. Costisella, *Tetrahedron*, **34**, 3081 (1978).

0022-3263/79/1944-3599$01.00/0

Scheme I[a]

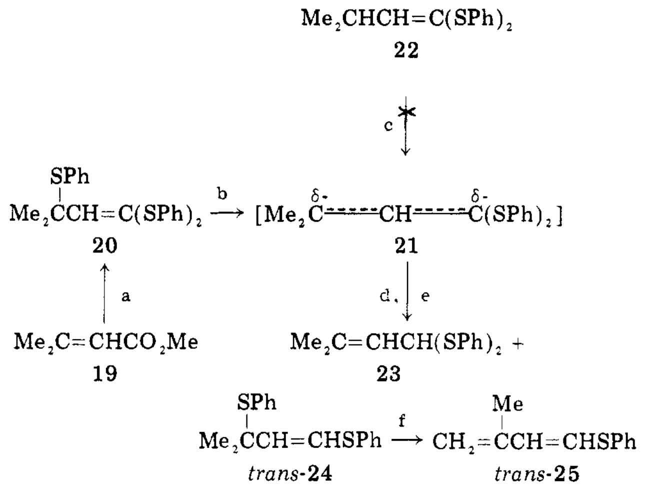


[a] a, $Al(SPh)_3$, xylene, Δ; b, *s*-BuLi, THF, TMEDA, −70 → 0 °C; c, MeOH, −70 °C; d, cat. BF_3, CCl_4, 25 °C; e, MeI, −70 °C; f, Cu^+, Cu^{2+}, MeCN, H_2O, reflux; g, Cu^+, diisopropylethylamine, C_6H_6/THF 19:1, 0 °C; h, PhSSPh, −70 °C; i, *n*-BuLi, −70 → 0 °C, 30 min.

greatly increased when the two sulfur atoms are not incorporated into a ring. In the accompanying paper, it is shown that ketene bis(phenylthio)acetals are very readily reductively lithiated by lithium naphthalenide to produce sulfur-stabilized vinyllithiums, valuable acyl anion equivalents.[10] In the present paper, we reveal other examples of the independent manipulation of the phenylthio groups, and we provide demonstrations of the synthetic utility of the tris(phenylthio)alkenes **5**.

The allylic anion arising from deprotonation[5,11] of the ketene thioacetal **8** (Scheme I), derived from cyclohexanecarboxylic acid or ester, reprotonates almost exclusively at the α position to yield the thioacetal (**9**) of cyclohexenecarboxaldehyde.[12] Treatment of the crude product with a catalytic quantity of boron trifluoride converts **9** cleanly to **10**, the product of thiallylic rearrangement;[13-15] recrystallization from hexane results in an 84% yield (from **8**) of pure **10** (mp 49.0–49.5 °C). Deprotonation[15,16] of the latter and methylation of the anion provide a 93% yield (NMR) of a 10:1 mixture of **11** and **12**. Hydrolysis of this mixture with combined cuprous and cupric triflate[17] in aqueous acetonitrile yields (*E*)-2-ethylidenecyclohexanone (**13**) in 54% yield from **10**, after chromatographic separation from the enal produced by the

Scheme II[a]



[a] a, $Al(SPh)_3$, PhH, Δ; b, Li naph, −70 °C, THF; c, see text; d, MeOH, −70 °C; e, chromatography on silica gel; f, Cu^+, diisopropylethylamine, C_6H_6/THF, 5:1.

hydrolysis of **12** and 16% of **14**. The overall yield in the conversion of cyclohexanecarboxylic acid to **13** is 45%, and this could almost certainly be improved considerably if **14** were to be separately converted to **13** by pyrolysis of the sulfoxide.[18] Another use of **10** is described in ref 3b.

1,4-Elimination of thiophenol from **9** by the use of anhydrous cuprous triflate[19] provides the spectroscopically pure sulfur-substituted diene **15** in 73% yield. A more reactive diene (**17**) is produced from **8** by sulfenylation of

---

(10) T. Cohen and R. B. Weisenfeld, *J. Org. Chem.*, accompanying paper.

(11) D. Seebach, *Synthesis*, 17 (1969); D. Seebach, M. Kolb, and B.-T. Gröbel, *Tetrahedron Lett.*, 3171 (1974).

(12) Corey and Kozikowski have executed a similar transformation.[5]

(13) S. Warren, *Acc. Chem. Res.*, 11, 401 (1978).

(14) H. Kwart and T. J. George, *J. Am. Chem. Soc.*, **99**, 5214 (1977).

(15) T. Cohen, D. A. Bennett, and A. J. Mura, Jr., *J. Org. Chem.*, **41**, 2506 (1976).

(16) E. J. Corey, B. W. Erickson, and R. Noyori, *J. Am. Chem. Soc.*, **93**, 1724 (1971); E. J. Corey and R. Noyori, *Tetrahedron Lett.*, 311 (1970); K. Oshima, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, **48**, 1567 (1975); R. G. Carlson and W. S. Mardis, *J. Org. Chem.*, **40**, 817 (1975).

(17) The reagent is readily prepared by reduction of cupric trifluoromethanesulfonate with copper metal in acetonitrile and dilution of the clear solution with water; T. Cohen and I. Cristea, *J. Am. Chem. Soc.*, **98**, 748 (1976). Neither salt by itself gave satisfactory results in this case, whereas a number of other compounds of this type gave better results than those observed in this case by the use of cuprous triflate in aqueous acetonitrile; ref 15 and unpublished work of R. E. Gapinski.

(18) H. J. Reich and J. M. Renga, *J. Chem. Soc., Chem. Commun.*, 135 (1974); B. M. Trost and R. A. Kunz, *J. Org. Chem.*, **39**, 2648 (1974); P. A. Grieco and M. Miyashita, *ibid.*, **40**, 1181 (1975).

(19) T. Cohen, A. J. Mura, Jr., D. W. Shull, E. R. Fogel, R. J. Ruffner, and J. R. Falck, *J. Org. Chem.*, **41**, 3218 (1976); T. Cohen, R. J. Ruffner, D. W. Shull, E. R. Fogel, and R. J. Falck, *Org. Synth.*, in press. The cuprous triflate can now be purchased from Strem Chemicals, Inc., P.O. Box 108, Newburyport, MA 01950.

its conjugate base with diphenyl disulfide to provide a 68% yield of **16** (which should be attainable in one step by treatment of methyl cyclohexene-1-carboxylate with aluminum thiophenoxide) and elimination of thiophenol by the agency of cuprous triflate. The conjugated ketene thioacetal, **17**, adds *n*-butyllithium,[20] and the resulting allylic anion becomes protonated almost exclusively on the thioacetal carbon atom (as expected from the results of the conversion of **8** to **9**) to provide pure **18**, which is an alkylated analogue of **9** and the thioacetal of 3-*n*-butylcyclohexene-1-carboxaldehyde, in 84% yield from **16** (57% overall yield from cyclohexanecarboxylic acid).

Similar conversion of isovaleric acid to sulfur-substituted diene **25** (Scheme II) was frustrated by the resistance of its derived ketene thioacetal (**22**) to removal of the tertiary allylic proton[21] required for the production of the sulfur-stabilized allylic anion **21**. However, this anion could be produced cleanly from the ketene thioacetal **20**, derived from the corresponding conjugated ester **19**, by reductive lithiation at −70 °C, using lithium naphthalenide (Li naph).[22] Protonation of the anion **21** with methanol at −70 °C resulted in a 71% yield of the thioacetal (**23**) of 3-methyl-2-butenal. During chromatographic separation on silica gel of naphthalene from **23**, the latter partially rearranged to *trans*-**24**. Treatment of the mixture of **23** and **24** with cuprous triflate[19] in the presence of diisopropylethylamine caused elimination of thiophenol and the production of 76% (46% from the unsaturated ester) of the purely trans diene **25**,[24] a sulfur-bearing isoprene unit which should be of use in the construction of terpenes by the Diels-Alder reaction.

Only a few of the many uses that may be envisioned for the now easily prepared sulfur-separated ketene thioacetals such as **8** and **20** have been demonstrated in this and the accompanying communication.[10] The value of the transformations revealed here is enhanced by a report which appeared while our work was being prepared for publication; Mendoza and Matteson have discovered a connective method for producing ketene bis(phenylthio)acetals from ketones utilizing anions derived from bis(phenylthio)methaneboronic esters.[25] Finally, this work demonstrates the power of reductive lithiation for the production of anions that are not accessible by the conventional deprotonation procedure.

Acknowledgment. We thank Messrs. Glen Herman and Daniel Ouellette for recording the mass spectra and the National Institutes of Health for support of this work.

Registry No. **1**, 15821-77-9; **2** ($R = H$; $R_1 = CH_3$; $R_2 = H$), 79-09-4; **2** ($R = H$; $R_1 = CH_2CH_3$; $R_2 = H$), 107-92-6; **2** ($R = H$; $R_1 = C_6H_{11}$; $R_2 = H$), 5292-21-7; **2** ($R = H$; $R_1 = R_2 = CH_3$), 79-31-2; **2** ($R = CH_3$; $R_1 = R_2 = CH_3$), 547-63-7; **3** ($R_1 = CH_3$; $R_2 = H$), 71341-78-1; **3** ($R_1 = CH_2CH_3$; $R_2 = H$), 71341-79-2; **3** ($R_1 = C_6H_{11}$; $R_2 = H$), 71341-80-5; **3** ($R_1 = R_2 = CH_3$), 41563-50-2; **5** ($R_3 = CH_3$; $R_4 = H$), 71341-81-6; **5** ($R_3 = Ph$; $R_4 = H$), 71341-82-7; **8**, 69190-57-4; **9**, 71341-83-8; **10**, 71341-84-9; **11**, 71341-85-0; **12**, 71341-86-1; **13**, 7417-55-2; **14**, 71369-95-4; **15**, 71341-87-2; **16**, 71341-88-3; **17**, 71341-89-4; **18**, 71341-90-7; **19**, 924-50-5; **20**, 71341-91-8; **21**, 71341-92-9; **22**, 71341-93-0; **23**, 71341-94-1; **24**, 71341-95-2; **25**, 16627-79-5; cyclohexanecarboxylic acid, 98-89-5; methyl cyclohexanecarboxylate, 4630-82-4; isovaleric acid, 503-74-2; 3–cyclohexenylideneketene diphenyl thioacetal, 71341-96-3; 3–cyclohexanecarboxylic acid, 4771-80-6; methyl 3–cyclohexencarboxylate, 6493-77-2; methyl crotonate, 18707-60-3; methyl cinnamate, 103-26-4; methyl 3–methyl–2–butenoate, 924-50-5.

Theodore Cohen,* Richard E. Gapinski
Robert R. Hutchins

Department of Chemistry
University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Received July 24, 1979

---

(20) D. Seebach, M. Kolb, and B.-T. Gröbel, *Angew. Chem., Int. Ed. Engl.*, **12**, 69 (1973); D. Seebach, R. Bürstinghaus, B.-T. Gröbel, and M. Kolb, *Justus Liebigs Ann. Chem.*, 830 (1977); B. Cazes and S. Julia, *Tetrahedron Lett.*, 4065 (1978).

(21) The following bases were used in the presence of TMEDA: *sec*-butyllithium in the presence and absence of lithium diisopropylamide in THF and *tert*-butyllithium in hexanes. In the former cases, substrate was recovered; in the latter, lithium thiophenoxy exchange appears to have occurred.

(22) We[10,23a] and Screttas[23b] have used this readily prepared reagent previously for the production of sulfur-stabilized anions. However, this is the first report of the formation by this means of an anion further stabilized by allylic resonance.

(23) (a) T. Cohen, W. M. Daniewski, and R. B. Weisenfeld, *Tetrahedron Lett.*, 4465 (1978); (b) C. G. Screttas and M. Micha-Screttas, *J. Org. Chem.*, **44**, 713 (1979).

(24) E. Guittet and S. Julia, *Tetrahedron Lett.*, 1155 (1978); T. J. Jacobs and A. Mihailovski, *ibid.*, 2607 (1967); C. Huynh, V. Ratovelomanana, and S. Julia, *Bull. Soc. Chim. Fr.*, 710 (1977).

(25) A. Mendoza and D. S. Matteson, *J. Org. Chem.*, **44**, 1352 (1979).

The Conversion of Carboxylic Acids and Esters into Acyl Anion Equivalents via Reduction Lithiation of Their Ketene Phenylthioacetal Derivatives

Summary: Treatment of ketene bis(phenylthio)acetals with lithium naphthalenide produces sulfur-stabilized vinyllithiums which can react with a variety of electrophiles.

Sir: We have recently reported that readily available[1] cyclopropanone bis(phenylthio)ketals are rapidly reduced to sulfur-stabilized cyclopropyl anions at −70 °C by the use of lithium naphthalenide,[2] and Screttas has shown that pentanal bis(phenylthio)acetal behaves similarly with this reagent.[3] We now report that ketene bis(phenylthio)acetals (**1**), which are readily available in high yield by the reaction of carboxylic acids or esters with aluminum thiophenoxide,[4,5] are reductively lithiated with comparable ease by lithium naphthalenide (Li naph). The resulting lithio derivatives (**2**) are potential acyl anion equivalents since they react with a variety of electrophiles (E) to yield substituted vinyl sulfides (**3**; Table I),[6] a type of functionality which is hydrolyzable to a ketone.[7]

Sulfur-stabilized vinyllithiums such as **5** are usually produced by deprotonation of enol thioethers of aldehydes[8-11] (**4**), but, except for those cases in which the

---

(1) T. Cohen and W. M. Daniewski, *Tetrahedron Lett.*, 2991 (1978).

(2) T. Cohen, W. M. Daniewski, and R. B. Weisenfeld, *Tetrahedron Lett.*, 4665 (1978).

(3) C. G. Screttas and M. Micha-Screttas, *J. Org. Chem.*, **44**, 713 (1979). The preparation of simple alkyllithiums from phenyl thioethers by this procedure is also demonstrated in this paper as well as in C. G. Screttas and M. Micha-Screttas, *ibid.*, **43**, 1064 (1978), and C. G. Screttas, Abstract 56, Seventh International Conference on Organometallic Chemistry, Venice, Italy, Sept. 1975.

(4) T. Cohen, R. E. Gapinski, and R. R. Hutchins, *J. Org. Chem.*, accompanying paper.

(5) Connective methods for the production of this type of thioacetal are also available: D. Seebach, M. Kolb, and B.-T. Gröbel, *Chem. Ber.*, **106**, 2277 (1973); B.-T. Gröbel, R. Bürstinghaus, and D. Seebach, *Synthesis*, 121 (1976); A. Mendoza and D. S. Matteson, *J. Org. Chem.*, **44**, 1352 (1979).

(6) New compounds were characterized by ^1H NMR, IR, and mass spectroscopy and by their exact masses as determined by high-resolution mass spectroscopy.

(7) B.-T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).

(8) K. Oshima, K. Shimoji, H. Takahashi, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95**, 2694 (1973).

(9) R. Muthukrishnan and M. Schlosser, *Helv. Chim. Acta*, **59**, 13 (1976).

0022-3263/79/1944-3601$01.00/0