Table I. Characteristics of Acetylenic Diethyl Acetals

| RMgBr, R = | solvent[a] | $RCH(OC_2H_5)_2$,[b] R = | yield (%) | bp/mmHg | $n^{20}_D$ | NMR ($\delta$) $HC(OC_2H_5)_2$ |
|---|---|---|---|---|---|---|
| $n$-$C_4H_9C{\equiv}C$ | a | $n$-$C_4H_9C{\equiv}C$ | 80 | 97/12 | 1.4370 | 5.05 t |
| $C_6H_5C{\equiv}C$ | a | $C_6H_5C{\equiv}C$ | 90 | 108/4 | 1.5170 | 5.33 s |
| $CH_3OCH_2C{\equiv}C$ | a/b | $CH_3OCH_2C{\equiv}C$ | 70[c] | 93/11 | 1.4335 | 5.15 t |
| $(CH_3)_2NCH_2C{\equiv}C$ | a/b | $(CH_3)_2NCH_2C{\equiv}C$ | 80[c] | 100/10 | 1.4410 | 5.15 t |
| $(CH_3)_2C(OMgBr)C{\equiv}C$ | a/b | $(CH_3)_2C(OH)C{\equiv}C$ | 85[c] | 117/12 | 1.4415 | 5.10 s |

[a] a = ether; b = dichloromethane. [b] All compounds gave satisfactory elemental analyses.[4] [c] In ether only complex polymeric material formed.[7]

temperature sensitive to distillation or just difficult to separate in good yields from the decomposition products that accompany such reactions, especially during prolonged distillation.[3,4] As an example, the preparation of $n$-butylpropiolaldehyde diethyl acetal[3] is prepared by heating an equimolar mixture of 1-hexyne and triethyl orthoformate, containing catalytic amounts of zinc chloride–zinc iodide, under autogenous pressure at 190 °C for 3 h. Under such conditions a product yield of 32% was obtained. Using the method reported here, the author has obtained $n$-butylpropiolaldehyde diethyl acetal in yields greater than 80%.[4,5]

The modified procedure for the general synthesis of acetylenic diethyl acetals is as follows. The commonly used ortho ester, triethyl orthoformate, is replaced by the mixed ortho ester, phenyl diethyl orthoformate [$HC(OC_2H_5)_2OC_6H_5$] and reacted at room temperature with the appropriate alkynyl Grignard reagent ($RC{\equiv}CMgBr$) in ether. This modification eliminates both the necessity for using a zinc halide catalyst and the harsh reaction conditions of distillation.

To illustrate the method, the preparation of phenylpropargylaldehyde diethyl acetal is given (yield > 90%). The optimum yield for this acetal, using $ZnI_2$ catalyst, is 72–78%.[3]

It is found[4-6] that polymerization occurs in the preparation of some acetylenic diethyl acetals in ether. This can be eliminated, and the appropriate diethyl acetal obtained in excellent yield (Table I), when the solvent is dichloromethane.[7]

## Experimental Section

**General Methods.** All organometallic reactions were carried out under dry nitrogen. Reagent preparation and instrumentation have previously been reported.[5,7] Product isolation was by distillation under reduced pressure.[5] The NMR results are expressed in parts per million ($\delta$) downfield from internal tetramethylsilane, followed by the signal shape: s, singlet, and t, triplet.

**General Procedure for Preparation of Acetylenic Diethyl Acetals—Preparation of Phenylpropargylaldehyde Diethyl Acetal.** To an ether solution (50 mL) of ethylmagnesium bromide (0.1 mol),[8] in a 250 mL three-necked round-bottom flask was added dropwise with stirring an ether solution (25 mL) of phenylacetylene (5.6 g, 0.055 mol). The contents were heated under reflux until evolution of ethane had ceased[5] and then left to attain room temperature.[9] To this stirred alkynyl Grignard solution was added dropwise at room temperature in its volume of ether phenyl diethyl orthoformate (7.32 g, 0.03 mol). The reaction was slightly exothermic. The contents were stirred for 4 h at room temperature and then hydrolyzed with a cold saturated aqueous solution of ammonium chloride (80 mL), followed by extraction with ether (3 × 150 mL). The organic phase was washed with 20% sodium hydroxide (2 × 10 mL) and water (100 mL) and dried over potassium carbonate. The solvent was removed under reduced pressure and the acetal isolated by vacuum distillation (5.4 g, 88%): bp 108 °C (4 mmHg); $n^{20}_D$ 1.5170 (lit.[3] $n^{25}_D$ 1.5153–1.5158); IR (neat) 2970 (s), 2240 (m), 2490 and 2440 (m), 1120–1000 (br, s) 755 and 690 (s); NMR ($CCl_4$) $\delta$ 7.53–7.06 (m, 5 H), 5.36 (s, 1 H), 4.06–3.26 (m, 4 H), 1.23 (t, 6 H).

**Acknowledgment.** I thank Professor P. Miginiac and Drs. F. Barbot and F. L. Wimmer for helpful discussions.

**Registry No.** $n$-$C_4H_9C{\equiv}CMgBr$, 32359-01-6; $C_6H_5C{\equiv}CMgBr$, 6738-06-3; $CH_3OCH_2C{\equiv}CMgBr$, 32666-87-8; $(CH_3)_2NCH_2C{\equiv}CMgBr$, 86111-72-0; $(CH_3)_2C(OMgBr)C{\equiv}CMgBr$, 920-01-4; $n$-$C_4H_9C{\equiv}CCH(OC_2H_5)_2$, 18232-30-9; $C_6H_5C{\equiv}CCH(OC_2H_5)_2$, 6142-95-6; $CH_3OCH_2C{\equiv}CCH(OC_2H_5)_2$, 53281-61-1; $(CH_3)_2NCH_2C{\equiv}CCH(OC_2H_5)_2$, 5799-77-9; $(CH_3)_2C(OH)C{\equiv}CCH(OC_2H_5)_2$, 25938-06-1; ethylmagnesium bromide, 925-90-6; phenylacetylene, 536-74-3; phenyl diethyl orthoformate, 14444-77-0.

(2) Aiegenbein, W. "Chemistry of Acetylenes", Viehe, H. C., Ed.; Marcel Dekker: New York, 1969; Chapter 3, p 205 and references therein.
(3) Howk, B. W.; Sauer, J. C. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, p 801.
(4) Poncini, L. Ph.D. Dissertation, University of Poitiers, France, 1981.
(5) Barbot, F.; Poncini, L.; Randrianoelina, B.; Miginiac, P. *J. Chem. Res., Miniprint* **1981**, 4016.
(6) Viehe, H. G.; Reinstein, M. *Chem. Ber.* **1962**, *95*, 2557.
(7) Poncini, L. *N. Z. J. Sci.* **1983**, *26*, 31.
(8) Julia, S.; Julia, M.; Linstrumelle, G. *Bull. Soc. Chim. Fr.* **1966**, *3*, 3499.
(9) For some acetylenic diethyl acetals, susceptible to polymerization (see Table I), the ether solvent was removed by evaporation and replaced with dichloromethane (50 mL).

## Preparation of $\alpha$-Chloro Ketones from Enol Silyl Ethers with Sulfuryl Chloride Fluoride and Sulfuryl Chloride[1]

George A. Olah,* Lena Ohannesian, Massoud Arvanaghi, and G. K. Surya Prakash

*Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089*

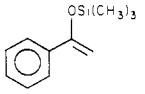
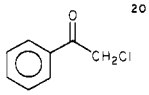
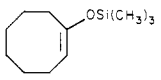
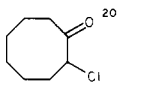
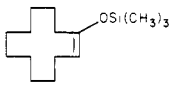
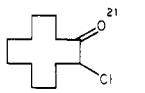
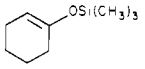
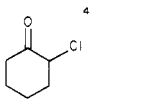
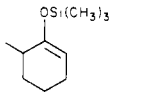
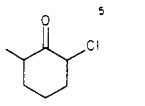
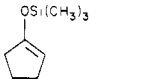
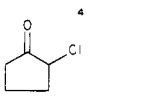
*Received October 24, 1983*

$\alpha$-Chloro ketones are versatile synthetic intermediates. They have been prepared by the reaction of the parent ketone with chlorine, $N$-chlorosuccinimide, copper(II) chloride, sulfuryl chloride, selenium oxychloride, or *tert*-butyl hypochlorite.[2] Chloro ketones have also been obtained by treating epoxides and enamines with a variety of electrophilic chlorinating agents such as chlorine,[3a] $N$-chlorosuccinimide,[3g] *tert*-butyl hypochlorite,[3a] chlorodimethylsulfonium chloride,[4] or hexachloroacetone.[5] Enol

(1) Synthetic Methods and Reactions. 123. For part 122, see: Olah, G. A.; Arvanaghi, M.; Ohannesian, L.; Prakash, G. K. S. *Synthesis*, in press.
(2) (a) House, H. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972. (b) Shaefer, J. P.; Sonnenberg, F. *J. Org. Chem.* **1973**, *28*, 1128.
(3) (a) Paul, L.; Schuster, E.; Hilgetag, G. *Chem. Ber.* **1967**, *100*, 1087. (b) Gabbard, R. B.; Jensen, E. V. *J. Org. Chem.* **1958**, *23*, 1406. (c) Pederson, R. L.; Johnson, J. L.; Holysaz, R. P.; Ott, A. C. *J. Am. Chem. Soc.* **1957**, *79*, 115. (d) Kuehne, M. E. *J. Am. Chem. Soc.* **1961**, *83*, 1492. (e) Speziale, A. J.; Smith, L. R. *J. Org. Chem.* **1963**, *28*, 3492. Ott, G. H. Ibid. **1967**, *33*, 2858. Huang, S. J.; Lessard, M. V. *J. Am. Chem. Soc.* **1968**, *90*, 2432.
(4) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Tetrahedron Lett.* **1979**, 3653.

0022-3263/84/1949-2032$01.50/0 

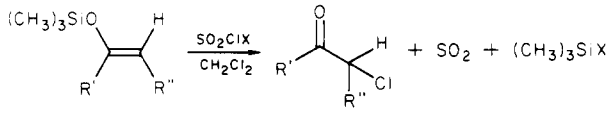
Table I. Preparation of α-Chloro Ketones from Enol Silyl Ethers

| substrate | product[ref] | yield,[a] % $SO_2ClF$ | yield,[a] % $SO_2Cl_2$ | (mp)[b] or bp/torr, °C |
|---|---|---|---|---|
|  |  [20] | 90 | 85 | (55.0) |
|  |  [20] | 86 | 80 | 72-74/2.4 |
|  |  [21] | 67 | 52 | 114-117/1.3 |
|  |  [4] | 72 | 80 | 79-81 /10 |
|  |  [5] | 61 | 62 | 85-87/3 |
|  |  [4] | | 69 | 55-56/2.3 |

[a] Purified products; product purity determined by TLC (silica, hexane:benzene), IR and $^1H$ NMR analysis. [b] Melting points are uncorrected.

silyl ethers are also known to give chloro ketones when treated with chlorine, *N*-chlorosuccinimide, or cupric or ferric chloride.[6]

Sulfuryl chloride fluoride ($SO_2ClF$) has found extensive use as a solvent of low nucleophilicity in the preparation of stable carbocations.[7] Recently we demonstrated the use of $SO_2ClF$ as a convenient reagent for the dehydration of oximes to nitriles,[8] preparation of amides from carboxylic acids,[9] cleavage of thioketals to ketones,[10] oxidation of phosphines to phosphine oxide,[11] and esterification[12] and oxidation of thiols to disulfides.[13] It has also been used as a chlorinating agent for alcohols[14] and enones,[15] although the latter reaction was found to be rather complex. We now report that enol silyl ethers react with $SO_2ClF$ to yield α-chloro ketones under mild conditions in dichloromethane solution. For comparison we also carried out the chlorination with $SO_2Cl_2$.



X = Cl, F

Both reactions work well with a wide variety of enol silyl ethers. The regioselectivity of the method is demonstrated by the chlorination of 2-methylcyclohexanone at the six position through the corresponding enol silyl ether. In contrast, direct chlorination of 2-methylcyclohexanone with $SO_2Cl_2$ gives only 2-chloro-2-methylcyclohexanone.[16] The reaction works well even in the case of medium and large sized rings without any concomitant transannular rearrangement.[17] The yields obtained are shown in Table I. The presently developed method should serve as a useful alternative procedure for the chlorination of enol silyl ethers to α-chloro ketones.

## Experimental Section

All the enol silyl ethers used were prepared from the corresponding carbonyl compounds following literature procedures.[18] Sulfuryl chloride fluoride was prepared from sulfuryl chloride and HF/pyridine.[19]

**General Procedure for the Preparation of α-Chloro Ketones.** To a stirred solution of $SO_2ClF$ or $SO_2Cl_2$ (16 mmol) in 50 mL of dry dichloromethane at −78 °C under nitrogen was added the corresponding enol silyl ether (15 mmol) in 10 mL of dry dichloromethane over a period of 5 min. After the addition was complete the stirred mixture was slowly warmed to room temperature and stirred for an additional 30 min. Subsequently, the reaction mixture was quenched with 50 mL of ice-cold water and extracted with dichloromethane (3 × 50 mL). The extract was washed several times with ice-cold water (3 × 100 mL). The organic layers were combined and dried over anhydrous $MgSO_4$ and evaporated to provide the crude α-chloro ketones. The α-chloro ketones were further purified either by crystallization or distillation.

(5) Laskovics, F. M.; Schulman, M. *Tetrahedron Lett.* **1977**, 759.
(6) (a) Reuss, R. H.; Hassner, A. *J. Org. Chem.* **1974**, *39*, 1785. (b) Blanco, L. Amice, P.; Conia, J. M. *Synthesis* **1976**, 194. (c) Lazukina, L. A.; Kuhar, V. P.; Pesotskaya, G. V. *J. Gen. Chem. USSR (Engl. Trans.)* **1975**, *45*, 2065. (d) Itoh, Y.; Nakatskuka, M.; Saegusa, T. *J. Org. Chem.* **1980**, *45*, 2022.
(7) (a) Olah, G. A. "Carbocations and Electrophilic Reaction"; Wiley: New York, 1974. (b) Olah, G. A.; Donovan, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 5163.
(8) Olah, G. A.; Narang, S. C.; Garcia-Luna, A. *Synthesis* **1980**, 659.
(9) Olah, G. A.; Narang, S. C.; Garcia-Luna, A. *Synthesis* **1980**, 661.
(10) Olah, G. A.; Narang, S. C.; Garcia-Luna, A.; Salem, G. F. *Synthesis* **1981**, 146.
(11) Olah, G. A.; Gupta, B. G. B.; Garcia-Luna, A.; Narang, S. C. *J. Org. Chem.* **1983**, *48*, 760.
(12) Olah, G. A.; Narang, S. C.; Garcia-Luna, A. *Synthesis* **1981**, 790.
(13) Olah, G. A.; Karpeles, R.; Narang, S. C. *Synthesis* **1982**, 963.
(14) Sokilskii, G. A. *Zh. Obshch. Khim.* **1966**, *36*, 860.
(15) Loustalot, M. F. G.; Iratcabal, P.; Metras, F.; Petrissans, J. *Synthesis* **1976**, 33.
(16) McDonald, R. N.; Tabor, T. E. *J. Am. Chem. Soc.* **1967**, *89*, 6573.
(17) Cope, A. C.; Grisar, J.; Peterson, P. *J. Am. Chem. Soc.* **1959**, *81*, 1640 and references cited therein.
(18) Rubottom, G. M.; Mott, R. O.; Krueger, D. S. *Synth. Commun.* **1977**, 327.
(19) Olah, G. A.; Bruce, M. R.; Welch, J. *Inorg. Chem.* **1977**, *16*, 2637.
(20) *Methoden Org. Chem. (Houben-Weyl)* **1962**, *5/3*, 620–621.
(21) Zakharkin, I.; Korneva, L. A. *Bull. Acad. Sci. USSR, Hiv. Chem. Sci. (Engl. Transl.)* **1962**, 1817.

**Acknowledgment.** Support of our work by the National Science Foundation is gratefully acknowledged.

**Registry No.** Acetophenone trimethylsilyl enol ether, 13735-81-4; cyclooctanone trimethylsilyl enol ether, 50338-42-6; cyclododecanone trimethylsilyl enol ether, 51584-36-2; cyclohexanone trimethylsilyl enol ether, 6651-36-1; 2-methylcyclohexanone trimethylsilyl enol ether, 19980-33-7; cyclopentanone trimethylsilyl enol ether, 19980-43-9; α-chloroacetophenone, 532-27-4; 2-chlorocyclooctanone, 4828-34-6; 2-chlorocyclododecanone, 35951-28-1; 2-chlorocyclohexanone, 822-87-7; 2-chloro-6-methylcyclohexanone, 73193-05-2; 2-chlorocyclopentanone, 694-28-0; $SO_2ClF$, 13637-84-8; $SO_2Cl_2$, 7791-25-5.

---

# A New Approach for the Regiospecific Annelation of Butenolides

Aede de Groot* and Ben J. M. Jansen

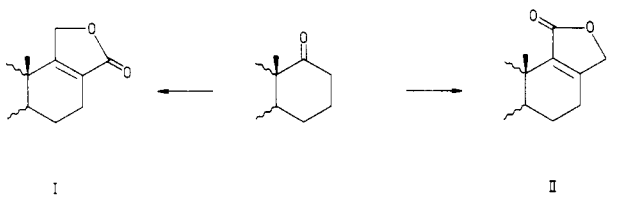
*Department of Organic Chemistry, Agricultural University, De Dreijen 5, 6703 BC Wageningen, The Netherlands*

*Received November 14, 1983*

The regiospecific annelation of butenolides forms part of the problems in the total synthesis of, for instance, triptolide and congeners[1] of a number of drimane sesquiterpenes[2] and eventually of spongianes[3] and scalaranes.[4] Recently an efficient procedure was described for the construction of butenolides of type I (Figure 1), starting from a ketone.[1b] We have developed a method for the annelation of butenolides with the opposite regiochemistry (type II), starting from the same type of ketone.[2e]

This procedure, outlined in Scheme I, starts with formylation of the ketone followed by protection of the aldehyde group as the (*n*-butylthio)methylene derivative **2**.[5] Reaction of **2** with [(phenylthio)methyl]lithium followed by hydrolysis of the adduct affords the γ-(phenylthio)-α,β-unsaturated aldehyde **3**. This hydrolysis can be performed at reflux temperature in a few hours. When acid-sensitive groups are present in the molecule, as in **3c**, longer reaction times at room temperature can be applied.[2e,6] Oxidation of the sulfide **3** with $NaIO_4$ in methanol–water[7] gives the sulfoxide **4**, which can be transformed in a Pummerer-type reaction into the (phenylthio)furan **5** by heating in acetic anhydride at 110 °C. The hydrolysis of the (phenylthio)furan is complete in 4 h at reflux temperature,[8] but up to 10% of the other regioisomer is isolated under these circumstances. Hydrolysis at room temperature takes about 1 day to 1 week to complete the reaction, but only one regioisomer is formed under these conditions.

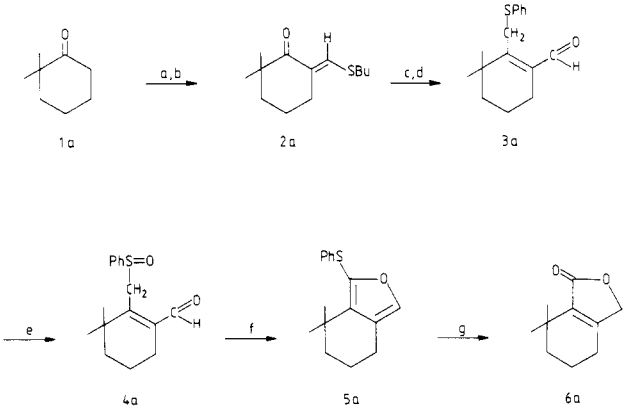
The butenolide **6** can be obtained from the ketone **1** in an overall yield of 30–40%. The utility of this procedure



I II

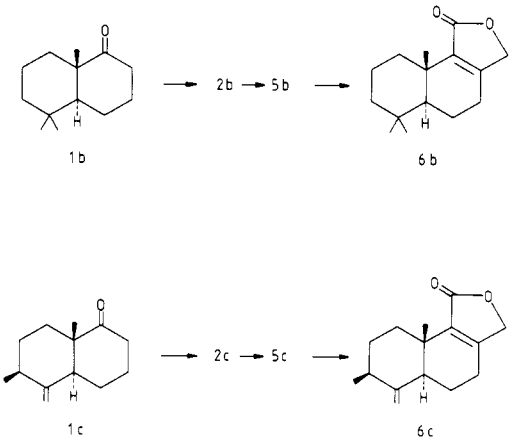
**Figure 1.**

**Scheme I**[a]



[a] (a) NaH, HCOOEt; (b) $H^+$, *n*-BuSH; (c) $PhSCH_2Li$; (d) $H^+$, $H_2O$, $HgCl_2$; (e) $NaIO_4$; (f) $Ac_2O$, 110 °C, (g) $H^+$, $H_2O$, $HgCl_2$.

**Scheme II**



is illustrated by the total syntheses of isodrimenin (**6b**) and colorata-4(13),8-dienolide (**6c**), starting from the ketones **1b** and **1c** (Scheme II).

## Experimental Section

$^1H$ NMR spectra were recorded on a Varian AM-390 or a Perkin-Elmer R 24B spectrometer with tetramethylsilane as an internal standard. Mass spectra and accurate mass measurements were obtained with an AEI MS-902 spectrometer. GC/MS spectra were obtained from a VG Micromass 7070-F spectrometer. Melting points are uncorrected.

**(*n*-Butylthio)methylene Ketones 2a–c.** The starting compounds **1a**,[5] **1b**,[9] and **1c**[2e] were prepared as described. The (*n*-butylthio)methylene ketones **2a**,[5] **2b**,[10] and **2c** were prepared following the procedure of Ireland and Marshall.[5]

**Compound 2c**:[2e] yield 84%; mp 54–55 °C; $^1H$ NMR ($CDCl_3$) δ 0.87 (s, 3 H), 0.93 (t, $J$ = 6 Hz, 3 H), 1.06 (d, $J$ = 6 Hz, 3 H), 1.2–2.7 (m, 14 H), 2.85 (t, $J$ = 6 Hz, 2 H), 4.70 (d, $J$ = 0.9 Hz, 1 H), 4.84 (d, $J$ = 0.9 Hz, 1 H), 7.57 (br s, 1 H); mass spectrum, $m/z$ (relative intensity) 292 (30), 253 (100), 203 (10), 175 (12), 161 (24), 159 (11), 129 (12); accurate mass calcd for $C_{18}H_{28}OS$

(1) (a) Van Tamelen, E. E.; Demers, J. P.; Taylor, E. G.; Koller, K. *J. Am. Chem. Soc.* **1980**, *102*, 5424. (b) Garver, L. C.; Van Tamelen, E. E. *Ibid.* **1982**, *104*, 867. (c) Tokoroyama, T.; Kondo, A.; Ezaki, Y. *Chem. Lett.* **1983**, 203.

(2) (a) Burton, L. P. J.; White, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 3226. (b) Akita, H.; Naito, T.; Oishi, T. *Chem. Lett.* **1979**, 1365. (c) Ley, S. V.; Mahon, M. *Tetrahedron Lett.* **1981**, *22*, 4747. (d) Nakano, T.; Maillo, M. A. *Synth. Commun.* **1981**, 463. (e) De Groot, Ae.; Broekhuysen, M. P.; Doddema, L. L.; Vollering, M. C.; Westerbeek, J. J. M. *Tetrahedron Lett.* **1982**, *23*, 4831.

(3) Nakano, T.; Hernandez, M. I. *J. Chem. Soc., Perkin Trans. 1* **1983**, 135.

(4) (a) Herz, W.; Siva Prasad, J. *J. Org. Chem.* **1982**, *47*, 4171. (b) Croft, K. D.; Ghisalberti, E. L.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Perkin Trans. 1* **1983**, 155.

(5) Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615.

(6) Sowerby, R. L.; Coates, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 4758.

(7) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282.

(8) Okazaki, R.; Negishi, Y.; Inamoto, N. *Chem. Commun.* **1982**, 1055.

(9) Reuvers, J. T. A.; De Groot, Ae. *J. Org. Chem.* **1984**, *49*, 1110.

(10) Ley, S. V.; Mahon, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1379.

0022-3263/84/1949-2034$01.50/0 