stances,[8,9] it follows that the shape of the given reactivity profiles should be mainly determined by an increasingly greater strain in the smaller rings. Thus, the present data would suggest that the strain energies of the given cyclophane compounds regularly increase on decreasing the chain length, without any indication of the existence of a strain maximum, as predicted by Allinger[5] for the medium-sized [n]paracyclophanes. The presence of two oxygen atoms in our systems should be a relatively unimportant factor in this respect, since the reactivity profiles bear a close similarity to that displayed by the formation of a series of (2,5)-thiophenophan-1-ones by intramolecular acylation of ω-thienyl-2-alkanoic acids,[10] in spite of the different reaction type and of the presence of an all-carbon chain in the latter system.

Experimental Section

Most apparatuses were as before.[4] All materials used in this work, except those listed below, were reagent-grade commercial samples.

1,16-Dibromohexadecane was prepared by the symmetric anodic coupling of 9-bromononanoic acid[11] in a modification[12] of Woolford's procedure.[13] The cell was that previously described.[9] The compound was obtained in 30% yield, mp 51.5–52.5 °C, from hexane [lit.[13] mp 53.5–55.0 °C].

***m*- and *p*-(ω-Bromoalkoxy)phenols (1 and 3, respectively).** The 12-bromododecyl ethers 1, m = 12, and 3, m = 12, were available from a previous investigation.[4] All the other compounds were prepared by monoalkylation of resorcinol and hydroquinone with the proper α,ω-dibromoalkane in KOH/EtOH as previously reported.[4] Purification was made very difficult by the presence of several impurities, as shown by TLC analysis. Pure samples for analytical and kinetic purposes were obtained by repeated elutions on silica gel using several eluants until pure (TLC), followed by crystallization or microdistillation in vacuo with the ball tube. Low yields (3 to 20%) of isolated pure materials were obtained, since several fractions containing the given products in a low purity state were discarded. Consistent with the expected structures, all the compounds showed ^{1}H NMR spectra similar to those of the dodecamethylene homologues previously reported,[4] with the corrected peak intensity ratios. No extra peaks were present.

Physical constants and UV spectral data in 99% Me_2SO solution are given below. For the new compounds analytical data (Br content) are also reported. 1, m = 8: mp 29–31 °C; UV λ_{max} 278 nm (log ε 3.39); Br +0.5% of theory. 1, m = 9: $n^{26.5}_D$ 1.5288; UV λ_{max} 278 nm (log ε 3.36); Br −0.7% of theory. 1, m = 10: mp 49.5–50.5 °C from light petroleum/ether [lit.[3b] mp 56 °C]; UV λ_{max} 278 nm (log ε 3.40).

3, m = 8: mp 61.5–62.5 °C from CCl_4 [lit.[3a] mp 65 °C]; UV λ_{max} 297 nm (log ε 3.48); **3**, m = 10: mp 70–71 °C from CCl_4 [lit.[3a] mp 76–77 °C]; UV λ_{max} 297 nm (log ε 3.49); **3**, m = 16: mp 84–85 °C from hexane; UV λ_{max} 297 nm (log ε 3.48); Br −0.2% of theory.

1,10-Dioxa[10]metacyclophane (Resorcinol Octamethylene Ether) (2, *m* = 8). This compound was prepared by cyclization of 1, m = 8, in a modification of an earlier procedure reported for the preparation of hydroquinone dodecamethylene ether,[4] with the difference that the reaction was run at 35 °C, the addition of the reactants was carried out by means of two motor-driven syringes operated by a Sage Instrument syringe pump Model 355, and the total addition time was 30 h. After workup with light petroleum–water, column chromatography on silica gel with benzene afforded the pure title compound in 41% yield, mp 99–100.5 °C, after sublimation in vacuo. In the ^{1}H NMR spectrum (CCl_4) the four aromatic protons are shown as two multiplets with relative areas 3:1 at δ 6.35–6.75 and 6.9–7.15, respectively. The four OCH_2 protons appeared as a partially resolved triplet centered at δ 4.1, whereas the other methylene protons are shown as a broad multiplet at δ 1.3–2.3, with a prominent peak at δ 1.55; m/e 220 (M^+).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.32; H, 9.17.

Kinetics and Product Analyses. The mixed solvent (99% aqueous Me_2SO, v/v) and the KOH stock solution (2×10^{-2} M in 93% aqueous Me_2SO) used for the in situ generation of the anions derived from compounds 1 and 3 were prepared and handled as previously reported.[9] In all cases initial concentrations were at least one order of magnitude lower than the corresponding EM values (Table I) to minimize polymerization. The kinetics were followed spectrophotometrically at wavelengths corresponding to the absorption maxima of the conjugate bases of the substrates, namely, λ 309 and 337 nm for the resorcinol and hydroquinone derivatives, respectively. The decrease of optical density of the solutions was found to follow clean first-order behavior for at least 2 to 3 half-lives. Yield determinations in the kinetic runs were carried out spectrophotometrically in the usual manner.[4,6] Further product analysis for the cyclization of 1, m = 8, was carried out as follows. A 1.2×10^{-4} M solution (50 mL) of the potassium salt of 1, m = 8, in 99% Me_2SO was kept at room temperature for 24 h. After workup with water–pentane, the residue was analyzed by VPC (internal standard) on a 1.5-m column packed with 2% SE-30 plus 0.4% FFAP on silanized Chromosorb W, 60–80 mesh, operated at 166 °C. The yield of cyclic product **2**, m = 8, was 88 ± 5%.

(9) Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591.
(10) Galli, C.; Illuminati, G.; Mandolini, L. *J. Org. Chem.* **1980**, *45*, 311.
(11) Galli, C.; Illuminati, G.; Mandolini, L. *J. Am. Chem. Soc.* **1973**, *95*, 8374.
(12) Galli, C.; Giovannelli, G.; Illuminati, G.; Mandolini, L. *J. Org. Chem.* **1979**, *44*, 1258.
(13) Woolford, R. G. *Can. J. Chem.* **1962**, *40*, 1846.

Communications

(Trimethylsilyl)allenes as Propargylic Anion Equivalents: Synthesis of Homopropargylic Alcohols and Ethers

Summary: (Trimethylsilyl)allenes react with ketones, aldehydes, and acetals in the presence of titanium tetrachloride to yield homopropargylic alcohols and ethers.

Sir: Substitution and addition reactions involving propargylic anion equivalents provide a potentially important synthetic route to acetylenic compounds. The utility of organometallic derivatives of type 1 in such methodology

$$\underset{\textbf{1a}}{R_1C{\equiv}CCR_2R_3M} \rightleftarrows \underset{\textbf{1b}}{R_1MC{=}C{=}CR_2R_3}$$

unfortunately is limited by the tendency of these ambident nucleophiles to combine with electrophiles to produce both allenic and acetylenic products.[1,2] For example, organo-

(1) Klein, J. In "The Chemistry of the Carbon–Carbon Triple Bond"; Patai, S., Ed.; Wiley: New York, 1978; pp 343–381.
(2) Alkylation of lithio-1-(trimethylsilyl)propyne yields acetylenic products, but reaction of this reagent with other electrophiles leads to mixtures of allenes and acetylenes: Corey, E. J.; Kirst, H. *Tetrahedron Lett.* **1968**, 5041. Kirst, H. Ph.D. Dissertation, Harvard University, Cambridge, MA, 1971. Ganem, B. *Tetrahedron Lett.* **1974**, 4467.

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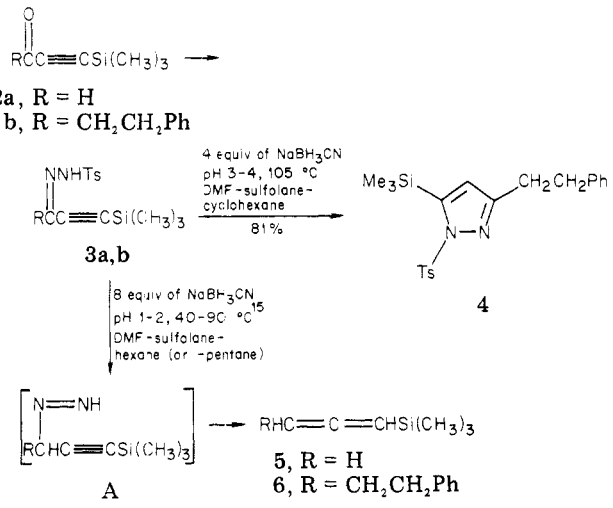
Scheme I



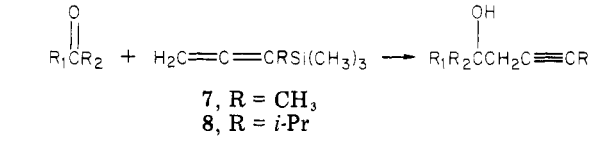
metallic reagents 1, M = Li, MgX, and $B(OR)_2$ (particularly substituted derivatives), react with ketones and aldehydes to afford mixtures of homopropargylic and homoallenic alcohols.[2,3]

In this communication we report that (trimethylsilyl)allenes react regiospecifically with ketones, aldehydes, and acetals in the presence of titanium tetrachloride to yield homopropargylic alcohols and ethers. In these reactions the (trimethylsilyl)allenes function as allyl- rather than vinylsilanes, in accord with orbital overlap considerations[4] and literature precedent.[5-7]

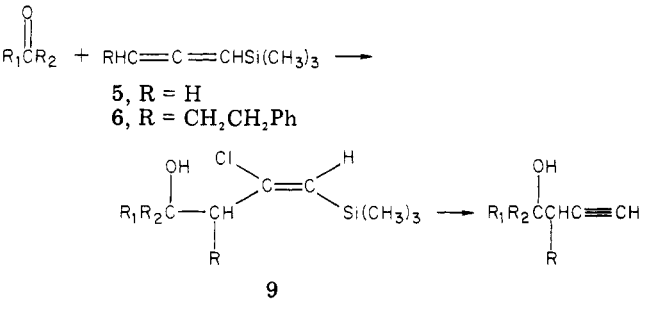
The 1-substituted (trimethylsilyl)allenes 7 and 8 employed in this study were conveniently prepared by the method of Westmijze and Vermeer.[8] Since no satisfactory procedure was available for the synthesis of pure (trimethylsilyl)allene 5 and its 3-alkyl derivatives (e.g., 6),[9] we have developed a new approach involving an adaptation of Hutchin's method for the reductive deoxygenation of α,β-unsaturated carbonyl compounds.[10] This reaction involves a *concerted* [1,5] sigmatropic rearrangement of a propargylic diazene intermediate (A) (Scheme I) and thus furnishes (trimethylsilyl)allene 5 and its 3-alkyl derivatives free of their acetylenic isomers.

Reaction of hydrocinnamyl chloride with cuprous (trimethylsilyl)acetylide[11] gave the ketone **2b**, which was converted to the tosylhydrazone **3b**, mp 105.5–107 °C, by treatment with 1.1 equiv of $TsNHNH_2$ in diethyl ether at 25 °C (86% overall yield).[12] Although reaction of **3b** with sodium cyanoborohydride according to Hutchin's procedure led to formation of the pyrazole **4**,[13,14] mp 97–98 °C, rearrangement to the desired (trimethylsilyl)allene (**6**) could be effected in 84% yield[12] by employing a modified procedure (**3b** → **6**). (Trimethylsilyl)allene (**5**) was prepared in 51% yield[12] from the aldehyde **2a**[16] in a similar fashion.

Exposure of 1-substituted (trimethylsilyl)allenes (7 or 8, 1.0–1.5 equiv) to a mixture of carbonyl compound and



1.0–1.5 equiv of titanium tetrachloride in methylene chloride leads directly to homopropargylic alcohols (Table I, method A).[17] Optimal reaction conditions vary from case to case. Unexpectedly, similar treatment of allenes **5** and **6** produced mixtures of homopropargylic alcohols and (trimethylsilyl)vinyl chlorides (**9**). However, exposure



of the crude reaction product to 2.0–2.5 equiv of potassium fluoride in dimethyl sulfoxide (25 °C, 4–24 h) furnished the desired homopropargylic alcohols (Table I, method B).[17]

This approach to homopropargylic alcohols should prove particularly useful in the synthesis of branched acetylenes, which are not accessible via alkylation of acetylide anions with alkyl halides and epoxides. (Trimethylsilyl)allenes also react with acetals to afford homopropargylic ethers (Table I, entry 4). However, the reaction of these allenes with α,β-unsaturated carbonyl compounds follows an unusual course, the details of which will be reported in a future communication.

In a typical reaction, a solution of hydrocinnamaldehyde

(3) For examples, see: Favre, E.; Gaudemar, M. *J. Organomet. Chem.* **1974**, *76*, 305. Creary, X. *J. Am. Chem. Soc.* **1977**, *99*, 7632. Perepelkin, O. V.; Kormer, V. A.; Bal'yan, Kh. V.; Petrov, A. A. *J. Org. Chem. U. S.S.R.* (*Engl. Transl.*) **1965**, *1*, 1730. Perepelkin, O. V.; Bal'yan, Kh. V. *Ibid.* **1966**, *2*, 1897. Pasternak, Y.; Delépine, M. *C. R. Hebd. Seances Acad. Sci.* **1962**, *255*, 1750.

(4) The C–Si bond in (trimethylsilyl)allene is oriented cis coplanar to only the *allylic* π bond and can thus only afford direct stabilization to the transition state resulting from electrophilic substitution at C_3.

(5) For a review of electrophilic substitution of organosilicon compounds, see: Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761.

(6) The sulfonylation of (trimethylsilyl)allene and similar reactions of polysilylallenes have been described: Bourgeois, P.; Calas, R.; Merault, G. *J. Organomet. Chem.* **1977**, *141*, 23. Bourgeois, P. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1974**, *278*, 969.

(7) In contrast to our results, it was recently reported that derivatives of (trimethylsilyl)allene yield only polymer on reaction with carbonyl compounds in the presence of Lewis acids: Montury, M.; Psaume, B.; Goré, J. *Tetrahedron Lett.* **1980**, 163.

(8) Westmijze, H.; Vermeer, P. *Synthesis* **1979**, 340. We thank James T. Kadonaga and Dr. Ajoy Basak for assistance in the preparation of allenes 7 and 8.

(9) Several methods exist for the synthesis of (trimethylsilyl)allenes contaminated with isomeric acetylenes: Bourgeois, P.; Merault, G.; Dunogues, J. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1972**, *274*, 857. Jaffee, F. *J. Organomet. Chem.* **1970**, *23*, 59. Yogo, T.; Koshimo, J.; Suzuki, A. *Tetrahedron Lett.* **1979**, 1781 and references cited therein.

(10) Hutchins, R. O.; Kacha, M.; Rua, L. *J. Org. Chem.* **1975**, *40*, 923. Hutchins, R. O.; Natale, N. R. *Ibid.* **1978**, *43*, 2299.

(11) Generated from (trimethylsilyl)acetylene by using 1 equiv of *n*-butyllithium and 1.1 equiv of $CuBr{\cdot}S(CH_3)_2$ ($THF{-}S(CH_3)_2$, 0 °C); see: Logue, M. W.; Moore, G. L. *J. Org. Chem.* **1975**, *40*, 131.

(12) Isolated yields of compounds purified by recrystallization or chromatography. Infrared, ^1H (and in some cases ^{13}C) NMR, and mass spectral data were fully consistent with the assigned structures.

(13) No reaction occurred upon exposure of **3b** to catecholborane under a variety of conditions; see Kabalka, Newton, Chandler, and Yang (*J. Chem. Soc., Chem. Commun.* **1978**, 726) for the application of this reagent to the synthesis of allenes.

(14) For other examples of the formation of pyrazoles from α,β-acetylenic hydrazones, see: Fusco, R. In "Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles, and Condensed Rings"; Wiley, R. H.; Ed.; Wiley: New York, 1967; pp 16–19.

(15) In the preparation of **5** the reaction mixture was heated at 40–45 °C for 30 h and then at 55–60 °C for 48 h. For the preparation of **6**, reaction was carried out at 50 °C for 25 h followed by 90 °C for 20 h.

(16) Komarov, N. V.; Yarosh, O. G.; Astaf'eva, L. N. *J. Gen. Chem. U.S.S.R.* **1966**, *36*, 920.

(17) Isomeric homoallenic alcohols were not detected in purified and crude reaction products by IR, ^1H NMR, or ^{13}C NMR.

Table I. Synthesis of Homopropargylic Alcohols and Ethers

entry	ketone, aldehyde, or acetal	allene	reaction conditions	method[a]	product (% yield[b])
1	$PhCH_2CH_2CHO$	5	−78 °C, 1 h	B	10 (84)
2	cyclohexanone	5	−78 → 25 °C, 2 h	B	11[c] (89)
3	$PhCH_2COCH_3$	5	−78 °C, 2 h	B	12 (72)
4	$PhCH_2CH_2CH(OCH_3)_2$	5	−78 °C, 1 h	B	13 (75)
5	CH_3COCH_3	6	−78 → 25 °C, 2 h	B	14 (38[d])
6	cyclohexanone	6	−78 → 25 °C, 2 h	B	15 (49)
7	*i*-$PrCOCH_3$	7	−78 → 25 °C, 1.5 h	A	16 (86)
8	$PhCH_2CH_2CHO$	7	−78 °C, 1 h	A	17 (85)
9	*i*-$PrCOCH_3$	8	−78 → 0 °C, 2.5 h	A	18 (51)
10	$PhCH_2CH_2CHO$	8	−78 °C, 1 h	A	19 (89)
11	cyclohexanone	8	−78 → 25 °C, 2 h	A	20 (84)

[a] For explanation, see text. [b] Isolated yields[12] based on carbonyl compound. [c] Ziele, K.; Meyer, H. *Chem. Ber.* **1942**, *75*, 356. [d] Yield based on allene.

(1.01 g, 7.5 mmol) and distilled $TiCl_4$ (1.57 g, 8.25 mmol) in 30 mL of CH_2Cl_2 (distilled from CaH_2) was stirred at −78 °C for 5 min and then treated with the allene **5** (1.01 g, 9.0 mmol). The resulting mixture was stirred at −78 °C for 1 h, diluted with aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organic layers were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated to afford 2.08 g of a yellow oil.[18] A solution of this material and KF (1.10 g, 18.4 mmol) in 25 mL of Me_2SO (distilled from CaH_2) was stirred at 25 °C for 4 h, then diluted with H_2O, and extracted with ether. The combined organic phases were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (elution with ethyl acetate–hexane) to afford 1.10 g of the homopropargylic alcohol **10** as a colorless oil.[19]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation for support of this research.

(18) IR (film) 3580, 3445, 3025, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H), 1.8 (m, 2 H), 2.1 (s, 1 H), 2.34–2.95 (m, 4 H), 3.9 (m, 1 H), 5.84 (s, 1 H), 7.25 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ −0.9, 32.0, 38.2, 46.8, 68.6, 125.8, 128.2, 128.3, 130.6, 141.7, 143.4.

(19) IR (film) 3545, 3400, 3025, 2118, 1603 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84 (m, 2 H, $PhCH_2CH_2$), 2.02 (t, 1 H, *J* = 3 Hz), 2.34 (m, 2 H, $CH_2C{\equiv}C$), 2.62 (s, 1 H, OH), 2.75 (m, 2 H, $PhCH_2$), 3.72 (m, 1 H, CHOH), 7.21 (m, 5 H).

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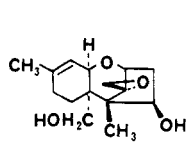
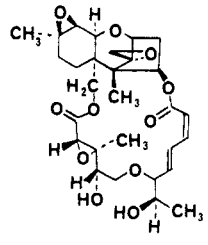
Studies on the Total Synthesis of Verrucarol: A Stereoselective Synthesis of 13,14-Dinor-15-hydroxytrichothec-9-ene

Summary: A stereoselective synthesis of 13,14-dinor-15-hydroxytrichothec-9-ene (**3**) is described.

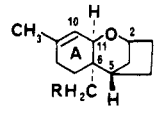
Sir: Verrucarol (**1**) possesses the 12,13-epoxytrichothecene skeleton common to the trichothecene family of terpene antibiotics.[1] The remarkable biological activities of certain macrocyclic di- and triester derivatives of **1** (one example being baccharin (**2**)[2]) has stimulated considerable interest in the synthesis of verrucarol.[3,4] We describe herein a synthetic approach to the trichothecene ring system, exemplified by stereospecific syntheses of **3** and the derived deoxy compound **4**, by a route involving annelation of ring



1



2



3 R = OH
4 R = H

A onto a preformed bicyclic precursor. A crucial element of this approach is that stereochemical control of C-6 relative to C-5 is achieved as a consequence of the sterically biased nature of bicyclic intermediate **7**. The remaining stereocenter at C-11 is introduced in a reaction (**14** → **3**) patterned after the last step in the biosynthesis of trichodermin.[5] Compound **3** is the first trichothecene derivative bearing a C-15 hydroxymethyl group to be synthesized.

The synthesis of **3** is outlined in Scheme I. Baeyer–Villiger oxidation of commercially available norcamphor (**5**) afforded **6**[6] (90%), formylation of which gave the highly crystalline **7**,[7a,b] mp 122–123 °C, in 85% yield. It is necessary to use *tert*-butyl formate[8] in the latter reaction, since with ethyl formate and KO-*t*-Bu **7** is obtained in lower yield (50%) together with a hydroxy ethyl ester (38%)

(1) (a) Bamburg, J. R.; Strong, F. M. "Microbial Toxins"; Kadis, S., Ciegler, A., Ajl, S. J., Eds.; Academic Press: New York, 1971; Vol. 3, pp 207–292. (b) Bamburg, J. R. *Adv. Chem. Ser., No. 149*, **1976**, 144. (c) Tamm, C. *Fortschr. Chem. Org. Naturst.* **1975**, *32*, 74.

(2) Kupchan, S. M.; Streetman, D. R.; Jarvis, B. B.; Daily, R. G., Jr.; Sneden, A. T. *J. Org. Chem.* **1977**, *42*, 4221.

(3) Synthetic studies on verrucarol: (a) Colvin, E. W.; Malchenko, S.; Raphel, R. A; Roberts *J. Chem. Soc., Perkin Trans. 1* **1978**, 658; (b) Snider, B. B.; Amin, S. G. *Synth. Commun.* **1978**, *8* 117; (c) Trost, B. M.; Rigby, J. H. *J. Org. Chem.* **1978**, *43*, 2938.

(4) Synthetic studies on other trichothecenes: (a) Still, W. C.; Tsai, M.-Y. *J. Am. Chem. Soc.* **1980**, *102*, 3655; (b) Colvin, E. W.; Malchenko, S.; Raphael, R. A.; Roberts *J. Chem. Soc., Perkin Trans. 1* **1973**, 1989; (c) Welch, S. C.; Wong, R. Y. *Tetrahedron Lett.* **1972**, 1583; *Synth. Commun.* **1972**, *2*, 291; (d) Goldsmith, D. J.; Lewis, A. J.; Still, W. C. *Tetrahedron Lett.* **1973**, 4807; (e) Fugimoto, Y.; Yokura, S.; Nakamura, T.; Morikawa, T.; Tatsuno, T. *Ibid.* **1974**, 2523; (f) Masuoka, E.; Kamikawa, T. *Ibid.* **1976**, 1691; (g) Pearson, A. J.; Rathby, P. R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 395.

(5) (a) Machoda, Y.; Nozoe, S. *Tetrahedron* **1972**, *28*, 5113. (b) Archilladelis, B. A.; Adams, P. M.; Hanson, J. R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1425. Masuoka and Kamikawa (ref 4f) have applied this biomimetic cyclization in a synthesis of vominotoxin.

(6) Meinwald, J.; Frauenglass, E. *J. Am. Chem. Soc.* **1960**, *82*, 5235.

(7) (a) All new compounds were fully characterized by NMR, IR, and mass spectroscopy. (b) This compound gave a satisfactory combustion analysis. (c) The elemental composition of this compound has been verified by high-resolution mass spectroscopy.

0022-3263/80/1945-3927$01.00/0