prepared by the published method[5] was added an equimolar solution of bromoacetaldehyde (1 M in hexane or THF). The reaction mixture was stirred at −78 °C for 15 min. Acetic acid was added. The solution was diluted with water and extracted twice with ether. The combined organic layers were dried over sodium sulfate, filtered, and concentrated in vacuo. The reaction products were generally very clean, requiring only rapid filtration through a small amount of silica gel for purification.

4-Bromo-3-hydroxy-1-phenylbutan-1-one: IR (film) 3080, 2970, 1690, 1300, 840, 750, 685 cm^{-1}; NMR ($CDCl_3$) δ 0.10 (s, 9 H), 3.15 (d, 2 H), 3.37 (d, 2 H), 3.42 (p, 1 H), 7.35 (m, 3 H), 7.83 (m, 2 H).

(2-Bromo-1-hydroxyethyl)benzene: IR (film) 3400, 1063, 755, 700 cm^{-1}; NMR ($CDCl_3$) δ 3.5 (dd, J = 6, 7 Hz, 2 H), 4.07 (br s, 1 H), 4.77 (dd, J = 2.5, 2.5 Hz, 1 H), 7.25 (s, 5 H); high-resolution mass spectrum, C_8H_9BrO requires m/e 199.98368, found m/e 199.9837.

1-Bromo-2-hexanol: IR (film) 3500, 2960, 2930, 2870, 1030 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (br t, 3 H), 1.43 (m, 6 H), 2.39 (br s, 1 H), 3.49 (d, 2 H), 3.63 (m, 1 H); high-resolution mass spectrum, $C_8H_{18}BrSiO$ (trimethylsilyl ether derivative − CH_3) requires m/e 237.03103, found m/e 237.03134.

***tert*-Butyl 4-Bromo-3-hydroxybutyrate**: IR (film) 3380, 2900, 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (s, 9 H), 2.53 (dd, J = 0.0, 0.5 Hz, 2 H), 3.48 (d, 2 H), 4.16 (br p, 1 H); high-resolution mass spectrm, $C_7H_{12}BrO_3$ (P − CH_3) requires m/e 222.99748, found m/e 222.99697.

Ethyl 6-Bromo-5-hydroxy-3-oxohexanoate: IR (film) 3460, 2980, 1735, 1715 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (t, 3 H), 2.80 (d, 2 H), 3.40 (d, 2 H), 3.47 (s, 2 H), 4.13 (q superimposed on m, 4 H); high-resolution mass spectrum, $C_8H_{11}BrO_3$ (P − H_2O) requires m/e 234.98915, found m/e 234.98950.

1-Bromo-2-hydroxy-4-heptanone: IR (film) 3430, 2980, 1715 cm^{-1}; NMR ($CDCl_3$) δ 0.92 (br t, 3 H), 1.52 (m, 2 H), 2.48 (m, 4 H), 3.43 (dd, J = 5.5 Hz, 2 H), 4.0 (br m, 1 H); high-resolution mass spectrum, $C_4H_6BrO_2$ (P − 43) requires m/e 164.95511, found m/e 164.95467.

Acknowledgment. We thank the National Institutes of Health for partial support of this work.

Registry No. Bromoacetaldehyde, 17157-48-1; 1,4-dibromo-*trans*-2-butene, 821-06-7; 4-bromo-3-hydroxy-1-phenylbutan-1-one, 85565-73-7; (2-bromo-1-hydroxyethyl)benzene, 2425-28-7; 1-bromo-2-hexanol, 26818-04-2; *tert*-butyl 4-bromo-3-hydroxybutyrate, 85565-74-8; ethyl 6-bromo-5-hydroxy-3-oxahexanoate, 85565-75-9; 1-bromo-2-hydroxy-4-heptanone, 85565-76-0; $PhCOCH_2^-Li^+$, 55905-98-1; PhLi, 591-51-5; BuLi, 109-72-8; $t\text{-}BuOCOCH_2^-Li^+$, 53503-61-0; $EtOCOCH^-COCH_2^-\cdot 2Li^+$, 83925-49-9; $CH_3(CH_2)_2COCH_2^-Li^+$, 85565-72-6.

---

(5) Ketone and ester aldols: Stork, G.; Kraus, G. A.; Garcia, G. A. *J. Org. Chem* **1974**, *39*, 3459. Ethylacetaoacetate dianion: Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082. Acid dianions: Pfeffer, P. E.; Silbert, L. S.; Chirinko, J. M. *J. Org. Chem.* **1972**, *37*, 451. In our case no HMPA was used.

Instability of Anhydrous Tetra-*n*-alkylammonium Fluorides

Ramesh K. Sharma and James L. Fry*

Bowman-Oddy Laboratories, Department of Chemistry, The University of Toledo, Toledo, Ohio 43606

Received September 2, 1982

Quaternary ammonium fluoride salts are gaining increasing importance in chemistry as organic-soluble sources of fluoride ion.[1] Of these, tetra-*n*-butylammonium fluoride (TBAF)[2] has found widespread use as a reagent to promote various silylation/desilylation reactions, often under aprotic or anhydrous conditions.[3-12] TBAF is an extremely hygroscopic material. It has been prepared by fluoride exchange with tetra-*n*-butylammonium bromide[13] or, more commonly, by neutralization of aqueous tetra-*n*-butylammonium hydroxide with aqueous hydrogen fluoride followed by removal of water under vacuum.[3-7,14,15] It is also available commercially as the trihydrate.[16]

Because many of the literature uses of TBAF have reportedly been preceded by attempts to dry it under vacuum for extended periods at temperatures above ambient,[4,5,11,14,15] we report our observations concerning the stability of TBAF.

Results and Discussion

Our interest in studying the species formed from the interaction of various silicon compounds with fluoride ion in dichloromethane solution led us to attempt a preparation of anhydrous tetra-*n*-butylammonium fluoride. In accord with the method used by earlier workers, a sample of the trihydrate[16] was heated in a drying pistol with P_2O_5 at 77 °C (2 torr) for 15 h. Upon being cooled to 0 °C, the glassy liquid product formed white crystals which melted at 30–32 °C. Unfortunately, when this material was dissolved in dichloromethane, it did not display the reactivity toward our silicon compounds which we had expected from a source of "naked" fluoride ion.

Examination of the crystalline material in CD_2Cl_2 solution by ^1H, ^{13}C, and ^{19}F NMR spectroscopy established that this product was entirely tetra-*n*-butylammonium *bifluoride* instead of the expected anhydrous TBAF.[17-20]

In additional experiments with TBAF trihydrate at 77 °C (2 torr) we noted not only mass loss as a function of time but also changes in physical appearance as well. For example, when placed at 77 °C, the crystalline trihydrate immediately melted to a colorless liquid from which bubbles evolved. After 15 min, the liquid abruptly turned cloudy. It has lost 17.2% of its mass at this time. Examination of the sample at this stage by ^{19}F NMR spectroscopy showed it to contain both F^- and FHF^-. Continued heating of the sample caused the cloudy melt to form a yellow liquid with steady evolution of bubbles. After 3 h

---

(1) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.

(2) Fowler, D. L.; Lobenstein, W. V.; Pall, D. B.; Krause, C. A. *J. Am. Chem. Soc.* **1940**, *62*, 1140.

(3) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem Soc.* **1972**, *94*, 6190.

(4) Nakamura, E.; Murofushi, T.; Shimizu, M.; Kumajima, I. *J. Am. Chem. Soc.* **1976**, *98*, 2346.

(5) Nakamura, E.; Shimizu, M.; Kuwajima, I. *Tetrahedron Lett.* **1976**, 1699.

(6) Kuwajima, I.; Murofushi, T.; Nakamura, E. *Synthesis* **1976**, 602.

(7) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1977**, 1265.

(8) Colvin, E. W.; Seebach, D. *J. Chem. Soc., Chem. Commun.* **1978**, 689.

(9) Hosomi, A.; Shirahata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 3043.

(10) Schinzer, D.; Heathcock, C. H. *Tetrahedron Lett.* **1981**, *22*, 1881.

(11) Seitz, D. E.; Milius, R. A.; Quick, J. *Tetrahedron Lett.* **1982**, *23*, 1439.

(12) Pornet, J. *Tetrahedron Lett.* **1981**, *22*, 455.

(13) Mohr, S. C.; Wilk, W. D.; Barrow, G. M. *J. Am. Chem. Soc.* **1965**, *87*, 3048.

(14) Kent, P. W.; Young, R. C. *Tetrahedron* **1971**, *27*, 4057.

(15) Clark, J. H.; Miller, J. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2063.

(16) Obtained from Fluka Chemical Corp.

(17) Martin, J. S.; Fujiwara, F. Y. *Can. J. Chem.* **1971**, *49*, 3071.

(18) Fujiwa, F. Y.; Martin, J. S. *J. Am. Chem. Soc.* **1974**, *96*, 7625.

(19) Martin, J. S.; Fujiwa, F. Y. *J. Am. Chem. Soc.* **1974**, *96*, 7632.

(20) Emsley, *J. Chem. Soc. Rev.* **1980**, *9*, 91.

(21) Miller, W. T., Jr.; Fried, J. H.; Goldwhite, H. *J. Am. Chem. Soc.* **1960**, *82*, 3091.

0022-3263/83/1948-2112$01.50/0

there was a 44.9% mass loss. By the end of a 15-h period, bubbling had ceased, mass loss was constant at 53.8%, and the melt was again clear. Only FHF^- was present as judged by ^{19}F NMR spectroscopy.

The decomposition was conducted on a vacuum line, and all volatile products were collected in cold traps and examined spectroscopically. After 15 h at 77 °C, the nonvolatile residue had retained 46.2% of the original mass and was found to be pure tetra-*n*-butylammonium bifluoride. The trapped volatile fraction, totaling 53% of the original mass, was separated into two additional fractions on the vacuum line. The less volatile fraction consisted of a mixture of water and tri-*n*-butylamine. The more volatile fraction was pure 1-butene.

Additional experiments were performed at temperatures between 40 and 77 °C with qualitatively similar results. In no cases were we able to obtain pure anhydrous TBAF. Similar results were obtained during our attempts to dehydrate tetraethylammonium fluoride dihydrate.

Overall, these results indicte that hydrated TBAF can be dehydrated (eq 1) but that when the last of the water

$$(n\text{-}C_4H_9)_4N^+F^-\cdot 3H_2O \rightarrow (n\text{-}C_4H_9)_4N^+F^- + 3H_2O \tag{1}$$

$$2(n\text{-}C_4H_9)_4N^+F^- \rightarrow (n\text{-}C_4H_9)_4N^+FHF^- + (n\text{-}C_4H_9)_3N + CH_3CH_2CH{=}CH_2 \tag{2}$$

molecules stabilizing the fluoride ion are removed, fluoride ion's strong base properties[22,23] cause a rapid E2 elimination which eventually results in the formation of the thermodynamically very stable bifluoride ion (eq 2).[24-27]

The mass loss by water represented in eq 1 amounts to 17.1% of the original mass. By subjecting samples of TBAF trihydrate to a vacuum of at least 2 torr at 40 °C, we found that we could slowly approach that value. For example, after 147 h, one sample had lost 16.5% of its original mass. Although its ^{19}F NMR spectrum taken immediately in CD_2Cl_2 solution showed F^- ion with no more FHF^- ion than that originally present in the starting $TBAF\cdot 3H_2O$,[28] the IR spectrum showed OH absorption remaining in the region 3200–3600 cm^{-1}.

Solutions of this "almost anhydrous" TBAF in CD_2Cl_2 were quite unstable at room temperature. Within 12 h, only the decomposition products of eq 2 were in solution. No FDF^- ions were detected by ^{19}F NMR spectroscopy,[18] so it is likely that the abstraction of β-protons from the tetra-*n*-butylammonium ion by fluoride ion[23] predominates over deuteron abstraction from solvent. This salt suffered similar but somewhat slower decomposition in anhydrous tetrahydrofuran. After 8 days, FHF^- was present to the extent of about 75%. Storage of the "dry" TBAF as a solid under vacuum for 4 days at room temperature followed by dissolution into THF and immediate examination showed that FHF^- had been formed to the extent of about 80%.

References both to the difficulty of removing water from tetraalkylammonium fluorides[1,13,23] and to their instability[1,17,18,21] are found in the literature. These, together with our present observations, force us to conclude that it is very unlikely that pure, anhydrous tetraalkylammonium fluoride salts have ever, in fact, been produced in the case of ammonium ions susceptable to E2 elimination. Rather, reactions which have been reported to proceed in the presence of "naked" fluoride ion generated from such sources have probably actually been caused either by hydrated fluoride ion or by bifluoride ion.

For these reasons we would urge those who require the use of anhydrous fluoride ion uncontaminated with bifluoride ion to subject their source material to analysis prior to use. Moisture may easily be monitored by the IR spectrum. The distinctive doublet in the ^{19}F NMR spectrum (δ −148, J = 123 Hz) and triplet in the ^1H NMR spectrum (δ 16.1, J = 123 Hz) taken of CD_2Cl_2 solutions containing FHF^- at −80 °C make determination of bifluoride ion quite simple.[17-20]

Experimental Section

Nuclear magnetic resonance spectra were obtained on a JEOL FX-90Q Fourier transform spectrometer. Most were obtained by using CD_2Cl_2 as a solvent and lock in 5-mm tubes. ^1H chemical shifts are related to the center of the triplet of $CHDCl_2$, taken to be 5.32 ppm from external Me_4Si. ^{13}C chemical shifts are related to the center of the quintet of CD_2Cl_2, taken to be 53.8 ppm from external Me_4Si. ^{19}F chemical shifts are related to capillary $CFCl_3$, taken to be 0 ppm. A few ^1H and ^{13}C spectra were obtained in $CDCl_3$ and referenced to internal Me_4Si. Infrared spectra were obtained on a Pye Unicam SP3-200 instrument with 0.1-mm NaCl cells.

Commercial tetra-*n*-butylammonium fluoride trihydrate[16] was examined by ^{19}F NMR spectroscopy as a ca. 10% solution in CD_2Cl_2 at −80 °C. The singlet for F^- appeared at δ −113.1. Depending on the sample, or even the crystal chosen within a given sample, a doublet centered at δ −149.5 (J_{HF} = 123.3 Hz) was seen with an integrated intensity of 0–26%. This was attributed to the presence of 0–13 mol % of FHF^- ion in the hydrated sample. After storage of the solution for several days at room temperature, the intensity of the doublet did not increase for such hydrated sample solutions. Hydrated samples were also stable in THF solution.

Attempted Dehydration of $TBAF\cdot 3H_2O$ at 77 °C. A 2.00-g sample of $TBAF\cdot 3H_2O$ was placed in a drying pistol containing P_2O_5 and held at 77 °C (refluxing CCl_4) at a pressure not exceeding 2 torr. The sample was withdrawn periodically from the drying pistol and weighed. The following percent residual masses were found at the indicated times: 0.25 h, 82.8%; 1 h, 59.7% 3 h, 55.1%, 6 h, 51.4%, 10 h, 47.5%, 15 h, 46.2%. The ^{19}F NMR spectrum of a 10% solution of the final residue (mp 30–32 °C) in CD_2Cl_2 at −80 °C consisted only of a doublet at δ −147.5 (J_{HF} = 123.3 Hz) which collapsed to a singlet upon proton irradiation. The ^1H NMR spectrum contained, in addition to signals for the tetra-*n*-butylammonium ion, a triplet centered at δ 16.12 (J_{HF} = 122.7 Hz). The IR spectrum (CH_2Cl_2) had a strong band at 1460 cm^{-1}. These spectral features are consistent with the formation of tetra-*n*-butylammonium bifluoride.[17-20]

Another 2.000-g sample of commercial $TBAF\cdot 3H_2O$ was heated on a vacuum line at 77 °C for 1.5 h. At the end of that time, 0.879 g (44.0%) of nonvolatile, crystalline residue remained. NMR examination showed it to be exclusively tetra-*n*-butylammonium bifluoride. The volatile decomposition products, trapped at −196 °C, weighed 1.06 g (53% of original mass). Vacuum transfer of the most volatile fraction at room temperature into a cold NMR tube gave a sample whose spectra were consistent only with pure 1-butene: ^1H NMR ($CDCl_3$) δ 6.1–5.6 (1 H, m), 5.1–4.8 (2 H, m), 2.1 (2 H, q), 1.0 (3 H, t); ^{13}C NMR ($CDCl_3$) δ 13.1, 26.7, 113.1, 140.6. A rough fractional distillation of the less volatile components gave water, boiling about 100 °C, and a fraction boiling about 216 °C whose NMR spectra were consistent only with tri-*n*-butylamine: ^1H NMR ($CDCl_3$) δ 2.3 (2 H, t), 1.3 (4 H, m), 0.83 (3 H, t); ^{13}C NMR ($CDCl_3$) δ 54.3, 29.8, 20.7, 13.8.

Attempted Dehydration of $TBAF\cdot 3H_2O$ at 40 °C. A 2.000-g sample of $TBAF\cdot 3H_2O$, containing about 13 mol % of FHF^- by ^{19} NMR spectroscopy, was held at 40 °C (2 torr). The following

---

(22) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250.

(23) Bartsch, R. A. *J. Org. Chem.* **1970**, *35*, 1023.

(24) The hydrogen bond energy for FHF^- is on the order of 50 kcal/mol.[20,25-27]

(25) Emsley, J.; Hoyte, O. P. A.; Overill, R. E. *J. Chem. Soc., Chem. Commun.* **1977**, 225.

(26) Emsley, J.; Hoyt, O. P. A.; Overill, R. E. *J. Chem. Soc., Perkin Trans. 2* **1977**, 2079.

(27) Emsley, J.; Jones, D. J.; Miller, J. M.; Overill, R. E.; Waddilove, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 24.

(28) Different commercial samples of $TBAF\cdot 3H_2O$ received by us contained 0–13 mol % of FHF^- ions as judged by ^{19}F NMR spectroscopy (−80 °C, CD_2Cl_2).

percent residual masses were found at the indicated times: 3 h, 96.9%; 27 h, 91.1%; 51 h, 89.6%; 75 h, 88.2%; 99 h, 86.5%; 123 h, 85.1%; 147 h, 83.5%. The IR spectrum (CH_2Cl_2) of the residue had some absorption in the region of 3200–3600 cm^{-1}. The ^{19}F NMR spectrum of a freshly prepared 10% solution of this material in CD_2Cl_2 at −80 °C consisted of a singlet for fluoride ion at δ −112.8 and a double for bifluoride centered at δ −148.5 (J_{HF} = 123 Hz). The bifluoride ion was present in about 13 mol % originally, but by the time the sample had remained at room temperature for 3 h, the amount of FHF^- had risen to about 61 mol %. Examination of the solution after 12 h at room temperature revealed that all of the fluoride was present as FHF^-. No free fluoride was in evidence.

Attempted Dehydration of Tetraethylammonium Fluoride Dihydrate at 77 °C. Tetraethylammonium fluoride dihydrate (Eastman) was examined by ^{19}F NMR spectroscopy and found to contain no bifluoride ion. A 2.000-g sample of this material was held at 77 °C (2 torr) and weighed as a function of time as was done with TBAF·$3H_2O$. The following percent residual masses were found as a function of time: 0.25 h, 85.6%; 0.5 h, 81.7%; 3 h, 69.9%; 12 h, 52.1%; 24 h, 43.5%. The ^{19}F NMR spectrum of a CD_2Cl_2 solution of the final product at −70 °C showed only the doublet at δ 147.7 (J_{HF} = 123.3 Hz) for FHF^-. Similar results were obtained when the dihydrate was heated at 56 °C.

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

Registry No. Tetra-*n*-butylammonium fluoride, 429-41-4; tetraethylammonium fluoride, 665-46-3.

Total Synthesis of Leukotrienes. An Effective Procedure for the Synthesis of Conjugated Dienals by Four-Carbon Homologation

E. J. Corey* and John O. Albright

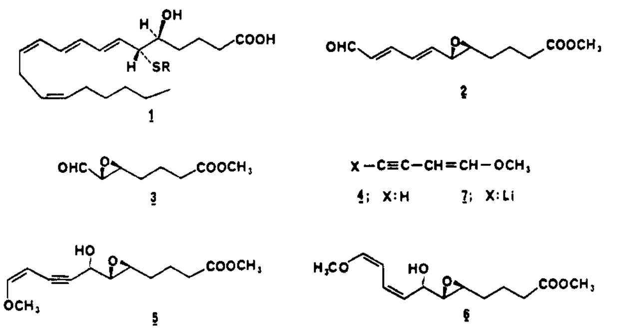
Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

Received December 13, 1982

The total synthesis[1] of the spasmogenic leukotrienes (LTs, formally termed slow-reacting substances of anaphylaxis) LTC, LTD, and LTE is of significance not only as a proof of structure but also since it makes available these rare substances for biological study.[2] These leukotrienes, of general formula 1 (Chart I), were made from the epoxy dienal 2 that in turn was obtained by four-carbon chain extension involving the lithio reagent from 1-(tributylstannyl)-4-methoxy-(*E*,*E*)-1,3-butadiene.[3] Although the conversion of 3 to 2 was accomplished in 63% yield under optimum conditions, the process involved several highly critical variables including not only the purity of reactants but also precise reaction and workup details. Because of the importance of the dienal 2 we have searched for a simpler and less critical procedure for its synthesis from 3. The method that is described herein has been used on many occasions in these laboratories and has proven to be experimentally straightforward and reproducible as well as efficient.

1-Methoxybut-1-en-3-yne (4) was isolated from the commercially available methanolic solution and converted to the corresponding lithio acetylide (7) in tetrahydrofuran (THF) solution. Reaction of 7 with epoxy aldehyde 3 produced the formyl adduct 5 in 92% crude yield, which without purification was hydrogenated over Lindlar catalyst to form the dienal 6 (97% crude yield). Mesylation of 6 followed by solvolysis with aqueous bicarbonate afforded the dienal 2 in 97% yield and >95% purity by NMR analysis. This sequence does not require chromatography and is easily scaled up.

Chart I



Experimental Section

Purification of 1-Methoxybut-1-en-3-yne (4).[4] A 100-mL (90 g) portion of commercial 4 (Aldrich) was partitioned between water (35 mL) and 35% (v/v) ether–pentane (3 × 50 mL). The combined organic layers were washed with water (2 × 30 mL) and dried over anhydrous calcium chloride (9 g) and calcium carbonate (1 g) at 4 °C overnight. The dark red solution was filtered, calcium carbonate (1 g) was added, and the solvents were distilled through a 10-cm Vigreux column at atmospheric pressure under argon (distillate 34–36 °C).[5] The remaining oil was distilled at 102 torr (aspirator pressure with an argon bleed), with the fraction boiling at 67–69 °C being collected. The resultant *colorless* liquid (16.5 g) was transferred via cannula to a dry bottle. The bottle was protected from light and stored in a desiccator at −20 °C. Samples were removed as required with a dry glass syringe previously flushed with argon:[6] NMR ($CDCl_3$) δ 6.32 (dd, 1 H, J = 6.5, 0.8 Hz), 4.50 (dd, 1 H, J = 6.5, 2.4), 3.78 (s, 3 H), 3.04 (dd, 1 H, J = 2.4, 0.8); IR (CCl_4): 3310 (vs), 2100 (m), 1630 (vs) cm^{-1}.

4-Lithio-1-methoxybut-1-en-3-yne (7). A dry reaction vessel was flushed with nitrogen and tared. Purified 4 (0.23 mL) was introduced and the vessel reweighed (+248 mg, 3.0 mmol of 4). Dry THF (6.7 mL) was added with stirring, and the resultant colorless solution was cooled to −40 °C.[7] To this solution was added slowly[8] 2.32 mmol (0.78 equiv) of *n*-butyllithium dropwise. After being stirred at −40 °C for 30 min, this solution was employed as 0.30 M in 7.[9,10]

Methyl 7-Hydroxy-11-methoxy-*trans*-5(*S*),6(*S*)-epoxyundeca-10(*Z*)-en-8-ynoate (5). Methyl *trans*-5(*S*),6(*R*)-oxido-7-oxoheptanoate (3, 155 mg, 0.90 mmol)[1] was azeotropically dried by the repeated evaporation in vacuo of a solution in benzene, dissolved in 20 mL of dry THF and cooled to −78 °C. To this

---

[1] Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarstrom, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436.

[2] See, for example: Weiss, J. W.; Drazen, J. M.; Coles, N.; McFadden, E. R., Jr.; Weller, P. F.; Corey, E. J.; Lewis, R. A.; Austen, K. F. *Science (Washington, D.C.)* **1982**, *216*, 196.

[3] Wollenberg, R. H. *Tetrahedron Lett.* **1978**, 717.

[4] Cf.: Cook, P. D.; Day, R. T.; Robin, R. K. *J. Heterocycl. Chem.* **1977**, *14*, 1295.

[5] Enyne 4 is *extremely* sensitive to air. Even brief contact with the atmosphere results in rapid decomposition (discoloration) of the material. Therefore *all* manipulations were performed under an inert atmosphere.

[6] This material could be kept for up to 1 month before requiring redistillation as per above.

[7] Below–40 °C and/or at higher concentrations the acetylide 7 precipitated from solution.

[8] Rapid addition of the *n*-butyllithium resulted in excessive warming and decomposition of the organometallic reagent.

[9] This mixture contained 30% excess 4 to insure the complete consumption of the *n*-butyllithium. Excess 4 was readily removed from the process at a later stage by evaporation.

[10] This reagent must be prepared immediately prior to use and must be maintained below −20 °C to minimize decomposition. It decomposes rapidly upon warming above −10 °C; however, in solution it could be transferred rapidly by using a dry, chilled syringe.

0022-3263/83/1948-2114$01.50/0 © 1983 American Chemical Society