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Reaction of 1-Bromo-1-alkynes with Alkoxide Ion. Generation of Vinylidene Carbenes[1]

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Abstract: Sodium alkoxides react with 1-bromo-1-alkynes in refluxing benzene, toluene, or xylene solutions by proton abstraction at C-3 generating an intermediate zwitterion-carbene, which in the presence of equimolar quantities of alcohol (or alkoxide) gives four products. Mechanisms involving nucleophilic attack by alcohol (alkoxide) on the ambident vinylidene carbene, prototropic rearrangement, and carbene insertion into the carbon–hydrogen bond α to the oxygen of the alcohol or alkoxide are proposed.

Substitution of bromine in 1-bromo-1-alkynes proceeds in good yield with a variety of nucleophiles[2a] (eq 1). Several mechanisms have been suggested

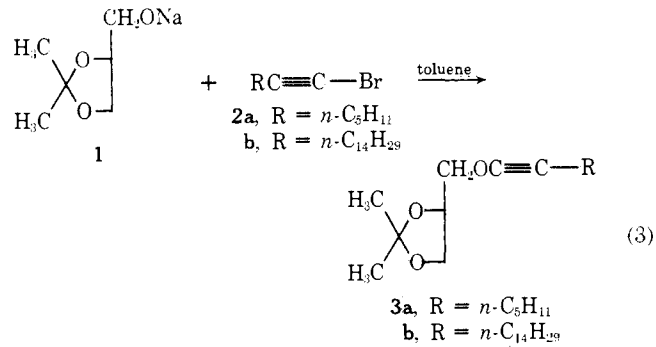
$$RC{\equiv}C{-}Br + X^- \longrightarrow RC{\equiv}C{-}X + Br^- \quad (1)$$
$$X = R'S^-,\ R'_2N^-,\ P(OR')_3$$

including α addition and β elimination[2b]; β addition, α elimination, and rearrangement;[2c] and attack on bromine followed by direct substitution[2d] (eq 2). Efforts to extend

$$RC{\equiv}CBr + X^- \longrightarrow RC{\equiv}C^- + XBr \quad (2)$$

the scope of this method to the preparation of acetylenic ethers ($X = R'O^-$) have been largely unsuccessful.[2d,3] Instead of substitution, 1-bromo-1-acetylenes react with alkali metal hydroxides or alkoxides to give the free acetylenes and recovery of starting materials.[3] Arens[2d] has attributed this to nucleophilic attack on bromine, which in protic solvents results in reversal of a useful preparative method based on hyprobromite–acetylene equilibria.

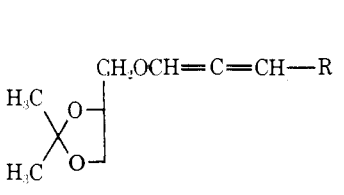
A notable exception to this generalization was reported by Preobrazhenskii and coworkers[4a] in which the preparation of **3a** was claimed as shown in eq 3. Unfortunately, lit-



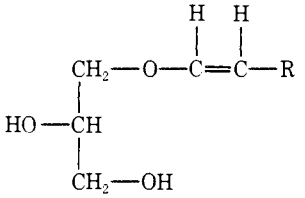
(3)

tle supporting evidence other than analytical data for the proposed structure was available. Chacko, *et al.*,[4b] reinvestigated this reaction and instead of **3a** obtained the isomeric allene (**4a**) in 27% yield. Again, incomplete spectral data and evidence of purity makes evaluation and comparison difficult. In a later communication, Preobrazhenskii, *et al.*,[5] restated their claim and extended the method to a longer carbon chain isolating **3b** in 6% yield. The solvent was refluxing xylene.

Our interest[6] in the synthesis of neutral plasmalogens (**5**) prompted a reinvestigation of this problem with the expectation of converting **3** to **5** by partial hydrogenation and removing the protecting group by hydrolysis with boric acid as suggested by Slotboom.[7] Although yields appeared to be low, this method would avoid more laborious multistep syntheses of **5** and at the same time allow controlled formation



4a, R = *n*-C_4H_9
b, R = *n*-$C_{13}H_{27}$



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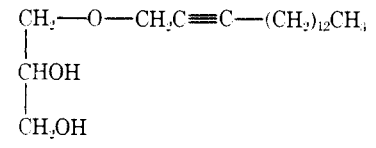
of the desired *cis*-alk-1-enyl linkage.[8] As plasmalogens commonly have long (R = $C_{14}H_{29}$ or $C_{16}H_{33}$) alkyl side chains,[8] 1-bromo-1-hexadecyne (**2b**) was initially chosen for study.

Results and Discussion

Repetition of the published procedure[5] (eq 3) using **2b** gave, in addition to 1-hexadecyne,[3f] a complex mixture of compounds from which it was possible to isolate an acetylenic and an allenic product in a ratio of about 1:10. The nmr spectrum of the acetylenic product differed from that expected for **3b**. In particular, a downfield two-proton triplet collapsed into a singlet upon spin decoupling with irradiation at δ 2.19, the position of a two-proton multiplet. This strongly indicated that the acetylenic product was in fact the propargyl ether **6b** rather than the ethynyl ether **3b**.

Removal of the ketal function from **6b** with boric acid[9] gave the acetylenic diol **7**, showing the expected ir absorption and nmr signals for the methylene protons adjacent to the triple bond similar to those for **6b**. Semihydrogenation of the triple bond in **7** using Lindlar catalyst gave the *cis*-olefin **8**. Both **7** and **8** yielded racemic chimyl alcohol on



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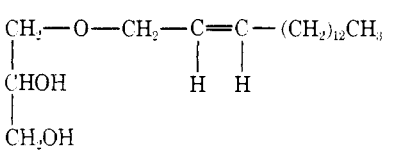
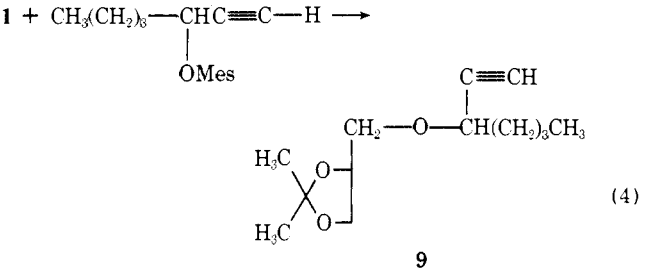


8

complete hydrogenation, thus confirming the carbon skeleton of **6b**. The position of the double bond in **8** was rigorously established by cleavage with both ozone and alkaline permanganate-periodate to give tetradecanal and myristic acid, respectively. In the nmr spectrum of **8**, the two olefinic protons appeared at δ 5.6 and irradiation at this position confirmed coupling to a two-proton doublet at δ 4.09 (C-1′ methylene) and a two-proton multiplet at δ 2.06 (C-4′ methylene). Repetition of the above procedures using the L enantiomer of **1** gave the D form of **6b**, which was converted to the D enantiomers of **7** and **8** and thence to optically pure D-chimyl alcohol.

The allenic product, although isomeric with the anticipated allenic ether (**4b**), showed ir absorption suggesting the presence of a hydroxyl group, confirmed by observation of an exchangeable (D_2O) proton in the nmr. From the above evidence, the structure **10b** may be inferred for the allene, and this is confirmed by the close similarity in spectral properties with the analogous compounds of structure **10** discussed below. In agreement with the postulated structure of **10b**, boric acid hydrolysis followed by complete hydrogenation afforded a saturated alcohol which on acetylation gave an acetate ester showing three acetate methyl groups in the nmr spectrum between 2.05 and 2.15 ppm.

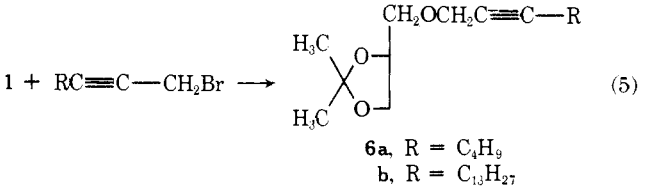
However, it was apparent that a more efficient method for isolation and estimation of the products was desirable. Accordingly, the reaction was reexamined using 1-bromo-1-heptyne (**2a**) in order to give more volatile derivatives suitable for treatment by gas chromatography. In our hands, a mixture of four products (**4a, 6a, 9,** and **10a**) in the ratio of 6:2:1:11 (total yield 19%) was obtained under these conditions.[10] All products were isomers of molecular formula $C_{13}H_{22}O_3$. Compounds **4a** and **10a** were particularly sensitive to air and thermally labile which may explain the divergent results from different laboratories. For example, distillation of the reaction mixture, as reported by Chacko,[4] at 80–90° effected almost complete decomposition of **10a**. The distillate obtained contains 85–90% of **4a** and small quantities of **6a** and **9** which were not easily detected except by glpc. All of these components were ultimately isolated by preparative glpc and characterized by chemical and spectral methods. Glpc analysis was successful only under carefully controlled conditions (see Experimental Section).



(4)

9

Compound **9** was assigned the terminal acetylenic propargylic ether structure (a doublet at 2.42 ppm (J = 2.5 Hz) in the nmr spectrum was attributed to the acetylenic hydrogen coupled to the single hydrogen adjacent to oxygen), confirmed by independent synthesis (eq 4) from **1** and 1-heptyn-3-yl mesylate which was in turn prepared from the alcohol by the general method of Crandall.[11] **6a** was independently synthesized from 1-bromo-2-heptyne[12] (eq 5) and showed nmr absorption in accord with the propargylic ether structure.



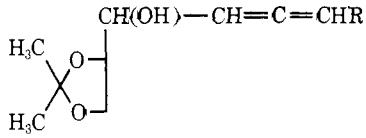
(5)

6a, R = C_4H_9
b, R = $C_{13}H_{27}$

The allenic ether structure for **4a** was confirmed by the nmr spectrum (multiplets at 6.65 and 5.83 ppm), which compares favorably with values of 6.77 and 5.77 ppm re-

ported for methyl propadienyl ether,[13a] and 6.60 and 5.74 ppm for ethyl 4,4-dimethyl-1,2-pentadienyl ether.[13b]

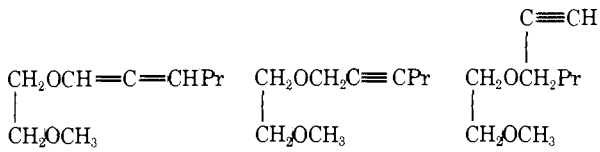
Ir bands suggested that **10a** was an allenic alcohol and



10a, R = n-C_4H_9
b, R = n-$C_{13}H_{27}$

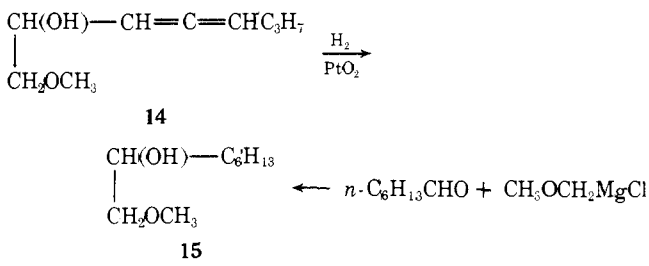
the nmr spectrum was consistent with this formulation. Glpc revealed that **10a** was a mixture of three partially resolved components which can be attributed to diastereomers.[14] Upon treatment with acetic anhydride in pyridine, these three peaks moved to longer retention times. Strong ir bands confirmed formation of the allenic acetates. Close agreement of integral ratios with theory and the presence of only two hydrogens in the region where methylenes adjacent to allenes are normally found[1a] argued against contamination by isomeric allenes or acetylenes. Evidence for other impurities was not detected in the mass spectrum.

Although this assignment appeared justified, further work on a simpler system was initiated. 1-Bromo-1-hexyne was treated with sodium 2-methoxyethanolate giving the anticipated products **11, 12, 13,** and **14.** Compound **14** had



11 **12** **13**

spectral properties similar to **10a** and glpc confirmed the presence of a mixture of two diastereomers as expected (dissymmetric allene and asymmetric center). Hydrogenation of **14** gave a single product identified as 1-methoxy-2-octanol (**15**) by comparison with material synthesized from methoxymagnesium chloride[15] and n-heptaldehyde.

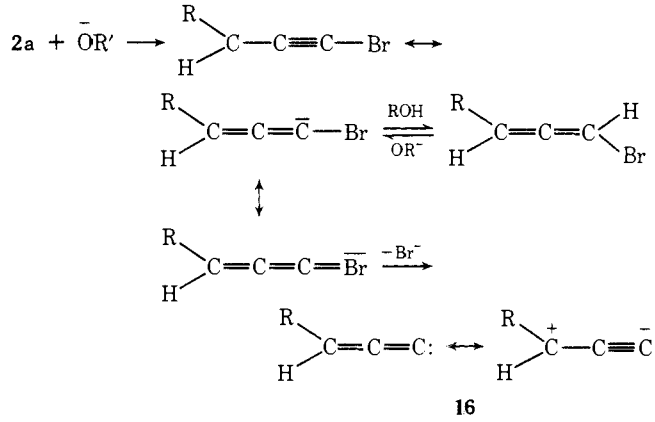


14 **15**

A priori, **4a** and **6a** could be derived from the acetylenic ether (**3a**) by a prototropic propargylic rearrangement under the basic reaction conditions; however, the formation of **9** and **10a** cannot be explained in this manner. Perkins and coworkers[4b] refluxed 1-methoxy-1-heptyne with sodium ethoxide but obtained no evidence for formation of the allenic ether, thus concluding that **4a** was not derived from **3a.** In addition to the mechanisms mentioned previously for substitution of 1-bromo-1-alkynes[2a-d] when X is a strong base, hydrogen abstraction at C-3 can occur and generate the zwitterion-carbene[17a,b] **16** either by 1,3 elimination of hydrogen bromide or by isomerization to 1-bromo-1,2-diene which then reacts rapidly with base to give the carbene (Scheme I).[18a] The ambident electrophile (**16**) may then react with alcohol (or alkoxide) at C-1 or C-3, giving **4** and **9**,[18b] respectively.

When the reaction was repeated using cyclohexene or toluene–cyclohexene as solvent, the major product formed in

Scheme I



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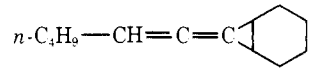
competition with the oxygenated compounds was the allenic cyclopropane (**17**). The ratio of **17** to other products was 4:



17

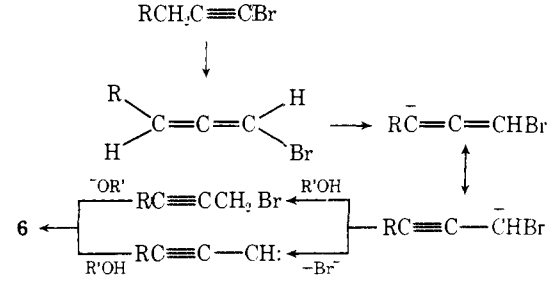
1 (total yield 17%). The strained allene structure of **17** was indicated by two strong ir bands.[19] Glpc indicated that **17** was a mixture of two partially resolved components which are probably endo and exo isomers.[20] Reaction of KO-t-Bu and **2a** in refluxing cyclohexene gave a 12% yield of **17.**

Other bases were of limited utility; no carbene-trapped product was obtained upon reaction of **2a** with n-butyllithium or sodium amide in cyclohexene at various temperatures, metalation being the presumed course of reaction.

Two plausible mechanisms for the formation of **6** were considered: (a) prototropic rearrangement of **4** to give **6;** and (b) rearrangement of **2** to bromodiene which then reacts as shown in Scheme II. Subjecting **6a** to the original reaction conditions (1 hr, equimolar quantity of base) led to recovery of starting material in 45% yield, but no trace of **4a** was detected. Similar treatment of **4a** gave a 51% yield of a mixture of **4a** and **6a** in the ratio 97:3. The partial recovery of material in both cases and the apparent lack of isomerization of **6a** can be explained in terms of the well-known 1,4 elimination of alcohol from propargylic ethers of this structure ($OCH_2C{\equiv}CCHR$) under strongly basic conditions which occurs faster than isomerization.[21,22] Although an unequivocal distinction between mechanisms a and b cannot be made, the alternative mechanism b seems less likely since the 1-H of the bromodiene is more acidic than the 3-H, and the bromodienes are known to react by α elimination. We therefore favor pathway a involving isomerization of **4a.** The results of the present study are thus compatible with a competition between **2a** and **6a** for a deficiency of base and concurrent slow isomerization of **4a.**

The formation of the allenic alcohol **10a** is indeed unexpected. In experiments using cyclohexene as solvent, the

Scheme II



yield of all four oxygenated products (**4, 6, 9,** and **10**) was greatly reduced while the relative ratios were unchanged strongly suggesting that **10a** is derived from the same intermediate (carbene). We suggest a mechanism involving insertion of the carbene into the carbon–hydrogen bond α to hydroxyl in the alcohol to explain the formation of **10a**. A more detailed description of this and other insertion reactions of vinylidene carbene is included in the following paper.[16]

In summary, all of the products obtained by reaction of 1-bromo-1-alkynes with sodium alkoxides are adequately explained by a zwitterion–carbene intermediate. We were unable to detect the presence of the reported 1-acetylenic ether (**3**) either by glpc and tlc or by spectral analysis of the crude reaction mixture.

Experimental Section[23]

General. Toluene, xylene, and benzene were distilled from calcium hydride prior to use. 2-Methoxyethanol and 2,2-dimethyl-1,3-dioxolane-4-methanol were distilled and stored over molecular sieves. Tetrahydrofuran was distilled from lithium aluminum hydride under nitrogen.

Analytical glpc determinations were made on a Varian Model 2100 chromatograph equipped with a flame ionization detector, using helium as the carrier gas at a flow rate of 25 ml/min. A 6 ft × ⅛ in. glass column packed with 3% carbowax 20M on 100–120 mesh Chromosorb W was used for all analyses. A Varian Aerograph A-700 was used for preparative separations with the following columns: column A, 10 ft × ⅜ in. aluminum column packed with 10% carbowax 20M on 40–60 mesh Chromosorb W; column B, 20 ft × ⅜ in. aluminum column packed with 20% OV-210 on 60–80 mesh Chromosorb W (AW); column C, 10 ft × ⅜ in. aluminum column packed with 10% QF-1 on 40–60 mesh Chromosorb W. Helium was used as carrier gas with flow rates of 120–140 ml/min.

1-Bromo-1-heptyne (2a). 2a was prepared as directed[24] in 63% yield, bp 57–59° (12 mm) [lit.[24] bp 69° (25 mm)]: ir (neat) 2215 cm^{-1} (-C≡C-); nmr ($CDCl_3$) δ 2.20 (m, 2 H, $CH_2C{\equiv}C$), 1.38 (m, 8 H, $-CH_2-$), and 0.91 ppm (m, 3 H, CH_3). Glpc showed a single peak (>99%). The absence of isomeric allene or acetylene impurities was apparent in the nmr and ir spectra. Portions were freshly distilled and checked for impurities before each reaction.

1-Heptyn-3-yl Mesylate. According to the general procedure of Crandall, *et al.*,[11] 15.8 g (0.12 mol) of methanesulfonyl chloride was added dropwise to a solution of 11.2 g (0.1 mol) of 1-heptyn-3-ol and 15 ml of pyridine with cooling in an ice bath. The mixture was stirred at 0° for 4 hr and then poured over ice and 25 ml of concentrated hydrochloric acid. The product was extracted with ether–benzene and worked up as usual to give 16.1 g (83%) of 1-heptyn-3-yl mesylate, bp 55–57° (0.005 mm): ir (neat) 3280 and 2142 cm^{-1} (C≡CH); nmr ($CDCl_3$) δ 5.13 (m, 1 H, CHC≡C), 3.08 (s, 3 H, SO_2CH_3), 2.83 (d, 1 H, C≡CH), 2.1–1.1 (broad m, 6 H, CH_2), and 0.90 (m, 3 H, CH_3).

Anal. Calcd for $C_8H_{14}O_3S$ (190.2); C, 50.09; H, 7.42. Found: C, 50.28; H, 7.16.

1-Bromo-1-hexadecyne (2b). To a solution of 93 g of mercuric chloride and excess potassium iodide in 225 ml of water at 50° was added 200 ml of 10% aqueous sodium hydroxide. The mixture was cooled to room temperature and 55 g (0.248 mol) of 1-hexadecyne dissolved in 1400 ml of methanol was added during 1 hr with stirring. The precipitate of bis(1-hexadecynyl)mercury was recovered by filtration and recrystallized from dimethylformamide, mp 95–96°.

Anal. Calcd for $C_{32}H_{58}Hg$: C, 59.74; H, 9.09. Found: C, 59.67; H, 8.90.

This material was suspended in 2500 ml of carbon tetrachloride and an equimolar amount of 10% bromine in carbon tetrachloride was added with cooling. After filtration the solvent was removed *in vacuo* and the residue was percolated through a short alumina column (hexane solvent) to remove traces of unreacted starting material. After removal of solvent **2b** was obtained by distillation, bp 95–96° (0.03 mm), 46.5 g (62%): ir (neat) 2210 cm^{-1} (-C≡C-); nmr ($CDCl_3$) δ 2.20 (m, 2 H, $CH_2C{\equiv}C$) and 1.3–0.89 ppm (broad m, 27 H, CH). Allenic or acetylenic impurities were not detected.

Anal. Calcd for $C_{16}H_{29}Br$ (301.3): C, 63.77; H, 9.70. Found: C, 63.75; H, 9.52.

Preparation of 2,2-Dimethyl-4-(1′-*n*-butyl-2′-propynyloxymethyl)-1,3-dioxolane (9). Sodium (0.726 g, 0.0316 mol) was added in small pieces to 2,2-dimethyl-1,3-dioxolane-4-methanol (6.15 g, 0.047 mol) in 50 ml of toluene under nitrogen. The mixture was slowly heated to reflux and then heated until all the sodium dissolved (3 hr). Then 6.0 g (0.0316 mol) of 1-heptyn-3-yl mesylate was added dropwise to the refluxing solution (15 min). Heating was continued for an additional hour followed by cooling and the normal work-up. Distillation of the oil remaining after removal of solvent gave 3.71 g (52%) of **9**, bp 72–74° (0.2 mm). Glpc indicated **9** was of 93% purity and contained 4% of **4a** and 3% of an unknown impurity having shorter retention time. The analytical sample was obtained by preparative glpc (column A, 150°): ir (neat) 3305 (C≡CH), 2115 (C≡C), and 1094 cm^{-1} (C-O-C); nmr ($CDCl_3$) δ 4.50–3.20 (m, 6 H, O-CH), 2.42 (d, 1 H, C≡CH), and 0.95 ppm (m, 15 H, CH).

Anal. Calcd for $C_{13}H_{22}O_3$ (226.3): C, 68.99; H, 9.80; mol wt, 226. Found: C, 68.77; H, 9.87; mol wt (mass spectrum), 226.

2,2-Dimethyl-4-(2′-heptynyloxymethyl)dioxolane (6a). 6a was prepared by a modification of the reported procedure.[12] The sodium alkoxide was prepared as in the previous section from 2.07 g (0.09 mol) of sodium and 13.5 g (0.1 mol) of 2,2-dimethyl-1,3-dioxolane-4-methanol. The mixture was transferred under nitrogen to a dropping funnel and added (30 min) to 17.5 g (0.1 mol) of 1-bromo-2-heptyne[25] in 50 ml of toluene at reflux. Heating was continued for an additional hour, followed by cooling and the normal work-up. Evaporation of solvent and distillation gave 10.6 g (47%) of **6a**, bp 82–85° (0.1 mm) [lit.[12] bp 84–86° (0.08 mm)]. Glpc indicated a purity of 95%. An analytically pure sample was obtained by glpc (column A, 155°): ir (neat) 2220, 2290 (C≡C), and 1091 cm^{-1} (C-O-C); nmr ($CDCl_3$) δ 4.17 (t, 2 H, J = 3 Hz, $OCH_2C{\equiv}C$), 4.4–3.4 (m, 5 H, CHO), 2.22 (m, 2 H, $CCH_2C{\equiv}C$), and 1.7–0.7 ppm (broad m, 13 H, CH): mol wt (mass spectrum), 226.

Reaction of 1-Bromo-1-heptyne (2a) and 1. The general procedure of Preobrazhenskii and coworkers[4] was employed. Sodium (0.54 g, 0.0235 mol) and 2,2-dimethyl-1,3-dioxolane-4-methanol (3.43 g, 0.0254 mole) were added to 50 ml of toluene under nitrogen at 25°. The mixture was heated at reflux until the sodium dissolved (3 hr) and 4.10 g (0.0234 mol) of **2a** dissolved in 10 ml of toluene was added dropwise (5 min). The mixture was heated for 2 hr, cooled, and worked up as usual. Evaporation of the solvent left an oil which consisted of six components as indicated by glpc analysis. These compounds were identified, in order of elution on a carbowax column at 90°, as **9**, **4a**, **6a**, and **10a** (mixture of three peaks). The total yield determined by glpc using 4-bromoacetophenone as internal standard was 19%. The ratio of **9**:**4a**:**6a**:**10a** was somewhat variable[15] but representative data are 1:6:2:11.

Partial separation was accomplished by distilling the ether products (**4a**, **6a**, and **9**), bp 81–88° (0.5 mm). The analytical samples were then obtained by preparative glpc (column A, 150°). The residual oil consisted largely of **10a** which was obtained by glpc as a mixture of diastereoisomers (column B, 130°). Careful control of injection port and column temperatures was essential to avoid excessive decomposition. Both **4a** and **10a** were very sensitive to air and thermally labile. Compounds **6a** and **9** had nmr and ir spectra and glpc retention times identical with those of the authentic samples. Data for **4a** and **10a** are as follows.

4a: ir (neat) 1952 (OCH=C=C) and 1186 and 1079 cm^{-1} (CHO); nmr ($CDCl_3$) δ 6.65 (m, 1 H, H(O)C=C=C), 5.83 (m, 1 H, OC=C=CH), 4.50–3.40 (m, 5 H, CHO), 2.08 (m, 2 H, $CH_2C{=}C{=}C$), and 2.6–0.7 ppm (m, 13 H, CH).

Anal. Calcd for $C_{13}H_{22}O_3$ (226.3): C, 68.99; H, 9.80. Found: C, 69.05; H, 9.63.

10a: ir (neat) 3450 (OH) and 1975 cm^{-1} (C=C=C); nmr ($CDCl_3$) δ 5.27 (m, 2 H, CH=C=CH), 4.4–3.7 (m, 4 H, OCH), 2.21 (m, 3 H, $C{=}C{=}CCH_2$, and OH) (one hydrogen disappears on addition of D_2O), and 2.7–0.7 ppm (m, 13 H, CH).

Anal. Calcd for $C_{13}H_{22}O_3$ (226.3): C, 68.99; H, 9.80; mol wt, 226.1569. Found: C, 68.73, H, 9.67; mol wt (mass spectrum), 226.1567.

Use of benzene or xylene as solvent in this procedure gave similar results with the reaction time varying from 30 min in xylene to 4 or 5 hr in benzene. The reaction was inconveniently slow at lower temperatures. In order to confirm that all of the components collectively assigned as **10a** were in fact alcohols, the aforementioned residual oil was treated with an excess of acetic anhydride in pyridine for 24 hr. Glpc confirmed the disappearance of the three alcohol peaks and revealed three new peaks of longer retention time. Collection of a small quantity of the new components by glpc (column B, 150°) gave material with ir bands at 1980 (C=C=C) and 1755 cm^{-1} (COOR) suggesting formation of the allenic acetates.

Reaction of 2a and 1 in Cyclohexene or Toluene–Cyclohexene. Repetition of the reaction (preceding section) in cyclohexene or toluene–cyclohexene gave, in addition to the aforementioned oxygenated products, a new compound subsequently identified as **17.** The ratio of **17** to the oxygenated products was 4:1 (total yield 17%). After simple distillation, **17** was isolated by glpc (column A, 140°): ir (neat) 2020 and 1995 cm^{-1} (allenic cyclopropyl); nmr ($CDCl_3$) δ 5.20 (m, 1 H, HC=C=C), and 2.4–0.7 ppm (broad m, 19 H, CH).

Anal. Calcd for $C_{13}H_{20}$ (176.2): C, 88.56, H, 11.44, mol wt, 176.1565. Found: C, 88.27, H, 11.56; mol wt (mass spectrum), 176.1565.

Analytical glpc showed that **17** was a mixture of two components (partially resolved) in approximately equal amounts which can be attributed to endo and exo isomers.[19] In another experiment, **2a** (4.38 g, 0.025 mol) was added in one portion to 5.17 g (0.025 mol) of potassium *tert*-butoxide suspended in 100 ml of refluxing cyclohexene under nitrogen. Heating was continued for 40 min and then the mixture was cooled, filtered, and worked up as usual. **17** was obtained in 8% yield (95% purity) by distillation, bp 65–69° (0.25 mm). Use of *n*-butyllithium or sodium amide at −80 or 0° gave no trace of **17**, metalation or attack on bromine being the probable course of reaction as large quantities of 1-heptyne were obtained.

Reaction of 1-Bromo-1-hexadecyne (2b) with Sodium 2,2-Dimethyl-1,3-dioxolane-4-methanolate (1). According to the directions of Preobrazhenskii, *et al.*,[5] 6.02 g (0.02 mol) of **2b** was added rapidly (5 min) to a refluxing solution of 0.02 mol of **1** (prepared from 0.46 g of sodium and 2.64 g of 2,2-dimethyl-1,3-dioxolane-4-methanol). The reaction mixture was heated for 30 min, cooled, and worked up as usual. After removal of solvent, the residue was chromatographed on silica gel to obtain, in order of elution, **2b** (20%), 1-hexadecyne (50%), a fraction containing a mixture of unidentified components, **6b** (2%), and **10b**, (20%). No evidence for the formation of the desired acetylenic ether was found in any fraction. Spectral and analytical data are as follows. **6b:** ir (neat) 2290, 2220 cm^{-1} (C≡C); nmr ($CDCl_3$) δ 4.21 (t, 2 H, J = 2 Hz, $OCH_2C{\equiv}C$), 4.41–3.40 (broad m, 5 H, CHO), 2.19 (m, 2 H, $CCH_2C{\equiv}C$), and 1.70–0.7 ppm (broad m, 31 H, CH). Irradiation at δ 2.19 caused the collapse of the signal at δ 4.21 to a singlet.

Anal. Calcd for $C_{22}H_{40}O_3$: C, 72.56; H, 12.18; mol wt, 352.2977. Found: C, 72.81; H, 12.24; mol wt (mass spectrum), 352.2981.

Treatment of **6b** with Brady's reagent gave only acetone 2,4-dinitrophenylhydrazone (melting point and mixture melting point).

10b: ir (neat) 3450 (OH) and 1970 cm^{-1} (C=C=C); nmr ($CDCl_3$) δ 5.33 (m, 2 H, CH=C=CH), 4.45–3.70 (m, 4 H, OCH), 2.44 (s, 1 H, OH, disappears on treatment with D_2O), 2.23 (m, 2 H, $CH_2C{=}C{=}C$), and 2.75–0.70 (broad m, 31 H, CH).

Anal. Calcd for $C_{22}H_{40}O_3$: mol wt, 352.2977. Found: mol wt (mass spectrum), 352.2984.

(±)-1-*O*-Hexadec-2′-ynylglycerol (7). A solution of **6b** (800 mg) in dry, redistilled 2-methoxyethanol was warmed on the steam bath overnight with a large excess of boric acid (saturated solution). The solvent was removed *in vacuo* and the residue taken up in ethyl acetate. The organic solution was washed (aqueous sodium carbonate, saturated aqueous potassium chloride), dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (chloroform solvent) to obtain pure **7** (500 mg), mp 35–36°: ir (neat) 3300, (OH), 2280, 2215 cm^{-1} (C≡C); nmr 4.21 (t, 2 H, J = 2 Hz, $OCH_2C{\equiv}C$), 2.20 (m, 2 H, $CCH_2C{\equiv}C$), 0.7–1.7 ppm (m, 25 H). Irradiation at δ 2.20 caused the collapse to a singlet of the signal at δ 4.21.

Anal. Calcd for $C_{19}H_{36}O_3$: C, 73.03, H, 11.61; mol wt, 312.2664. Found: C, 73.01, H, 11.53; mol wt (mass spectrum), 312.2669.

(±)-1-*O*-Hexadec-*cis*-2′-enylglycerol (8). A solution of **7** in ethyl acetate was hydrogenated for 1 week on the presence of Lindlar catalyst (100 mg) and 1,2-bis(2-hydroxyethylthio)ethane (0.5 mg). The catalyst was filtered off through Celite and the solution was evaporated. Purified hexane was added to the residue and the solution was allowed to stand overnight. The precipitated catalyst poison was filtered off through Celite and the solution was evaporated. The residue was chromatographed on silica gel (chloroform solvent) to obtain **8**, mp 27–28°: ir (neat) 3400 (OH), 1665, 735 cm^{-1} (HC=CH); nmr 0.7–1.7 ppm (m, 25 H), δ 2.06 (m, 2 H, $C{=}CCH_2C$), 4.09 (d, 2 H, J = 6.5 Hz, $OCH_2C{=}C$), 5.6 (m, 2 H, -HC=CH-). Irradiation at δ 5.6 showed coupling to the signals at δ 4.09 and 2.06.

Anal. Calcd for $C_{19}H_{38}O_3$: 314.2821. Found: (mass spectrum) 314.2819.

Cleavage of **8** with alkaline permanganate–periodate and subsequent esterification of the acidic product with diazomethane gave methyl myristate, identified by comparison with an authentic sample (glc and ir).

Hydrogenation (Adams' catalyst) of both **7** and **8** afforded racemic chimyl alcohol (melting point and mixture melting point).

Ozonolysis of **8** in ethyl acetate at −70° gave tetradecanal, identified as its 2,4-dinitrophenylhydrazone, mp and mmp 103–104°.

D-(+)-1-*O*-Hexadec-2′-ynylglycerol [(+)-7]. Prepared in the same way as **7**, but starting from L-2,2-dimethyl-1,3-dioxolane-4-methanol,[26] this had mp 47°, $[\alpha]^{22}D$ +0.9° (*c* 9.2, $CHCl_3$), and ir and nmr spectra identical with those of **7.**

Anal. Calcd for $C_{19}H_{36}O_3$: C, 73.03, H, 11.61; mol wt 312.2664. Found: C, 73.34, H, 11.44; mol wt (mass spectrum) 312.2667.

Hydrogenation of (+)-**7** (Adams' catalyst) gave D-(+)-chimyl alcohol, mp 66°, identified as the bis-4-nitrobenzoate, mp 58°, $[\alpha]^{22}D$ +29.4° (*c* 1.9, $CHCl_3$) [lit.[27] mp 58–59°, $[\alpha]^{16}D$ −29.8° (*c* 6.5, $CHCl_3$) for the enantiomer].

D-(+)-1-*O*-Hexadec-*cis*-2′-enylglycerol [(+)-8]. Prepared from (+)-**7** in the same manner as **8**, this had mp 34–35°, $[\alpha]^{22}D$ +0.7° (*c* 11, $CHCl_3$), and spectra identical with those of **8.**

Anal. Calcd for $C_{19}H_{38}O_3$: C, 72.56, H, 12.18; mol wt, 314.2821. Found: C, 72.81, H, 12.24; mol wt (mass spectrum), 314.2825.

Reaction of 1-Bromo-1-hexyne and Sodium 2-Methoxyethanolate. 1-Bromo-1-hexyne (20 g, 0.124 mol) in 20 ml of benzene was added over 5 min to a refluxing solution of sodium 2-methoxyethanolate (prepared from 2.85 g of sodium and 9.44 g of 2-methoxyethanol) in 200 ml of benzene. The mixture was heated at 80° for an additional 2 hr, cooled, and worked up as usual. The product distribution was analogous to that obtained from **2a** and **1.** The isolation technique was essentially the same except that the residual oil remaining after evaporation of the solvent was processed directly by preparative glpc (column B, 120–150° programmed). Thus in order of elution (on carbowax or QF-1), the following compounds were obtained: 2-methoxy(1′-*n*-propyl-2′-propynyloxy)ethane (**13**); 2-methoxy(1′,2′-hexadienyloxy)ethane (**11**); 2-methoxy(2′-hexynyloxy)ethane (**12**); and 1-methoxy-3,4-octadienol (**14**). The total yield was 14% and the product ratios are given in the following paper.[16] Spectral and analytical data for these compounds follow.

13: ir (neat) 3275 and 2119 cm^{-1} (C≡CH); nmr ($CDCl_3$) δ 3.90 (m, 5 H, OCH_2CH_2O, OCH), 3.37 (s, 3 H, OCH_3), 2.42 (d, 1 H, C≡CH) 1.9–1.1 (m, 4 H, $-CH_2-$), and 0.95 ppm (m, 3 H, CH_3).

Anal. Calcd for $C_9H_{16}O_2$ (156.2): C, 69.19; H, 10.32; mol wt 156. Found: C, 68.91; H, 10.44; mol wt (mass spectrum), 156.

11: ir (neat) 1965 cm^{-1} (OCH=C=CH); nmr ($CDCl_3$) δ 6.67 (m, 1 H, H(O)C=C=C), 5.83 (m, 1 H, OC=C=CH), 3.9–3.4 (m, 4 H, OCH_2CH_2O), 3.37 (s, 3 H, OCH_3), 2.19 (m, 2 H, C=C=CCH_2), 1.41 (m, 2 H, CH_2), and 0.94 ppm (m, 3 H, CH_3).

Anal. Calcd for $C_9H_{16}O_2$ (156.2): C, 69.19; H, 10.32; mol wt, 156. Found: C, 68.93; H, 10.09; mol wt (mass spectrum), 156.

12: ir (neat) 2285, 2230 (C≡C) and 1131, 1099 cm^{-1} (C–O–C); nmr ($CDCl_3$) δ 4.17 (t, 2 H, $C{\equiv}CCH_2O$), 3.8–3.4 (m, 4H, OCH_2CH_2O), 3.37 (s, 3 H, OCH_3), 2.22 (m, $CH_2C{\equiv}C$), 1.52 (m, 2 H, CH_2), and 0.99 ppm (m, 3 H, CH_3).

Anal. Calcd for $C_9H_{16}O_2$ (156.2): C, 69.19; H, 10.32; mol wt 156. Found: C, 68.96; H, 10.18; mol wt (mass spectrum), 156.

14: ir (neat) 3440 (OH) and 1980 cm^{-1} (C=C=C); nmr ($CDCl_3$) δ 5.20 (m, 2 H, CH=C=CH), 4.25 (m, 1 H, C*H*OH), 3.38 (d, 2 H, CH_2O), 3.37 (s, 3 H, OCH_3), 2.77 (broad, 1 H, OH, disappears on addition of D_2O), 2.3–1.1 (m, 4 H, CH_2CH_2), and 0.98 ppm (m, 3 H, CH_3).

Anal. Calcd for $C_9H_{16}O_2$ (156.2): C, 69.19; H, 10.32, mol wt, 156. Found: C, 69.05; H, 10.51; mol wt (mass spectrum), 156.

Preparation of 1-Methoxy-2-octanol (15). The general procedure of Normant, *et al.*,[15] was used. To a flask equipped with magnetic stirring, reflux condenser, two dropping funnels, and a nitrogen inlet was added 4.9 g (0.2 mol) of magnesium turnings, 0.2 g of mercuric chloride, and 30 ml of tetrahydrofuran. With cooling in an ice bath, a few milliliters of a solution of 16 g (0.2 mol) of chloromethyl methyl ether in 30 ml of THF was added. After initiation of the reaction the remainder of the chloromethyl methyl ether and 11.4 g (0.1 mol) of *n*-heptaldehyde in 20 ml of THF was added simultaneously (90 min). The mixture was then allowed to stand overnight at room temperature and hydrolyzed with saturated ammonium chloride solution. After the normal work-up and removal of solvent, the residue was distilled to give 10.1 g (63%) of material, bp 86–88° (6 mm), consisting of two components in the ratio of 92:8. The major component was isolated by preparative glpc (column B, 130°) and identified as **13**: ir (neat) 3440 (OH) and 1115 cm^{-1} (O-C); nmr ($CDCl_3$) δ 3.70 (m, 1 H, CHOH), 3.37 (s, 3 H, OCH_3), 3.30 (m, 2 H, CH_2O), 2.70 (s, 1 H, OH, disappears on treatment with D_2O), and 2.5–0.7 ppm (m, 13 H, CH).

Anal. Calcd for $C_9H_{20}O_2$ (160.3); C, 67.45; H, 12.58. Found: C, 67.35; H, 12.39. The minor component was not further investigated.

Hydrogenation of 14. 14 (300 mg, mixture of diastereomers), 25 ml of absolute ethanol, and 50 mg of platinum oxide were treated with hydrogen at an initial pressure of 30 psi in a Parr apparatus. After 2 hr the reaction was stopped and the catalyst filtered, and the absence of **14** was verified by glpc analysis. A single new peak of shorter retention time was apparent. The solution was concentrated by distillation through a short column for preparative glpc (column B, 130°). The material isolated was identical in ir, nmr, and glpc retention time (peak enhancement) with the authentic sample of **15**.

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