methylbuta-1,3-dien-4-yl(trimethyl)silane, 31734-55-1; *cis*-2-methylbuta-1,3-dien-4-yl(trimethyl)silane, 31734-56-2.

Acknowledgments.—The authors wish to express their appreciation for the support of this research through Grant GM-13421 of the Public Health Service.

Mass Spectrometry in Structural and Stereochemical Problems. CCIX.[1] Functional Group Interaction after Electron Impact. Anomalous Ether Cleavage in Bifunctional Benzyloxy Ethers[2]

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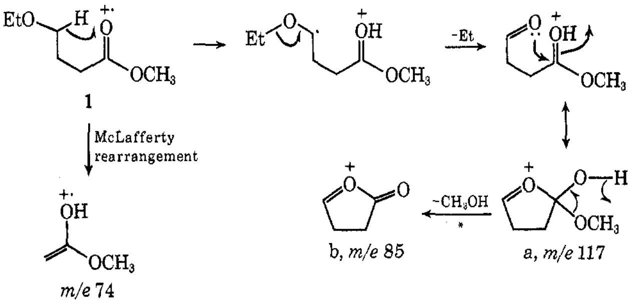
In a series of bifunctional benzyloxy ethers, the scope and limitations of the unexpected C–O cleavage at the ether function with charge retention on the benzyloxy moiety (*m/e* 107) has been investigated. Deuterium-labeling experiments indicated that simple C–O ether cleavage alone could not account for the formation of this ion. Its generation was found to be independent of the distance between the two functional groups. From these and other data, it was concluded that the structure of this ion was best represented as protonated benzaldehyde.

During the last decade the fragmentation patterns of almost every class of monofunctional compounds were thoroughly investigated,[4] and in the last few years the question of whether two functional groups in the same molecule would give rise to fragmentations independent of one another or to unique fragmentations resulting from direct interaction of the two groups has been the subject of several investigations.[5-14] As an extension of work reported earlier,[14] we became interested in pursuing further the nature of the process leading to the intense peaks at *m/e* 117 and 85 in the mass spectrum[15] (Figure 1) of methyl 4-ethoxybutyrate (**1**). With the

$EtO(CH_2)_3CO_2CH_3$ **1** $\qquad C_6H_5CH_2O(CH_2)_3CO_2CH_3$ **2**

aid of deuterium-labeling studies, high-resolution measurements, and metastable defocusing experiments,[16] the formation of these ions was rationalized as shown in Scheme I.

SCHEME I



It was reasoned that, if the ethyl ether portion of **1** were replaced with another substituent which would yield a radical more stable than ethyl, the process leading to ions of masses 117 and 85 should be enhanced. To this end methyl 4-benzyloxybutyrate (**2**) was synthesized and its mass spectrum (Figure 2) was recorded. These expectations were only partially fulfilled in that the peaks at *m/e* 117 and 85 were observed in Figure 2, but their intensities were no greater than in the spectrum (Figure 1) of **1**. Instead, a host of additional peaks was observed, most significant and interesting of which being the peak at *m/e* 107 (this peak becomes the base peak at 12 eV). High-resolution measurements indicated the composition of this ion to be C_7H_7O, which corresponds formally to cleavage of the C–O bond of the ether function with charge retention on the benzyloxy fragment. This finding was particularly unusual, since normally cleavage of an ether C–O bond with charge retention on the oxygen-containing fragment is a very unfavorable process[17] (in the spectrum of benzyl *n*-butyl ether, the *m/e* 107 peak is negligible—Σ_{40} 0.1%). Because of the uniqueness of this cleavage, we suspected that the ester function at the other end of the molecule was playing an unexpected role in this process and considered it of interest to determine the scope and limitations of this process.

Results and Discussion

It was felt that the two most obvious parameters which might influence the formation of the "anomalous" *m/e* 107 peak would be (a) the length of the hydrocarbon chain separating the two functions and (b) the nature of the functional group at the end of the chain. As a first step in this investigation, the effect of varying the chain length between the two functions on the relative intensity of the *m/e* 107 peak was probed. To this end

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(1) For paper CCVIII, see J. R. Dias, Y. Sheikh, and C. Djerassi, *J. Amer. Chem. Soc.*, in press.

(2) Financial support from the National Institutes of Health (Grant No. AM 04257) is gratefully acknowledged.

(3) (a) National Science Foundation Postdoctoral Fellow, 1969–1970. (b) National Institutes of Health Postdoctoral Fellow, 1967–1968.

(4) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

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(9) J. Diekman, J. B. Thomson, and C. Djerassi, *J. Org. Chem.*, **34**, 4091 (1969).

(10) R. G. Cooks, J. Ronayne, and D. H. Williams, *J. Chem. Soc. C*, 2601 (1967).

(11) R. H. Shapiro and K. B. Tomer, *Org. Mass Spectrom.*, **3**, 333 (1970).

(12) (a) R. J. Highet and P. F. Highet, *Tetrahedron Lett.*, 1803 (1970); (b) R. E. Wolff and A. Caspar, *ibid.*, 1807 (1970).

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(14) M. Sheehan, R. J. Spangler, M. Ikeda, and C. Djerassi, *J. Org. Chem.*, **36**, 1796 (1971).

(15) Mass spectra recorded at nominal voltages of 70 and 12 eV. Unless otherwise stated, only 70-eV spectra are shown.

(16) (a) J. H. Beynon, *Nature*, **204**, 67 (1964); (b) K. R. Jennings, "Some Newer Physical Methods in Structural Chemistry," R. Bonnett and J. G. Davis, Ed., United Trade Press, London, 1967, p 105.

(17) Reference 4, p 227.

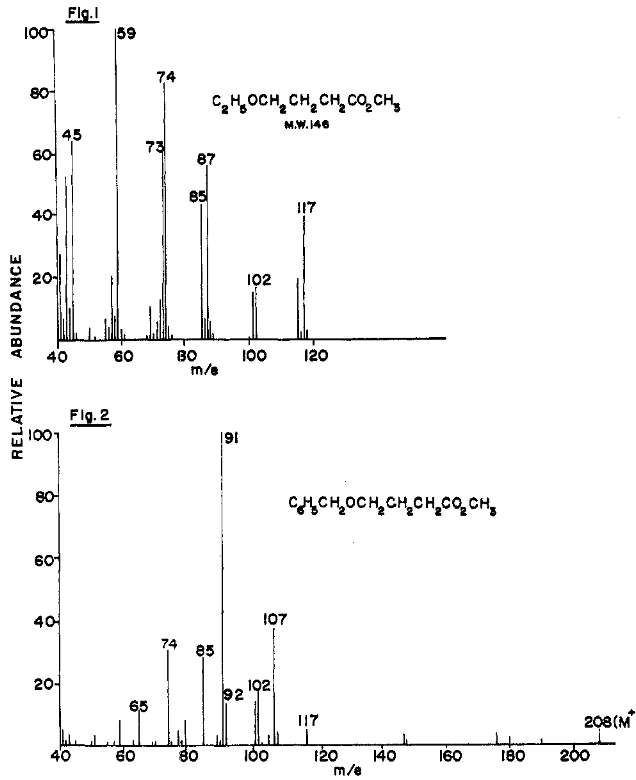


Figure 1.—Mass spectrum (70 eV) of methyl 4-ethoxybutyrate (**1**).

Figure 2.—Mass spectrum (70 eV) of methyl 4-benzyloxybutyrate (**2**).

the series of substances **3**–**6** were synthesized and their mass spectra recorded. Table I summarizes the pertinent spectral data regarding the m/e 107 peak for these compounds. From Table I it can be seen that the importance of the m/e 107 peak is not drastically affected by increasing the length of the hydrocarbon chain between the two functional groups. If it is assumed that the generation of the m/e 107 peak is a result of the interaction of the two functional groups, then analogies to solution chemistry would dictate that such interactions should be most favorable (with respect to entropy considerations) when a six-membered transition state is involved ($n = 3$) and should be very poor for a ten-membered transition state ($n = 7$). In point of fact, there is relatively little difference between these two cases. One explanation of these facts which has been previously postulated[14] is that after electron impact and expulsion of an electron from the parent molecule the resultant charge is actually shared between the two functions such that there is an attractive force holding the two ends of the molecule together, and that this force overrides any entropy consideration that might be made.

$C_6H_5CH_2O(CH_2)_nCO_2CH_3$
3, $n = 1$
4, $n = 2$
5, $n = 4$
6, $n = 7$

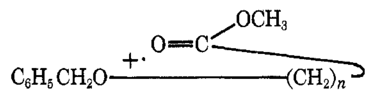
TABLE I

SPECTRAL DATA REGARDING THE m/e 107 PEAK FOR THE BENZYLOXY ESTERS

$C_6H_5CH_2O(CH_2)_nCO_2CH_3$

Compd no.	Σ_{40} m/e 107[a]	Base peak at 12 eV[b]
3, $n = 1$	21.0	107
4, $n = 2$	23.6	107
2, $n = 3$	11.5	107
5, $n = 4$	6.8	116 (m/e 107 is 70% of this peak)
6, $n = 7$	8.8	158 (m/e 107 is 50% of this peak)

[a] 70 eV. [b] Nominal voltage.



$$C_6H_5CH_2\overset{+\cdot}{O}\cdots O{=}C(OCH_3)(CH_2)_n$$

Accepting this model, it would be predicted that the spectra of substances in which the methoxycarbonyl group is replaced by another function capable of sharing charge should also exhibit prominent ions at mass 107. To test this notion, the series of substrates **7**–**12** was prepared and their mass spectra were recorded (Figures 3–8). Considering the first three substances (**7**–**9**), such was the case. That is, excluding the ubiquitous tropylium ion (m/e 91), the most intense ion in each spectrum was found at m/e 107 (Σ_{40} 23.0, 23.3, and 10.1%, respectively; base peak at low voltage). For R = OH and OCH_3, the effect of varying the length of the hydrocarbon chain between the two functional groups on the intensity of the m/e 107 peak was measured (see Table II), and again it was found that the intensity of this ion was more or less independent of the chain length. The only exception to this trend was found in the spectrum of benzyloxymethoxymethane (**17**) where no m/e 107 peak was encountered. In this instance, however, the two oxygen atoms are on the same carbon atom, and, hence, the compound is actually monofunctional (mixed acetal) and should be considered separately. In the spectra of the substrates **10**–**12** (Figures 6–8, respectively), it was found that the ion of mass 107 was either absent or unimportant. Various factors may be responsible for this deviation, but it is premature to speculate on the precise reasons at this time.

$C_6H_5CH_2O(CH_2)_nR$
7, $n = 3$; $R = CO_2H$
8, $n = 4$; $R = OH$
9, $n = 4$; $R = OCH_3$
10, $n = 2$; $R = N(CH_3)_2$
11, $n = 2$; $R = Br$
12, $n = 2$; $R = OSi(CH_3)_3$

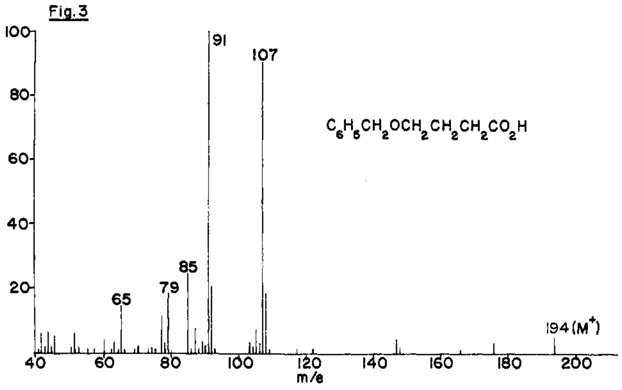
TABLE II

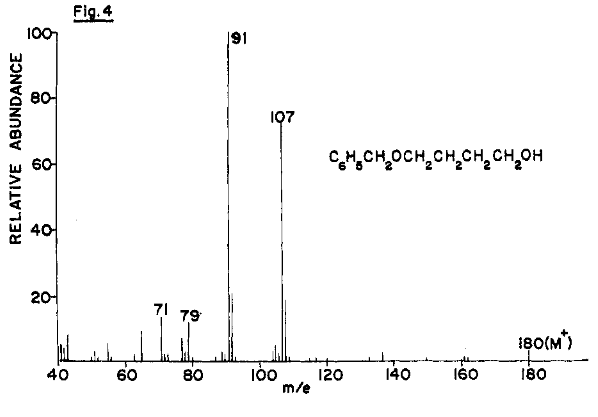
SPECTRAL DATA REGARDING THE m/e 107 PEAK FOR THE BENZYLOXY ALCOHOLS AND METHYL ETHERS

$C_6H_5CH_2O(CH_2)_nR$

Compd no.	Σ_{40} m/e 107[a]	Base peak at 12 eV, m/e[b]
13, R = OH; $n = 2$	10.7	152 (107 is 60% of this peak)
14, R = OH; $n = 3$	33.3	107
8, R = OH; $n = 4$	23.3	107
15, R = OH; $n = 5$	10.4	107
16, R = OH; $n = 8$	16.2	107
17, R = OCH_3; $n = 1$	0.1	91 (no 107 peak)
18, R = OCH_3; $n = 2$	11.0	107
9, R = OCH_3; $n = 4$	10.1	107

[a] 70 eV. [b] Nominal voltage.





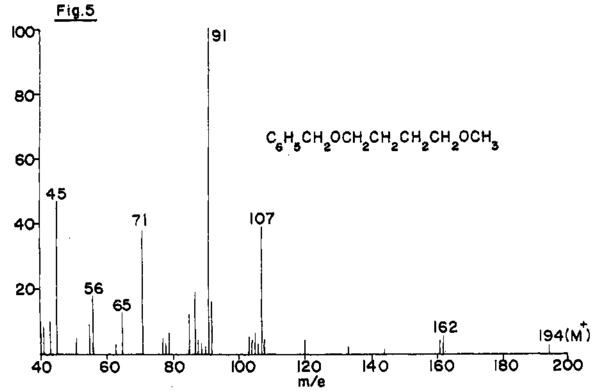
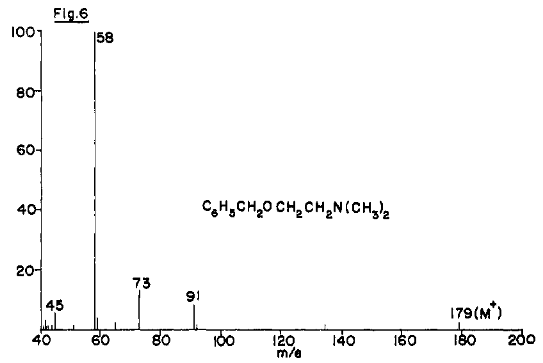
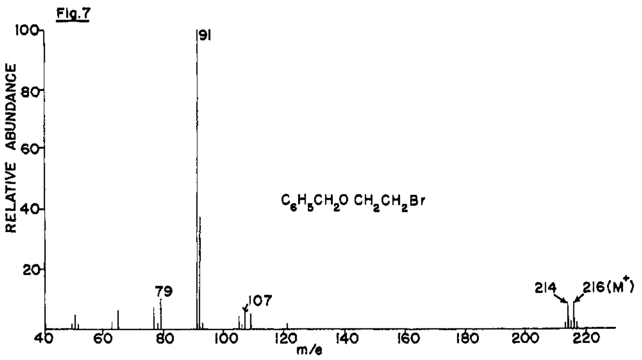


Figure 3.—Mass spectrum (70 eV) of 4-benzyloxybutyric acid (7).
Figure 4.—Mass spectrum (70 eV) of 4-benzyloxy-1-butanol (8).
Figure 5.—Mass spectrum (70 eV) of 4-benzyloxybutyl methyl ether (9).

One of the requirements for the generation of the *m/e* 107 peak in bifunctional benxyloxy substances appears to be an unhindered oxygen function on the terminus of the molecule. However, so far nothing has been stated about the actual details of the process leading to this ion. It was more or less assumed at the outset that this ion was not the result of direct C–O bond cleavage to give $C_6H_5CH_2O^+$ with its unfavorable sextet on oxygen; rather, it was felt that a rearrangement or reciprocal H transfer was probably occurring. To test this hypothesis and to elucidate the details of the process or processes leading to the *m/e* 107 peak in the substances mentioned above, several D-labeled analogs of **3**–**9** were synthesized (see Syntheses of Labeled Substrates) and their mass spectra recorded. Table III gives the structures of these substrates and lists the pertinent spectral data regarding the *m/e* 107 peak for each compound. In the absence of any reciprocal hydrogen transfers or rearrangements, it would be expected that the *m/e* 107 peak would shift completely to *m/e* 109 for α-d_2 labeled substrates and remain at 107 for any label in the hydrocarbon chain or functional group. For the most part, no scrambling of the labels was encountered. However, for the substrates **21**, **25**, **26**, and **27** considerable exchange was observed. Accounting for unlabeled substrate and ^{13}C isotope contributions, the following deuterium exchange was calculated: 0.7 D in **21**, 0.4 D in **25**, 0.67 D in **26**, and 0.70 D in **27**. These data suggest some type of reciprocal hydrogen transfer between the terminal hydroxyl group and the benzyl protons in the benzyloxy alcohols. This exchange did not seem to be affected by increased chain length, since significant exchange was also observed for the α-d_2 analog of 8-benzyloxy-1-octanol. One possible mechanism for the formation of the *m/e* 107 peak which is consistent with these data for the al-





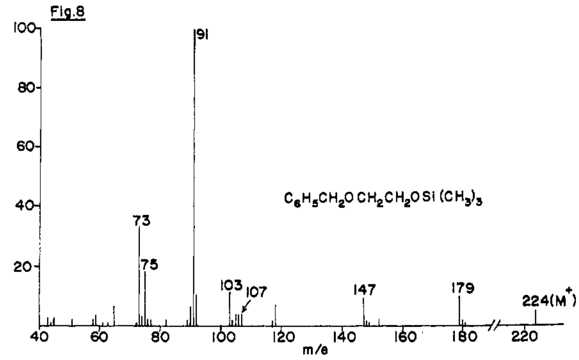


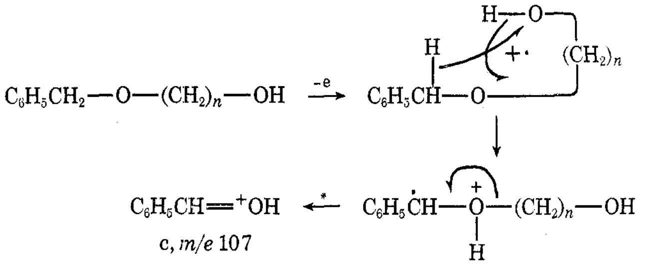
Figure 6.—Mass spectrum (70 eV) of 2-benzyloxyethyldimethylamine (10).
Figure 7.—Mass spectrum (70 eV) of 2-benzyloxyethyl bromide (11).
Figure 8.—Mass spectrum (70 eV) of 2-benzyloxyethyl trimethylsilyl ether (12).

TABLE III

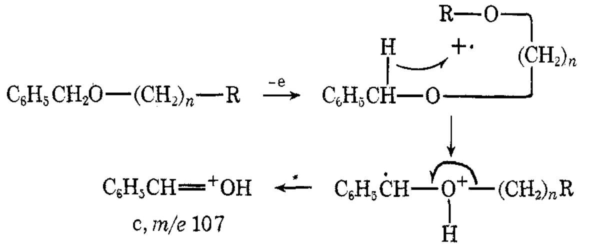
SPECTRAL DATA REGARDING THE *m/e* 107 PEAK FOR SOME DEUTERIUM-LABELED BENZYLOXY ESTERS, ALCOHOLS, AND METHYL ETHERS

Compd	No.	% isotopic purity	*m/e* (rel abundance) 105	106	107	108	109	110
$C_6H_5CH_2OCH_2CH_2CH_2CO_2CH_3$	**2**		3	1	37	4		
$C_6H_5CD_2OCH_2CH_2CH_2CO_2CH_3$	**19**	97 d_2	2			2	34	3
$C_6H_5CH_2OCD_2CH_2CH_2CO_2CH_3$	**20**	96 d_2	5	2	42	4		
$C_6H_5CH_2OCH_2CH_2CH_2CH_2OH$	**8**		5	3	72	19	1	
$C_6H_5CD_2OCH_2CH_2CH_2CH_2OH$	**21**	97 d_2	3	2	2	25	33	10
$C_6H_5CH_2OCD_{\alpha}CH_2CH_2CH_2OH$	**22**	96 d_2	3	2	78	20	2	
$C_6H_5CH_2OCH_2CD_2CD_2CH_2OH$	**23**	96 d_4	5	3	81	21	2	
$C_6H_5CH_2OCH_2CH_2CH_2CD_2OH$	**24**	98 d_2	5	2	48	12	1	
$C_6H_5CH_2OCH_2CH_2CH_2CH_2OD$	**25**	60 d_1	3	2	40	20	1	
$C_6H_5CH_2OCH_2CH_2OH$	**13**		2	1	20	2		
$C_6H_5CD_2OCH_2CH_2OH$	**26**	98 d_2			1	10	15	2
$C_6H_5CH_2OCH_2CH_2OD$	**27**	50 d_1	3	1	35	15	2	
$C_6H_5CH_2OCH_2CH_2OCH_3$	**18**		9	6	33	3		
$C_6H_5CD_2OCH_2CH_2OCH_3$	**28**	98 d_2	5	2	5	2	30	3
$C_6H_5CH_2OCH_2CH_2OCD_3$	**29**	98 d_3	8	7	35	4		

cohols is shown below. In accord with this mechanism, moderate metastable peaks were observed in the spectra



of most of these substrates for the transition $M^+ \rightarrow m/e$ 107. Whether this process is concerted or the exact structure of ion c is as shown is a matter of speculation at this point. Formation of the mass 107 ion from the benzyloxy esters, acids, and methyl ethers can be envisaged in an analogous manner, except that no reciprocal H transfer occurs (the benzyl proton protonating the benzyloxy oxygen directly).



It was felt that some driving force for the formation of the mass 107 ion in the above substances was provided by the particular stability of the intermediate benzyl radicals. Therefore, the question arose whether such intense *m/e* 107 peaks would also be observed after substitution of an alkyl group for the benzyl moiety. To answer this question, compounds **30–33** were synthesized and their mass spectra recorded (Figures 9–12). For ions of the general structure $R'CH=O^+H$, peaks at masses 45 for **30**, 59 for **31**, 73 for **32**, and 101 for **33** would be expected in the spectra of these substances, and such peaks were, in fact, found in **30–32**.

$RO(CH_2)_4OH$
30, R = C_2H_5
31, R = $CH(CH_3)_2$
32, R = n-C_4H_9
33, R = n-C_6H_{13}

In each instance, however, ions of the same mass could have been formed by other cleavage processes, and as yet no deuterium-labeling studies have been carried out to distinguish these from the cleavage in question. Only in the spectrum (Figure 12) of **33** could the peak at mass 101 be formed in only one way (excluding rearrangements) and perhaps give the ion corresponding to structure c. Inspection of Figure 12, however, reveals that formation of this peak is not a very favorable process (*m/e* 101, Σ_{40} 1.8% as compared to Σ_{40} 23.3% when R = $C_6H_5CH_2$). If this peak is formed by the same process as was postulated for the *m/e* 107 peak, then it would be expected that *m/e* 101 should be proportioned between 102 and 103 in the spectrum of 1,1-dideuterio-*n*-hexyl 4-hydroxy-*n*-butyl ether (**34**). In-

$CH_3CH_2CH_2CH_2CH_2CD_2OCH_2CH_2CH_2CH_2OH$
34

deed, the spectrum (not reproduced) of **34** shows that *m/e* 101 was shifted equally to 102 and 103 (deuterium content, 98% d_2). Whereas these data indicate that generation of ions of the general formula $R'CH=^+OH$ does occur, the low intensity of the *m/e* 101 peak in the spectrum of **33** suggests that a phenyl group is necessary to stabilize the incipient secondary radical.

While formation of protonated aldehyde ions of the general formula $R'CH=O^+H$ was not a very important process in the spectra of the 4-alkoxy-1-butanols, several interesting features were observed in these spectra which merit further discussion. In an earlier study[14] regarding the interaction of remote functional groups in acyclic systems upon electron impact, an intense peak (rel intensity 45% Σ_{40} 20%) was observed at *m/e* 58 in the spectrum of 4-methoxy-1-butanol (**35**). The structure and genesis of this ion were further studied by examining the spectra of **30–33** and of two deuterium-labeled analogs of **35**. In the spectra (not shown) of 4-methoxy-4,4-dideuterio-1-butanol (**36**) and 4-methoxy-1,1-dideuterio-1-butanol (**37**) it was found that the position of the *m/e* 58 peak was unchanged in **37** but shifted to *m/e* 59 in **36**. Furthermore, peaks corresponding to the loss of HDO and D_2O were observed for **36** but not for **37**, suggesting that loss of water in these substrates was occurring in the normal 1,4 manner.[18] Thus, formation

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[18] (a) W. Benz and K. Biemann, *J. Amer. Chem. Soc.*, **86**, 2375 (1964); (b) S. Meyerson and L. C. Leitch, *ibid.*, **86**, 2555 (1964).

Fig.9

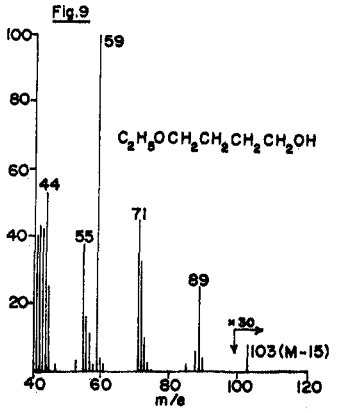


Fig.10

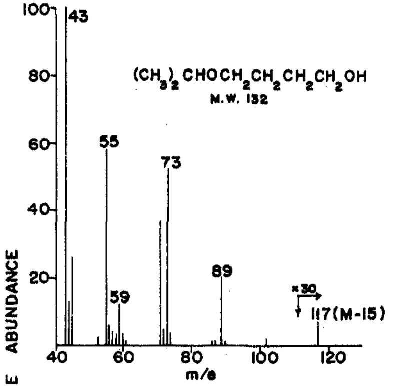


Fig.11

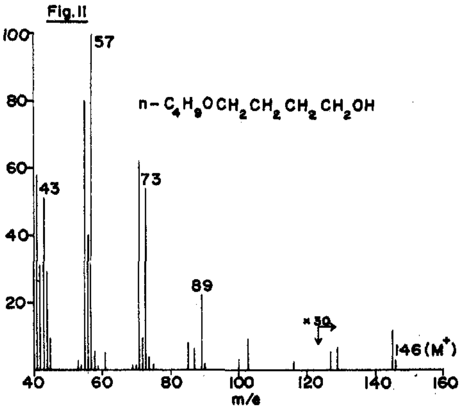


Fig.12

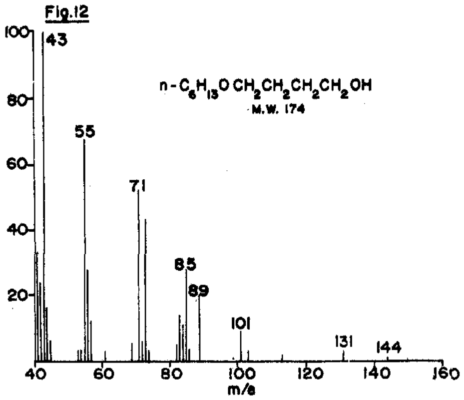
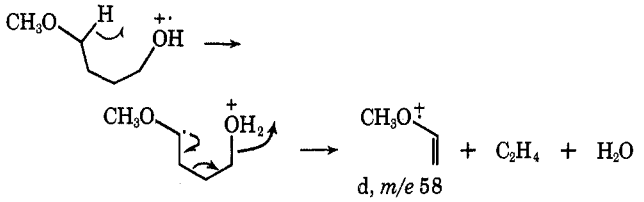


Figure 9.—Mass spectrum (70 eV) of 4-ethoxy-1-butanol (**30**).
Figure 10.—Mass spectrum (70 eV) of 4-isopropoxy-1-butanol (**31**).
Figure 11.—Mass spectrum (70 eV) of 4-*n*-butoxy-1-butanol (**32**).
Figure 12.—Mass spectrum (70 eV) of 4-*n*-hexoxy-1-butanol (**33**).

of the *m/e* 58 peak in the spectrum of **35** may be envisioned as transfer of the C-4 hydrogen atom to the terminal hydroxyl group followed by elimination of water and ethylene to give ion d, as shown below.

$CH_3OCH_2CH_2CH_2CH_2OH$
35

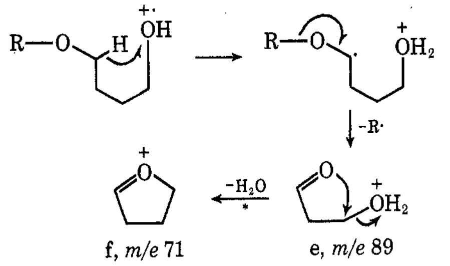
$CH_3OCD_2CH_2CH_2CH_2OH$ $CH_3OCH_2CH_2CH_2CD_2OH$
36 **37**



Metastable defocusing experiments indicated that the *m/e* 58 peak was formed from a precursor of mass 86 as well as from the molecular ion at *m/e* 104. Examination of the spectra (Figures 9–12) of **30–33** reveals that formation of ions analogous to d for these substances (*m/e* 72 for **30**, 86 for **31**, 100 for **32**, and 128 for **33**) is not general. That is, as the alkyl chain increases in length, the fragmentation process leading to these ions becomes unimportant. Instead, intense peaks were observed at *m/e* 89 and 71 (trivial peaks were observed at these values in the spectrum of **35**). Formally, loss of the ether alkyl group from the molecular ion affords the fragment of mass 89, and this fragment can then lose water to give the *m/e* 71 peak. In support of this notion, intense metastable peaks were observed at *m/e* 56.6–56.8 ($71^2/89 = 56.7$) in the spectra of **30–33**. Likewise, the position of these ions was unchanged in the spectrum **34**, whereas 89 was shifted to 91 and 71 to 73 in the spectrum of 4-*n*-butoxy-1,1-dideuterio-1-butanol (**38**). A plausible representation of

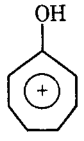
$n-C_4H_9OCH_2CH_2CH_2CD_2OH$
38

the structures and formation of these two ions is given below. It is probable that the low abundance of ions e and f in the spectrum of **35** is a reflection of the lower



stability of the methyl radical compared to the other alkyl radicals.

Summary.—The main purpose of this work was to investigate the scope and limitations of the process leading to the ion of mass 107 in the spectrum of **2**. Based on the findings that formation of this ion (1) was independent of the chain length between the two functional groups, (2) required an oxygen atom on the terminus of the molecule, and (3) involved the benzyl hydrogen atoms, it was concluded that direct C–O bond cleavage to give $C_6H_5CH_2O^+$ did not occur. Whether this ion is best represented by structure c is a matter of conjecture, since it is entirely possible that c immediately rearranges to the symmetrical tropylium alcohol ion g upon formation as was postulated for the M − 1 ion of benzyl alcohol.[19] Recently, the utility of ion

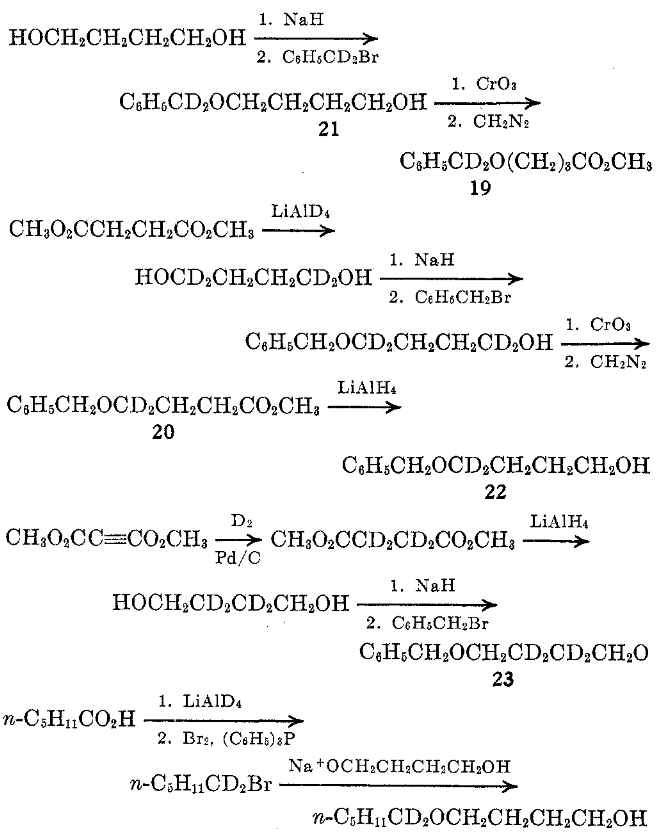


g

cyclotron resonance (icr) spectroscopy in distinguishing between isomeric ions has been dramatically proven,[20] and it is hoped that icr studies can be initiated in these laboratories to determine the exact structure of the mass 107 ion in the benzyloxy esters, alcohols, and methyl ethers.

Syntheses of Labeled Substrates.—For this investigation it was necessary to synthesize several deuterium-labeled substrates. The reaction pathways employed to obtain these substances are summarized in Scheme II, and the isotopic purity of the products is given in the appropriate table.

Scheme II



$$HOCH_2CH_2CH_2CH_2OH \xrightarrow[2.\ C_6H_5CD_2Br]{1.\ NaH} \underset{\mathbf{21}}{C_6H_5CD_2OCH_2CH_2CH_2CH_2OH} \xrightarrow[2.\ CH_2N_2]{1.\ CrO_3} \underset{\mathbf{19}}{C_6H_5CD_2O(CH_2)_3CO_2CH_3}$$

$$CH_3O_2CCH_2CH_2CO_2CH_3 \xrightarrow{LiAlD_4} HOCD_2CH_2CH_2CD_2OH \xrightarrow[2.\ C_6H_5CH_2Br]{1.\ NaH} C_6H_5CH_2OCD_2CH_2CH_2CD_2OH \xrightarrow[2.\ CH_2N_2]{1.\ CrO_3}$$

$$\underset{\mathbf{20}}{C_6H_5CH_2OCD_2CH_2CH_2CO_2CH_3} \xrightarrow{LiAlH_4} \underset{\mathbf{22}}{C_6H_5CH_2OCD_2CH_2CH_2CH_2OH}$$

$$CH_3O_2CC{\equiv}CO_2CH_3 \xrightarrow[Pd/C]{D_2} CH_3O_2CCD_2CD_2CO_2CH_3 \xrightarrow{LiAlH_4} HOCH_2CD_2CD_2CH_2OH \xrightarrow[2.\ C_6H_5CH_2Br]{1.\ NaH} \underset{\mathbf{23}}{C_6H_5CH_2OCH_2CD_2CD_2CH_2O}$$

$$n\text{-}C_5H_{11}CO_2H \xrightarrow[2.\ Br_2,\ (C_6H_5)_3P]{1.\ LiAlD_4} n\text{-}C_5H_{11}CD_2Br \xrightarrow{Na^+{}^-OCH_2CH_2CH_2CH_2OH} \underset{\mathbf{34}}{n\text{-}C_5H_{11}CD_2OCH_2CH_2CH_2CH_2OH}$$

Experimental Section

The low-resolution mass spectra were obtained by Mr. R. G. Ross using an AEI MS-9 double-focusing mass spectrometer (heated inlet 150°, ion source temperature 180°). The high-resolution data were obtained by Mr. Ross with the same instrument, and metastable transitions in the first field free region were observed with the aid of the metastable defocusing technique.[16] All substances were purified by vpc (5 ft × 0.25 in. SE-30, 5% on Chromosorb G) prior to spectral analyses.

Infrared spectral data were recorded with a Perkin-Elmer Model 700 spectrophotometer, and the nmr spectra were secured with a Varian Model T-60 spectrometer. All nmr measurements were made in CCl_4 solutions containing 1% TMS as an internal standard. Chemical shifts are reported in parts per million downfield from the standard, and coupling constants are reported in hertz.

4-Benzyloxy-1-butanol (**8**).—NaH (1 equiv) was added in small batches to excess 1,4-butanediol (Matheson, reagent) covered with a layer of dry benzene. After the addition was completed, the mixture was refluxed for 4 hr, and then 1 equiv of benzyl bromide was added and reflux was continued for 18 hr. The solution was cooled, excess water added, and the resultant mixture extracted with ether. Ether extracts were washed with water and saturated NaCl solution and dried. The solvent was removed under vacuum, and the resultant viscous oil was distilled to give **8** as a colorless oil: bp 95–105° (0.5 mm); ir (CCl_4) 3350 cm^{-1} (OH); nmr δ 7.24 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.52 (m, 4 H, OCH_2, CH_2OH), 1.80 (m, 4 H, CH_2CH_2); M^+ 180 ($C_{11}H_{16}O_2$).

4-Benzyloxybutyric Acid (**7**).—Jones oxidation[21] of **8** gave **7** as a colorless oil: bp 133–134° (0.5 mm); ir (film) 3100 cm^{-1} (broad, COOH); nmr δ 11.0 (s, 1 H, COOH), 7.2 (s, 5 H, C_6H_5), 4.4 (s, 2 H, $C_6H_5CH_2$), 3.4 (t, J = 6 Hz, 2 H, OCH_2), 2.4 (m, 2 H, CH_2CO_2), 1.9 (m, 2 H, $CH_2CH_2CH_2$); M^+ 194 ($C_{11}H_{14}O_3$).

Methyl 4-Benzyloxybutyrate (**2**).—Methylation of **7** with diazomethane in the usual manner gave **2** as a colorless oil: bp 110–113° (0.5 mm); ir (film) 1740 cm^{-1} (C═O); nmr δ 7.3 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.6 (s, 3 H, CO_2CH_3), 3.5 (t, J = 6 Hz, 2 H, OCH_2), 2.4 (m, 2 H, CH_2CO_2), 1.95 (m, 2 H, $CH_2CH_2CH_2$); M^+ 208 ($C_{12}H_{16}O_3$).

Methyl Benzyloxyacetate (**3**).—Potassium metal (1 equiv) was added to 1 equiv of benzyl alcohol dissolved in excess benzene. This mixture was refluxed for 3 hr, and then 1 equiv of methyl bromoacetate (Aldrich) was added slowly and the resultant solution was refluxed for an additional 12 hr. Work-up and distillation gave **3** as a colorless oil: bp 82–89° (4 mm); ir (CCl_4) 1740 cm^{-1} (C═O); nmr δ 7.3 (s, 5 H, C_6H_5), 4.6 (s, 2 H, $C_6H_5CH_2$), 4.0 (s, 2 H, CH_2CO_2), 3.7 (s, 3 H, CO_2CH_2); M^+ 180 ($C_{10}H_{12}O_3$).

Methyl Benzyloxy Esters 4, 5, and 6.—Esters **4**, **5**, and **6** were prepared from the corresponding glycols according to the procedure described above for the preparation of **2**. These esters were separated from their respective reaction mixtures by preparative vpc and were identified by their ir, nmr, and mass spectra. **Methyl 3-benzyloxypropionate** (**4**): ir (film) 1740 cm^{-1} (C═O); nmr δ 7.3 (s, 5 H, C_6H_5), 4.5 (, 2 H, $C_6H_5CH_2$), 3.7 (s, 3 H, CO_2CH_3), 3.7 (m, 2 H, OCH_2), 2.5 (t, J = 6 Hz, 2 H, CH_2CO_2); M^+ 194 ($C_{11}H_{14}O_3$). **Methyl 5-benzyloxyvalerate** (**5**): ir (CCl_4) 1735 cm^{-1} (C═O); nmr δ 7.28 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.6 (s, 3 H, CO_2CH_3), 3.5 (t, J = 6 Hz, 2 H, OCH_2), 2.35 (m, 2 H, CH_2CO_2), 1.9 (m, 4 H, CH_2CH_2); M^+ 222 ($C_{13}H_{18}O_3$). **Methyl 7-benzyloxyoctanoate** (**6**): ir (CCl_4) 1740 cm^{-1} (C═O); nmr δ 7.25 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.6 (s, 3 H, CO_2CH_3), 3.5 (m, 2 H, OCH_2), 2.4 (m, 2 H, CH_2CO_2), 1.8–2.0 (m, 10 H, CH_2); M^+ 264 ($C_{16}H_{24}O_3$).

4-Benzyloxybutyl Methyl Ether (**9**).—Treatment of **8** with 1 equiv of NaH and 1 equiv of methyl iodide in benzene for 24 hr at reflux afforded **9**: nmr δ 7.3 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.5 (s, 4 H, OCH_2), 3.4 (s, 3 H, OCH_3), 1.7 (m, 4 H, CH_2CH_2); M^+ 194 ($C_{12}H_{18}O_2$).

2-Benzyloxyethyldimethylamine (**10**).—To 1 equiv of neat 2-dimethylaminoethanol (Aldrich) was added 0.67 equiv of NaH under nitrogen and the mixture was refluxed for 1 hr. Benzyl bromide (1 equiv) in benzene was added, and reflux continued for 2 hr. Separation by vpc after work-up gave **10**: nmr δ 7.4 (s, 5, C_6H_5), 4.4 (s, 2 H, $C_6H_5CH_2$), 3.5 (t, J = 6 Hz, 2 H, OCH_2), 2.4 (t, J = 6 Hz, 2 H, CH_2N), 2.17 (s, 6 H, NCH_3); M^+ 179 ($C_{11}H_{17}NO$).

2-Benzyloxyethyl Bromide (**11**).—Treatment of **13** with triphenylphosphine and bromine according to the procedure of Wiley[22] afforded **11**, M^+ 214, 216 ($C_9H_{11}BrO$).

2-Benzyloxyethyl Trimethysilyl Ether (**12**).—A mixture of 1

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[19] Reference 4, p 119.

[20] (a) G. Eadon, J. Diekman, and C. Djerassi, *J. Amer. Chem. Soc.*, **92**, 6205 (1970), and references cited therein; (b) J. L. Beauchamp and R. C. Dunbar, *ibid.*, **92**, 1477 (1970).

[21] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[22] G. A. Wiley, *et al.*, *J. Amer. Chem. Soc.*, **86**, 964 (1964).

equiv of **13** and 0.5 equiv of hexamethyldisilazane was heated under reflux with 1 drop of trimethylchlorosilane until the evolution of ammonia ceased (1 hr). After work-up, **12** was isolated from the crude reaction mixture by preparative vpc: nmr δ 7.3 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.6 (m, 4 H, OCH_2CH_2O), 0.08 (s, 9 H, CH_3Si); M^+ 224.

Benzyloxy Alcohols 13, 14, 15, and 16.—Benzyloxy alcohols **13**, **14**, **15**, and **16** were prepared by treatment of the corresponding glycol with 1 equiv of NaH and 1 equiv of benzyl bromide. The monobenzyl ethers were then separated from starting material and dibenzyl ethers by preparative vpc and identified by their ir, nmr, and mass spectra. **2-Benzyloxyethanol (13)**: ir (film) 3375 cm^{-1} (OH); nmr δ 7.3 (s, 5 H, C_6H_5), 4.4 (s, 2 H, $C_6H_5CH_2$), 3.6 (m, 4 H, OCH_2, CH_2OH); M^+ 152 ($C_9H_{12}O_2$). **3-Benzyloxy-1-propanol(14)**: ir (CCl_4) 3450 cm^{-1} (OH); nmr δ 7.25 (s, 5 H, C_6H_5), 4.4 (s, 2 H, $C_6H_5CH_2$); 3.6 (m, 4 H, OCH_2, CH_2OH), 1.7 (m, 2 H, $CH_2CH_2CH_2$); M^+ 166 ($C_{10}H_{14}O_2$). **5-Benzyloxy-1-pentanol (15)**: ir (CCl_4) 3350 cm^{-1} (OH); nmr δ 7.3 (s, 5 H, C_6H_5), 4.5 (s, 2 H, $C_6H_5CH_2$), 3.6 (m, 4 H, OCH_2, CH_2OH), 1.8 (m 6 H, $CH_2CH_2CH_2$); M^+ 194 ($C_{12}H_{18}O_2$). **8-Benzyloxy-1-octanol (16)**: ir (film) 3400 cm^{-1} (OH); nmr δ 7.25 (s, 5 H, C_6H_5), 4.4 (s, 2 H, $C_6H_5CH_2$), 3.5–3.6 (m, 4 H, OCH_2, CH_2OH), 1.7–1.9 (m, 12 H, CH_2); M^+ 236 ($C_{15}H_{24}O_2$).

Benzyloxymethyl Methyl Ether (17).—A mixture of 20.0 g (0.185 mol) of benzyl alcohol, 6.0 g (0.185 mol) of methanol, 5.0 g of paraformaldehyde, and a trace (*ca.* 200 mg) of *p*-toluenesulfonic acid in 30 ml of reagent chloroform was stirred at room temperature for 48 hr. The reaction mixture was worked up as usual, and **17**, was obtained as a colorless liquid by distillation: bp 70–75° (4 mm) [lit.[23] bp 74° (5 mm)]; M^+ 152 ($C_9H_{12}O_2$).

2-Benzyloxyethyl Methyl Ether (18).—Preparation of **18** was carried out by treatment of **13** with 1 equiv of NaH followed by 1 equiv of methyl iodide. Work-up and vpc separation gave **18**: nmr δ 7.3 (s, 5 H, C_6H_5) 4.4 (s, 2 H, $C_6H_5CH_2$), 3.5 (s, 3 H, OCH_3), 3.3 (s, 4 H, OCH_2CH_2O); M^+ 166 ($C_{10}H_{14}O_2$).

4-Alkoxy-1-butanols.—All 4-alkoxy-1-butanols were prepared by treating the monosodium alkoxide of 1,4-butanediol with the corresponding alkyl bromide. In a typical run *ca.* 10 equiv of 1,4-butanediol was covered with benzene, and 1 equiv of NaH (54.7% mineral oil dispersion) was added with stirring. The mixture was heated at reflux 2–4 hr, and then 1–2 equiv of the appropriate alkyl bromide was added slowly and reflux was continued for 4–6 hr. The mixture was cooled, diluted with saturated NaCl solution, and extracted with ether. The ether extracts were combined, washed with saturated NaCl solution, and dried ($MgSO_4$). The 4-alkoxy-1-butanols were then separated from the crude reaction mixtures by distillation and preparative vpc and identified by their ir, nmr, and mass spectra. **4-Ethoxy-1-butanol (30)**: bp 68–71° (6 mm) [lit.[24] bp 72° (8 mm)]; ir (film) 3380 cm^{-1} (OH); nmr δ 3.42 (m, 6 H, CH_2O), 1.85 (m, 4 H, CH_2CH_2), 1.15 (t, J = 6 Hz, 3 H, CH_3CH_2). **4-Isopropoxy-1-butanol (31)**: bp 145–150° (lit.[25] bp 149–152°); ir (CCl_4) 3445 cm^{-1} (OH); nmr 3.50 (m, 5 H, CH_2O,CHO), 1.57 (m, 4 H, CH_2CH_2), 1.08 (d, 6 H, J = 6 Hz, $(CH_3)_2CH$). **4-*n*-Butoxy-1-butanol (32)**: bp 80–84° (6 mm) (lit.[26] bp 212–214°); ir (CCl_4) 3400 cm^{-1} (OH); nmr δ 3.55 (m, 6 H, CH_2O), 1.65 (m, 8 H, CH_2CH_2), 1.10 (t, 3 H, J = 6 Hz, CH_3CH_2). **4-*n*-Hexoxy-1-butanol (33)**: bp 110° (4 mm); ir (CCl_4) 3450 cm^{-1} (OH); nmr δ 3.4 (m, 6 H, CH_2O), 1.1–1.8 (m, 12 H, CH_2CH_2), 0.9 (m, 3 H, CH_3CH_2); M^+ 174 ($C_{10}H_{22}O_2$).

Preparation of Deuterium-Labeled Substrates.—Preparation of 1,1,4,4-tetradeuterio-1,4-butanediol and 2,2,3,3-tetradeuterio-1,4-butanediol was described earlier.[14] The α-d_2 labeled substrates **19**, **21**, **26**, and **28** were prepared using 98% α-d_2 benzyl bromide following the same procedures as for the unlabeled substances. Likewise, **20** and **23** were prepared using the appropriate butanediol-d_4 in place of unlabeled butanediol. Compound **22** was synthesized from **20** by $LiAlH_4$ reduction, and **24** from **2** by $LiAlO_4$ reduction. The synthesis of **29** was the same as that of **18**, except that CD_3I was used instead of CH_3I. Compound **34** was prepared from 2,2-dideuteriohexyl bromide and 1,4-butanediol in the same manner as was **33**, and the 2,2-dideuteriohexyl bromide was generated from hexanoic acid by $LiAlD_4$ reduction followed by bromination with triphenylphosphine and bromine.

Registry No.—**1**, 29006-04-0; **2**, 31600-42-7; **3**, 31600-43-8; **4**, 4126-60-7; **5**, 31662-20-1; **6**, 31662-21-2; **7**, 10385-30-5; **8**, 4541-14-4; **9**, 31600-47-2; **10**, 27058-12-4; **11**, 1462-37-9; **12**, 31600-50-7; **13**, 622-08-2; **14**, 4799-68-2; **15**, 4541-15-5; **16**, 31600-54-1; **17**, 31600-55-2; **18**, 31600-56-3; **19**, 31600-57-4; **20**, 31600-58-5; **21**, 31600-59-6; **22**, 31600-60-9; **23**, 31600-61-0; **24**, 31600-62-1; **25**, 31600-63-2; **26**, 31600-64-3; **27**, 31600-65-4; **28**, 31600-66-5; **29**, 31600-67-6; **30**, 111-73-9; **31**, 31600-69-8; **32**, 4161-24-4; **33**, 4541-13-3.

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