in 25 ml of Ansul ether 141. The reaction mixture was allowed to stir overnight at 70°. Excess methyl carbitol was added and the product distilled to give 2.3 g (61%) of isobutyl-1,1-d_2 alcohol, bp 108–109°.

To a solution of 3.04 g (0.030 mol) of triethylamine and 2.28 g (0.030 mol) of isobutyl-1,1-d_2 alcohol in 75 ml of dry benzene was added 2.86 g (0.025 mol) of methanesulfonyl chloride in 10 ml of benzene. The mixture was stirred overnight and worked up in the usual manner. The ester was distilled *in vacuo* giving 1.4 g (28%) of isobutyl-1,1-d_2 methanesulfonate: bp 58–59° (0.60 mm); nmr, τ 9.00 (d, 6), 8.00 (m, 1), 7.02 (s, 3).

Acknowledgment.—This investigation was supported by Public Health Service Grant No. CA-04536-08 and the U. S. Army Medical Research and Development Command under Contract No. DA-49-193-MD-2949.

Mass Spectrometry in Structural and Stereochemical Problems. CLIV.[1] Electron Impact Promoted Fragmentation of Alkyl Tetrahydropyranyl Ethers and Thioethers[2]

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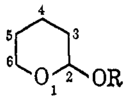
In view of the importance of tetrahydropyranyl ethers as protecting groups for alcohols, there was undertaken a study of the principal modes of fragmentation subsequent to electron impact of alkyl tetrahydropyranyl ethers and thioethers using specifically deuterated derivatives and high resolution mass spectrometry.

Tetrahydropyranyl ethers have been used in synthetic organic chemistry as base-stable, acid-labile protecting groups for hydroxylic functions. Although much research has been completed on the mass spectrometric fragmentation of alcohols,[3] ethers,[4] and thioethers,[5] only a preliminary description[6] of the processes following electron impact of alkyl tetrahydropyranyl ethers has been published. The present communication records the results of a detailed study, using specifically deuterated analogs supplemented by high resolution mass spectrometry, of the fragmentation of alkyl tetrahydropyranyl ethers and thioethers.

Discussion of Mass Spectra

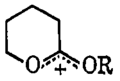
***n*-Alkyl Tetrahydropyranyl Ethers.**—Ethyl and *n*-butyl tetrahydropyranyl ethers (I and II) were prepared



I, R = C_2H_5
II, R = n-C_4H_9

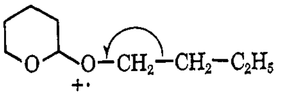
as typical representatives of this class of compound and their respective mass spectra are reproduced at both 70 and 12 eV in Figures 1, 1a, 2, and 2a. It was found necessary to use an all-glass heated inlet system in the determination of these spectra since we observed partial pyrolysis of these compounds to a mixture of dihydropyran (strong molecular ion at m/e 84) and the respective alcohol when using a metal heated inlet system.

The mass spectra (Figures 1 and 2) of ethyl and n-butyl tetrahydropyranyl ether (I and II) contain weak molecular ion peaks which are surpassed in intensity by an M − 1 species. Deuterium labeling established that the hydrogen atom eliminated in this process must originate from C-2 of the pyran ring as no loss of deuterium was observed in the analogs labeled in the alkyl chain or at C-3, C-4, or C-6 of the pyran ring. Therefore this ion can be represented by a.

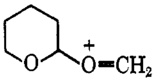


a, M − 1

α cleavage relative to the aliphatic ether oxygen atom is responsible (Table I) for the formation of the low abundance ion (represented by b) at mass 115 in the spectrum (Figure 2) of II and a metastable peak was recognized to verify this decomposition of the molecular ion.

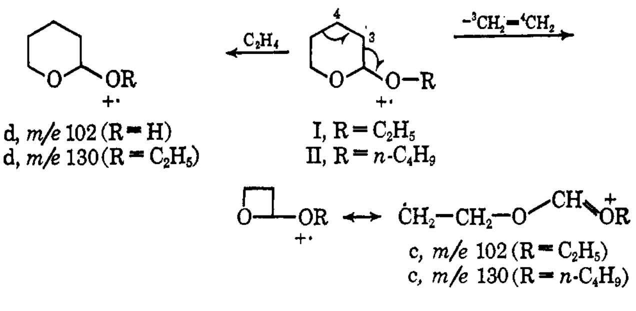


II



b, m/e 115

A peak of low abundance at m/e 102 (M − 28) in the spectrum (Figure 1) of ethyl tetrahydropyranyl ether (I) was shown by deuterium labeling to originate from loss of C-3 and C-4 of the pyranyl ring (c, 80%) supplemented by elimination of the alkyl chain less a terminal hydrogen atom (d, 20%). The analogous peak at m/e 130 in the spectrum (Figure 2) of the n-butyl homolog was less intense but 50% of its ion contribution arose from a process similar to I → c, the remainder of



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[1] For paper CLIII, see W. Carpenter, Y. M. Sheikh, A. M. Duffield, and C. Djerassi, *Org. Mass Spectry.*, **1**, 3 (1968).

[2] Financial assistance from the National Institutes of Health (Grants No. GM 11309 and AM 04257) is gratefully acknowledged.

[3] For a recent review of the mass spectrometry of alcohols, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, Chapter 2.

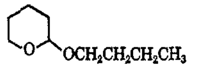
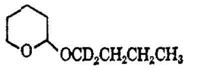
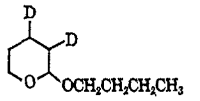
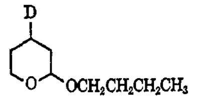
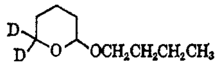
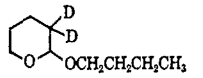
[4] See ref 3, Chapter 6.

[5] See ref 3, Chapter 7.

[6] See ref 3, pp 478, 479.

TABLE I

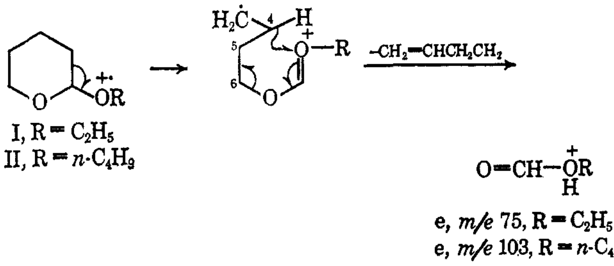
PRINCIPAL MASS SPECTRAL PEAKS IN *n*-BUTYL TETRAHYDROPYRANYL ETHER (FIGURE 2) AND DEUTERATED ANALOGS[a]

Compound	Isotopic purity	Relative abundance, % M	M − 1	M − 28	M − 43	M − 55	M − 58	M − 73	M − 74	M − 91	M − 101
	...	158	157	130	115	103	100	85	84	67	57
	98% d_2	160	159 (q)	130 (50%) 132 (50%)	117 (q)	105 (q)	102 (q)	85 (q)	84 (q)	67 (q)	59 (70%)
	98% d_2	160	159 (q)	130 (50%) 132 (50%)	115 (q)	105 (q)	102 (q)	85 (q)	84 (q)	67 (q)	59 (75%)
	98% d_2	160	159 (q)	132 (90%)	115 (q)	105 (q)	102 (q)	85 (q)	84 (q)	67 (q)	59 (70%)
	96% d_2	160	159 (q)	130 (50%) 132 (50%)	117 (q)	104 (15%) 103 (85%)	101 (q)	87 (q)	85 (~45%)	68 (50%) 69 (50%)	59 (25%)
	96% d_1	159	158 (q)	130 (50%) 131 (50%)	116 (q)	104 (15%) 103 (85%)	100 (q)	86 (q)	85 (~90%)	67 (90%) 68 (10%)	58 (25%)
	98% d_2	160	159 (q)	132 (q)	117 (q)	104 (25%) 103 (75%)	100 (q)	87 (q)	86 (q)	68 (60%) 69 (40%)	59 (30%)
	65% d_2 30% d_1	160	159 (q)	130 (50%) 132 (50%)	117 (q)	103 (10%) 104 (90%)	102 (q)	87 (q)	85 (~80%)	68 (~15%) 69 (~80%)	59 (25%)

[a] Isotopic purities were calculated from precursor compounds in the synthetic sequence whenever possible and these values checked against the displacement of the peak (Figures 1 and 2) at *m/e* 85. Numerical values are considered accurate to ±5% for peaks in excess of 20% relative abundance. The symbol q refers to a quantitative shift (>95%) while the absence of a value in the table indicates that no accurate assessment was possible.

the expelled ethylene emanating from C-1 and C-2 of the alkyl chain—a process which must involve an ethyl migration.[7]

Peaks of 56 and 7% relative abundance corresponding to the loss of 55 mass units occur in the spectra of I and II (*m/e* 75 in Figure 1; *m/e* 103 in Figure 2). In the case of the ethyl homolog (I) a high resolution mass measurement established the composition $C_3H_7O_2$ for the fragment of mass 75 and it is noteworthy that at low ionizing voltage (12 eV) this ion attains still greater abundance (Σ_{40} 14% *vs.* Σ_{40} 8%). In the ethyl and butyl analogs (I and II) deuterium labeling showed that the ions at mass 75 and 103, respectively, arose from fragmentation of the pyran ring as demonstrated by the total label retention in those derivatives containing deuterium in the side chain. Furthermore, isotopic labeling of the pyran ring indicated that 25% of the hydrogen at C-6 in both I and II were included in the charged species. The compound containing deuterium at C-4 of the pyran ring of I was unavailable but in view of the significant transfer (30%, Table I) from this ring position in the butyl derivative XVIIb it is likely that some similar transfer occurs in the ethyl analog. The remainder of the transferred hydrogen must embark from C-5 since no appreciable loss from C-3 (Tables I and II) was found. The general fragmentation sequence I → e (supplemented by hydrogen rearrangement from C-5 and C-6) is consistent with the observed results.



I, R = C_2H_5
II, R = n-C_4H_9

e, *m/e* 75, R = C_2H_5
e, *m/e* 103, R = n-C_4H_9

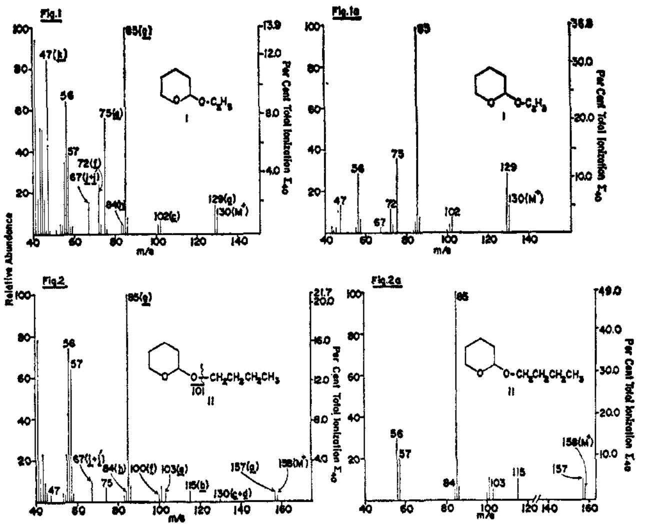


Figure 1.—Mass spectrum (70 eV) of ethyl tetrahydropyranyl ether (I).

Figure 1a.—Mass spectrum (12 eV) of ethyl tetrahydropyranyl ether (I).

Figure 2.—Mass spectrum (70 eV) of *n*-butyl tetrahydropyranyl ether (II).

Figure 2a.—Mass spectrum (12 eV) of *n*-butyl tetrahydropyranyl ether (II).

An ion equivalent to M − 58 (*m/e* 72, Figure 1; *m/e* 100, Figure 2) is present in the mass spectra of the tetra-

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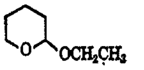
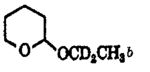
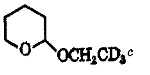
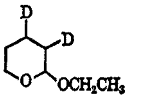
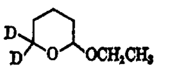
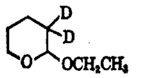
(7) P. Brown and C. Djerassi, *Angew. Chem.*, **79**, 481 (1967).

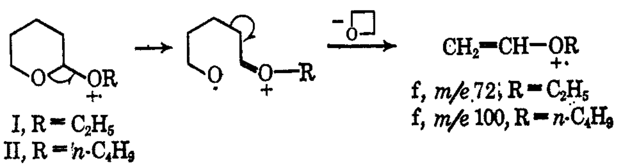
TABLE II

PRINCIPAL MASS SPECTRAL PEAKS IN ETHYL TETRAHYDROPYRANYL ETHER (FIGURE 1) AND DETERATED ANALOGS[a]

Compound	Isotopic purity	Relative abundance, % M⁺	M − 1	M − 28	M − 55	M − 58	M − 45	M − 46	M − 63	M − 73	M − 83
		130	129	102	75	72	85	84	67	57	47
 [b]	98% d_2	132	131 (q)	104 (80%) 102 (20%)	77 (q)	74 (q)	85 (q)	84 (q)	67 (q)	57 (q)	47 (80%) 48 (20%)
 [c]	98% d_3	133	132 (q)	105 (86%) 103 (14%)	78 (q)	75 (q)	85 (q)	84 (q)	67 (q)	57 (q)	47 (30%) 48 (70%)
	98% d_2	132	131 (q)	102 (80%) 104 (20%)	76 (20%) 75 (80%)	73 (q)	87 (q)	85 (∼50%) 86 (∼50%)	68 (30%) 69 (70%)	59 (∼40%)	47 (75%) 48 (20%)
	98% d_2	132	131 (q)	104 (q)	75 (75%) 76 (25%)	72 (q)	87 (q)	86 (q)	68 (55%) 69 (45%)	59 (∼70%)	47 (q)
	67% d_2 33% d_1	132	131 (q)	102 (85%) 104 (15%)	75 (90%) 76 (10%)	74 (q)	87 (q)	85 (∼90%)	68 (∼20%) 69 (∼70%)	59 (∼40%)	47 (90%) 48 (10%)

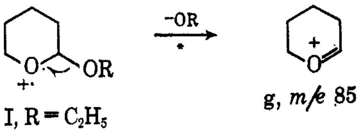
[a] See Table I, footnote *a*. [b] Registry no.: 16315-53-0. [c] Registry no.: 16315-54-1.

hydropyranyl ethers I and II and high resolution mass spectrometry identified the species in question as C_4H_8O in the case of the ethyl homolog. Deuterium labeling (Tables I and II) implicated the alkyl chain of both I and II with this ion and the rationalization depicted in I → f is consistent with the observed label retention.



I, R = C_2H_5
II, R = *n*-C_4H_9
f, *m/e* 72; R = C_2H_5
f, *m/e* 100, R = *n*-C_4H_9

The most abundant ion in the mass spectra (Figures 1 and 2) of ethyl and *n*-butyl tetrahydropyranyl ether (I and II) at both 70 and 12 eV occurs at mass 85 (C_5H_9O). The obvious representation for this ion is g and label retention in all the deuterated analogs examined supports this contention while the recognition of an appropriate metastable peak in the mass spectra of I and II testifies to the origin of this species by a single-step fragmentation of the parent ion.

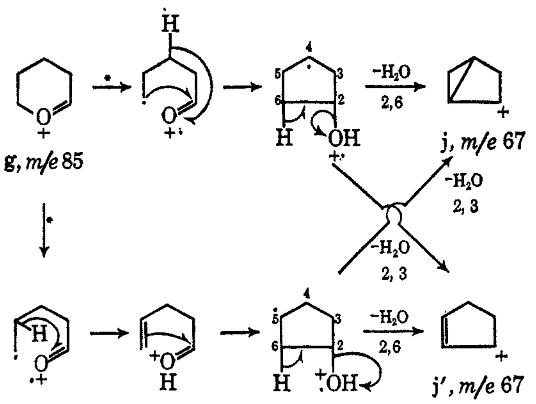


I, R = C_2H_5
II, R = *n*-C_4H_9
g, *m/e* 85

Whereas the elimination of an alkoxy radical from the molecular ion of I and II is a very important process in the electron impact promoted decomposition of these compounds, this loss accompanied by hydrogen abstraction from the pyranyl ring (M − ROH) assumes only minor importance (*m/e* 84, Figures 1 and 2). The major source of hydrogen in the butyl analog in this process is most likely C-3 of the ring (Table I) and this decomposition can be rationalized by the formation of dihydropyran (h, *m/e* 84). In view of our observation that alkyl tetrahydropyranyl ethers decomposed to dihydropyran when a metal heated inlet system was employed, we cannot eliminate the possibility that the low abundance of ion h observed actually arises from pyrolytic cleavage during passage through the all-glass heated inlet system.


I, R = C_2H_5
II, R = *n*-C_4H_9
h, *m/e* 84

A metastable peak was present in the spectra of I and II corresponding to the loss of water from the ion of mass 85 (g) with the generation of the species of mass 67 (C_5H_7). Low ionizing energy (12 eV) resulted in the virtually complete suppression (Figures 1a and 2a) of this ion. Label retention in the deuterated analogs (XII, XVIb, XVIIb, and XXb) of the butyl homolog implicated the hydrogen atoms attached to C-4 (90%), C-6 (60%), and C-3 (∼15%) of the pyranyl ring, the remainder possibly arising from C-5, the only position of the ring not tagged with deuterium. The following rationalization (g → j + j′, *m/e* 67) is consistent with the shifts of the peak at *m/e* 67 in the deuterated compounds examined.



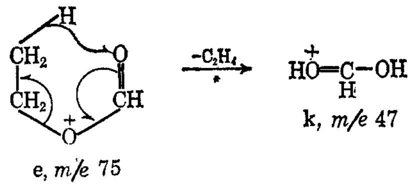
The peaks at *m/e* 57 in the spectra (Figures 1 and 2) of ethyl and *n*-butyl tetrahydropyranyl ether (I and II) correspond to C_4H_9 and C_3H_5O, the percentage of hydrocarbon being 50% in I and 90% in II. In the butyl homolog approximately 70% of the C_4H_9 species arises from the alkyl chain; the remainder arises from the pyranyl ring plus one hydrogen atom. This latter explanation also accounts for the C_4H_9 ion in the mass spectrum of the ethyl derivative I.

The oxygen containing species of mass 57 in the spectra (Figures 1 and 2) of I and II is formed, at least in part (since a metastable ion was recognized), by the loss of 28 mass units from g (*m/e* 85). Deuterium labeling in the ethyl homolog indicated that ethylene is possibly lost from g by multiple pathways and in view of the difficulty in calculating precise percentage shifts in the 3,4-d_2 derivative of I no accurate assessment can be given for this process. Loss of C-4 and C-5 as ethylene formally corresponds to an electron impact sponsored retro Diels–Alder process.[8]

High resolution mass spectrometry showed the peak at *m/e* 56 in the spectra (Figures 1 and 2) of the tetrahydropyranyl ethers I and II to be C_4H_8 (>90%). Deuterium labeling suggested that this ion arose from the pyranyl ring carbon atoms in ethyl tetrahydropyranyl ether (I) while in the *n*-butyl compound (II) approximately 70% arose in this fashion, the remainder originating from the butyl side chain.

The peak at *m/e* 55 in the spectra (Figures 1 and 2) of I and II is a doublet of composition C_4H_7 (80%), C_3H_3O (20%); and C_4H_7 (85%), C_3H_3O (15%), respectively. It was impossible to calculate precise shifts in the position of this peak in the isotopically labeled compounds studied but as anticipated for the ethyl compound (I) the pyranyl ring carbon atoms are the major source of the C_4H_7 ion while in the *n*-butyl analog better than 70% of this ion results from fragmentation of the alkyl side chain.

Because of its lack of adjacent neighbors the peak at *m/e* 47 in the mass spectra (Figures 1 and 2) of I and II is easily identified and high resolution mass spectrometry established its composition as CH_3O_2. In view of the presence of a metastable peak in the spectrum (Figure 1) of the ethyl analog I this ion must be formed, at least in part, by ejection of ethylene from e, (*m/e* 75). In this instance deuterium labeling was instrumental in determining that 20% of the hydrogen at C-1 and 70% of that at C-2 of the alkyl chain were involved with the charged species at mass 47. The following process will rationalize the formation of 70% of the ion current at mass 47 in the spectrum of ethyl tetrahydropyranyl ether (I).



***n*-Alkyl Tetrahydropyranyl Thioethers.**—Ethyl and *n*-butyl tetrahydropyranyl thioethers (III and IV) were examined as typical examples of this class of compound[9] and their mass spectra (Figures 3 and 4) determined. Over-all these spectra show a strong general resemblance to their oxygenated counterparts, two obvious differences being the anticipated[5] relative increase of the molecular ion in the butyl analog and especially the absence of an M − 1 species in both the thio compounds.

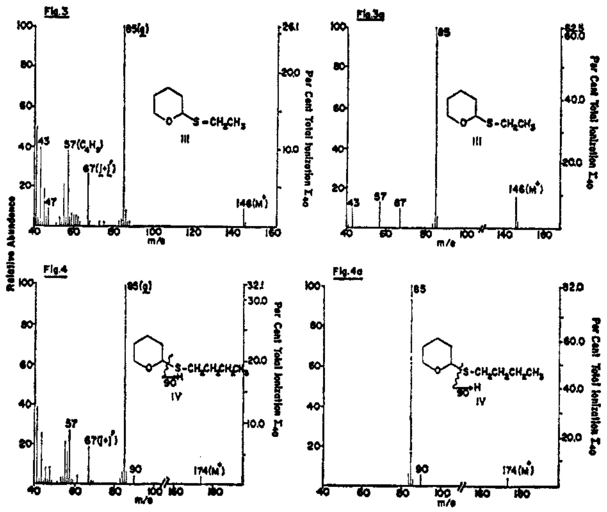
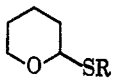


Figure 3.—Mass spectrum (70 eV) of ethyl tetrahydropyranyl thioether (III).

Figure 3a.—Mass spectrum (12 eV) of ethyl tetrahydropyranyl thioether (III).

Figure 4.—Mass spectrum (70 eV) of *n*-butyl tetrahydropyranyl thioether (IV).

Figure 4a.—Mass spectrum (12 eV) of *n*-butyl tetrahydropyranyl thioether (IV).



III, R = C_2H_5
IV, R = n-C_4H_9

By far the most abundant peak in the mass spectra (Figures 3 and 4) of the tetrahydropyranyl thioethers (III and IV) examined occurs at *m/e* 85 and this species can be rationalized by g, the eliminated neutral entity being a thioalkyl radical. At low ionizing energy this ion remains as the dominant feature of the spectra (Figures 3a and 4a) of III and IV.

A metastable peak at *m/e* 53.0 in the spectra (Figures 3 and 4) of the thioethers III and IV demonstrated that at least some of the charged species of mass 67 arose from the expulsion of water from g, *m/e* 85. In the absence of extensive isotopic labeling one would expect that this process proceeds in a manner analogous to that described for *n*-butyl tetrahydropyranyl ether (II).

The prominent ions at mass 57 in the spectra (Figures 3 and 4) of the thioethers III and IV correspond to C_4H_9 in greater than 90% yield. In the butyl thioether, dideuterated at C-6 of the pyran ring, 90% of the ion current at mass 57 is displaced to 59 thus establishing that this ion results from fragmentation of the pyran ring supplemented by a hydrogen-transfer process. This result conflicts with the mechanism operative in formation of the ion of mass 57 (C_4H_9) in the spectrum of *n*-butyl tetrahydropyranyl ether (II) in which 70%

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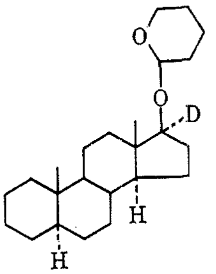
[8] H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965).

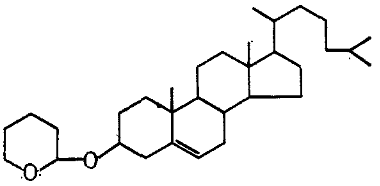
[9] E. L. Eliel, B. N. Nowak, and R. A. Daignault, *J. Org. Chem.*, **30**, 2448 (1965).

is generated from fragmentation of the butyl side chain. It is also noteworthy that there was no evidence of carbon–sulfur fission with charge retention on sulfur in any of the spectra, in marked contrast to the propensity of simple thioethers[10] for this type of cleavage.

Steroid Tetrahydropyranyl Ethers.—Tetrahydropyranyl ether derivatives of some steroids such as cholesterol and androstan-17β-ol were prepared and their mass spectra determined. A weak molecular ion peak was visible (0.3% relative abundance) in the spectrum of androstan-17β-ol tetrahydropyranyl ether (V) but a parent ion was absent in the cholesterol derivative VI. The only prominent ions in the mass spectra of these compounds corresponded to the product of elimination of 2-hydroxydihydropyran and the ubiquitous ion (g) of the tetrahydropyranyl ether at mass 85. From these results it would appear that tetrahydropyranyl ether derivatives are not the ones of choice for mass spectral identification of larger molecular weight hydroxylated compounds.



V

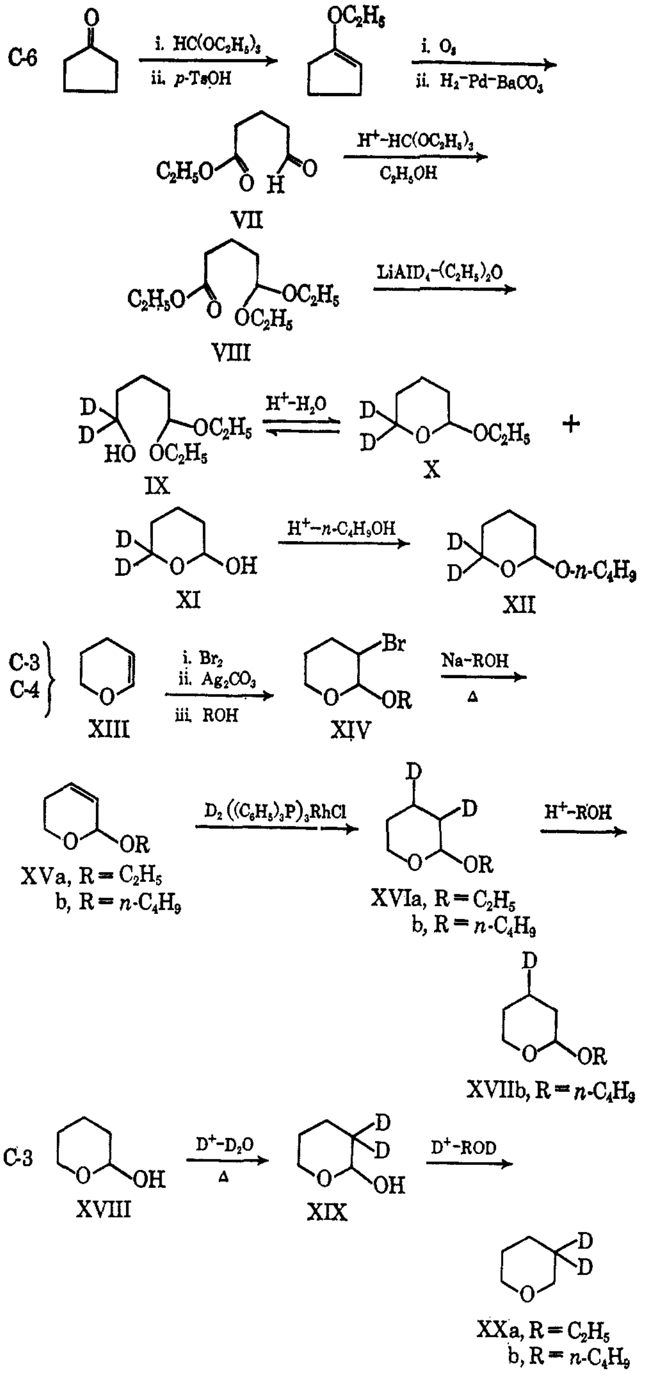


VI

In summary it can be stated that tetrahydropyranyl ethers and thioethers subsequent to electron impact cleave preferentially α to the ring oxygen atom (formation of g, m/e 85). The occurrence of a strong peak at m/e 84 in the mass spectrum of a tetrahydropyranyl ether is indicative of thermal fragmentation of the compound to dihydropyran and the corresponding alcohol in the heated inlet system (or ion source) of the mass spectrometer.

Synthesis of Deuterated Tetrahydropyranyl Ethers.—The compounds labeled in the alkyl chain were conveniently prepared by acid-catalyzed condensation of a specifically deuterated alcohol[11] with dihydropyran or alternatively by addition of the deuterated alcohol to 2-hydroxytetrahydropyran and azeotropic distillation with benzene of the water produced. Introduction of deuterium into the pyranyl ring at positions C-3, C-4, and C-6 was accomplished according to Scheme I.

Scheme I



n-butyl alcohol[11] by acid-catalyzed condensation with 2-hydroxytetrahydropyran (Aldrich).

Experimental Section

Low resolution mass spectra were obtained with a CEC 103-C mass spectrometer (ion source temperature 250°) attached to a heated all-glass inlet system (100°) while high resolution mass measurements were determined on an MS-9 instrument (inlet temperature 120°) by Mr. R. G. Ross and were accurate to within 3 ppm. Low-voltage spectra refer to nominal electron volt values. Samples were purified by vpc on a 15% Apiezon L column and isotopic purities are included in Tables I and II.

Side Chain Labeled Tetrahydropyranyl Ethers.—Ethyl and *n*-butyl tetrahydropyranyl ethers (I and II) labeled in the side chain with deuterium were prepared from the labeled ethanol[11] or *n*-butyl alcohol[11] by acid-catalyzed condensation with 2-hydroxytetrahydropyran (Aldrich).

Ethyl and *n*-Butyl Tetrahydropyranyl-6,6-d_2 Ether (X and XII).—5,5-Diethoxyvaleric acid ethyl ester (VIII) was prepared according to the method of Schmidt and Grafen[12] and 3.4 g (15.6 mmol) reduced with lithium aluminum hydride (0.76 g, 18.2 mmol) in refluxing anhydrous ether solution for 2 hr followed by decomposition of excess reagent with saturated sodium sulfate solution to give 5,5-diethoxypentanol-1,1-d_2 (IX) (yield 2.4 g, 87%). Attempted hydrolysis of IX using 1 *N* aqueous hydrochloric acid (11 ml) at room temperature for 2.5 hr afforded ethyl tetrahydropyranyl-6,6-d_2 ether (X) as the major product which was purified by vpc. 2-Hydroxytetrahydropyran-6,6-d_2 (XI) was isolated by vpc as a minor constituent (100 mg) of the reaction mixture. This material (23 mg) was converted into *n*-butyl tetrahydropyranyl-6,6-d_2 ether (XII) by refluxing overnight with *n*-butyl alcohol containing 1 drop of concentrated hydrochloric acid in benzene and the product (XII) (yield 21 mg, 57%) purified by vpc.

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[10] S. D. Sample and C. Djerassi, *J. Amer. Chem. Soc.*, **88**, 1937 (1966).

[11] For the preparation of specifically deuterated alcohols, see A. M. Duffield, R. Beugelmans, H. Budzikiewicz, D. A. Lightner, D. H. Williams, and C. Djerassi, *ibid.*, **87**, 805 (1965).

[12] U. Schmidt and P. Grafen, *Ann.*, **656**, 97 (1962).

Ethyl and *n*-Butyl Tetrahydropyranyl-3,4-d_2 Ether (XVIa and XVIb).—2-Ethoxy- and 2-butoxy-Δ^3-dihydropyran (XVa and XVb) were prepared by the method of Woods and Sanders[13] and each was deuterated by homogenous catalysis[14] using $[(C_6H_5)_3P]_3RhCl$ (25 mg) in acetone (10 ml) at room temperature for 18 hr, the solvent and the labeled tetrahydropyranyl ethers (XVIa and XVIb) being separated by vpc.

***n*-Butyl tetrahydropyranyl-4-d_1 ether (XVIIb)** was prepared from *n*-butyl tetrahydropyranyl-3,4-d_2 ether (XVIb) by stirring overnight with *n*-butyl alcohol containing a trace of concentrated hydrochloric acid. The solvent alcohol was fractionally distilled and XVIIb isolated by preparative vpc.

Ethyl and *n*-Butyl Tetrahydropyranyl-3,3-d_2 Ether (XXa and XXb).—2-Hydroxytetrahydropyran (XVIII, 0.5 g) was heated under reflux for 1.5 hr with deuterium oxide (15 ml) containing deuteriohydrochloric acid (8.8 *N*, 5 drops) and then continuously extracted with ether. Isolation by preparative vpc yielded 2-hydroxytetrahydropyran-3,3-d_2 (XIX, 0.27 g). Condensation of XIX (50 mg) with an excess of ethanol-O-*d* and deuterium oxide containing 3 drops of deuteriohydrochloric acid yielded ethyl tetrahydropyranyl-3,3-d_2 ether (XXa). Similar treatment of *n*-butanyl alcohol-O-*d* with 2-hydroxytetrahydropyran-3,3-d_2 (XIX) afforded *n*-butyl tetrahydropyranyl-3,3-d_2 ether (XXb).

Registry No.—I, 4819-83-4; II, 1927-68-0; III, 16315-51-8; IV, 16315-52-9; X, 16315-55-2; XVIa, 16315-56-3; XXa, 16315-57-4.

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[13] G. F. Woods and H. Sanders, *J. Amer. Chem. Soc.*, **68**, 2483 (1946).

[14] W. Voelter and C. Djerassi, *Chem. Ber.*, **101**, 58 (1968).

Mass Spectrometry in Structural and Stereochemical Problems. CLV.[1] Electron Impact Induced Fragmentations and Rearrangements of Some Trimethylsilyl Ethers of Aliphatic Glycols and Related Compounds[2]

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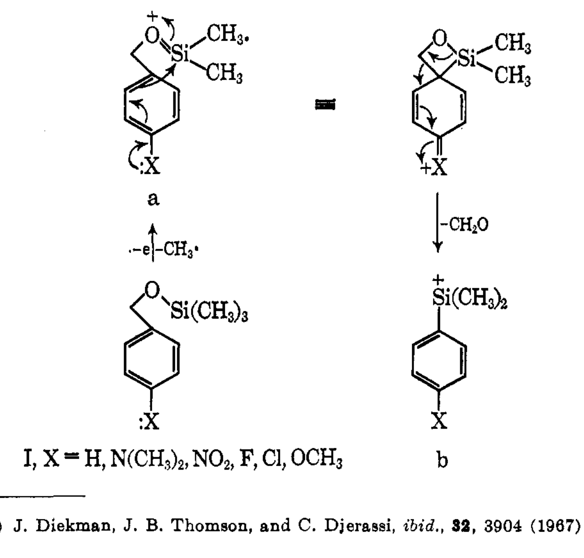
In view of the importance of trimethylsilyl ethers in gas chromatography, the basic fragmentation modes incurred upon electron bombardment of polymethylene glycol bistrimethylsilyl ethers (III, $n = 2$–8) were elucidated; in all cases ($n = 2$–8), there is encountered a characteristic rearrangement ion (g) of mass 147 involving expulsion of the central portion of the molecule. Electron bombardment of the corresponding methoxy- (XI, $n = 2,4,5$), ethoxy- (XIV), and phenoxy- (XVIII, $n = 2$–7) polymethylene trimethylsilyl ethers also produced intense rearrangement peaks analogous to g; and in all instances there was encountered a remarkable insensitivity toward ring size (five to eleven membered) in the cyclic transition state. Deuterium and oxygen-18 labeling was employed to elucidate the fragmentation patterns exhibited by XI, XIV, and XVIII. The trimethylsiloxy function of 2-phenoxyethyl trimethylsilyl ether (XVIII, $n = 2$) was replaced with the triethylsiloxy and trimethylgermanyl groups in order to assess their effect upon the mass spectral behavior of XVIII ($n = 2$). Likewise, the effect of substitution of nitrogen and sulfur atoms for both the phenoxy and trimethylsiloxy oxygen atoms was examined. Finally, deuterium labeling was employed to elucidate the electron impact induced fragmentation modes of 2-(cyclohexyloxy)ethyl trimethylsilyl ether (XXIX).

In recent years, trimethylsilyl ethers have been extensively employed to facilitate gas chromatographic separation of nonvolatile materials. The development[4] and widespread usage of mass spectrometers capable of making direct measurements of gas chromatographic effluents has made mass spectral investigations of trimethylsilyl ethers particularly relevant and several studies concerning the mass spectra of trimethylsilyl derivatives of a variety of natural products have recently appeared.[5] Interest in our laboratory initially focussed on the characteristic fragmentations encountered in sterol trimethylsilyl ethers.[6] During this work, it became evident that a thorough study of the electron impact promoted fragmentation of various trimethylsilyl ether types must be undertaken in order to permit more precise structural deductions. In a subsequent study[7] the fragmentation modes of certain alcohol derivatives were accurately elucidated utilizing deuterium-labeled pentanol trimethylsilyl ethers. Also discussed in that report were several electron impact induced skeletal rearrangements of which the sequential loss of a methyl radical and of formaldehyde in benzyl ether derivatives (I → a → b) is typical (Scheme I).

SCHEME I



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[1] For paper CLIV, see S. J. Isser, A. M. Duffield, and C. Djerassi, *J. Org. Chem.*, **33**, 2266 (1968).

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

[3] (a) National Science Foundation Predoctoral Fellow (1966–1967); National Institutes of Health Predoctoral Fellow (1967–1968). (b) National Institutes of Health International Postdoctoral Fellow (1965–1966) on leave from University College, Dublin.

[4] For review, see S. Ställberg-Stenhagen and E. Stenhagen in "Topics in Organic Mass Spectrometry," A. L. Burlingame, Ed., Interscience Publishers, Inc., New York, N. Y., 1968, Chapter 5.

[5] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, pp 471–477.

[6] J. Diekman and C. Djerassi, *J. Org. Chem.*, **32**, 1005 (1967).

[7] J. Diekman, J. B. Thomson, and C. Djerassi, *ibid.*, **32**, 3904 (1967).