Mass Spectrometry in Structural and Stereochemical Problems. CXLI.[1] The Electron Impact Induced Fragmentations and Rearrangements of Trimethylsilyl Ethers, Amines, and Sulfides[2]

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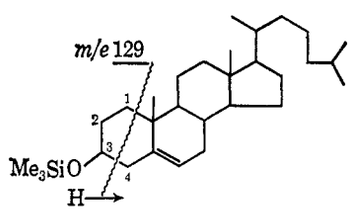
Using deuterium labeling, the basic fragmentation modes incurred upon electron bombardment of pentan-1-ol and pentan-2-ol trimethylsilyl ethers were elucidated. The mass spectra of these simple trimethylsilyl ethers exhibit peaks which appear in the spectra of practically all trimethylsilyl ether derivatives; the elucidation of the nature of these fragment ions provides a foundation for structural deductions of more complicated trimethylsilyl derivatives. Electron bombardment of trimethylsilyl benzyl ether likewise exhibits these typical fragmentation patterns as well as an abundant rearrangement caused by elimination of the central portion of the molecule from an M − CH_3 precursor with formation of a phenyl–silicon bond. This rearrangement is also abundant in the mass spectrum of N-(trimethylsilyl)benzylamine, but weak to moderate in the spectra of *p*-substituted benzyl ethers and α-methylbenzylamine, and weak in the case of α-substituted benzyl ethers. The amount of rearrangement ion decreases rapidly with increasing length of the alkyl side chain in both ethers and amines. The rearrangement is a minor feature in the spectrum of trimethylsilyl benzyl sulfide and is not observed in trimethylsilyl β-phenylethyl sulfide. Some triethylsilyl ethers have also been examined and found to behave quite differently from their trimethyl counterparts.

In recent years, trimethylsilyl ether derivatives of alcohols have been used extensively for purification and identification purposes. Not only does the greatly increased volatility of the trimethylsilyl ether as compared to the parent alcohol, lend itself to gas chromatographic separation,[4] but the trimethylsilyl group appears to direct characteristic mass spectral fragmentation patterns in many cases.[5] Trimethylsilyl ether derivatives have been especially useful with respect to the recently developed technique of direct mass spectral measurements of gas chromatographic effluents.[6] This method has found application in a variety of fields but has been particularly relevant to steroid metabolites; consequently, our previous interests[7] have been concerned with the fragmentation sequences directed by the trimethylsiloxy group in some steroid trimethylsilyl ethers. It was shown, for instance, by the use of deuterium labeling and high resolution mass measurements that the intense *m/e* 129 peak, which is a characteristic feature in the mass spectra of trimethylsilyl ethers of Δ^5 -3-hydroxy steroids, corresponded to a fragment containing carbon atoms 1, 2, and 3 of ring A of the steroid framework, accompanied by a hydrogen transfer from C-2 of the charge-retaining moiety I.



I

In the course of this work it became evident that certain of the more intense peaks in the mass spectra of trimethylsilyl ether derivatives were characteristic of practically all trimethylsilyl ethers regardless of the nature of the parent alcohol. Because of the ever-increasing use of trimethylsilyl ethers it is important to have available information regarding the very basic fragmentation modes of typical representatives of this class so that their mass spectra may be employed for structural deductions. Therefore it was decided to investigate thoroughly the mass spectral fragmentation of some structurally simple trimethylsilyl ethers by means of deuterium labeling in order to ascertain the exact nature of the peaks appearing in practically all of the mass spectra of trimethylsilyl ether derivatives. In the early stages of this research it became evident that in many cases the trimethylsilyl ethers underwent very interesting skeletal rearrangements upon bombardment by electrons in the mass spectrometer. In the light of the current interest in such rearrangements,[8] it was also decided to examine a series of benzyltrimethylsilyl ethers, amines and sulfides and some related compounds with particular emphasis on their skeletal rearrangements.

Pentanol Trimethylsilyl Ethers.—It was felt that a representative example of a structurally simple trimethylsilyl derivative which exhibits a mass spectral pattern characteristic of alkyl trimethylsiloxy compounds might be pentan-1-ol trimethylsilyl ether (II). The mass spectra of the trimethylsilyl ethers of a number of aliphatic alcohols, including pentan-1-ol, were studied in 1957 by Sharkey and his collaborators[9]

(1) For paper CXL, see J. K. MacLeod and C. Djerassi, *J. Org. Chem.*, **32**, 3485 (1967).

(2) Financial assistance from the National Institutes of Health (Grant No. CA-07195) is gratefully acknowledged.

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

(4) T. Luukainen, W. J. A. VandenHeuvel, E. O. A. Haahti, and E. C. Horning, *Biochim. Biophys. Acta*, **52**, 599 (1961); E. C. Horning, W. J. A. VandenHeuvel, and B. G. Creech, *Methods Biochem. Analy.*, **11**, 69 (1963); P. P. Nair, C. Bucana, S. deLeon, and D. A. Turner, *Anal. Chem.*, **37**, 631 (1965); A. Rozanski, *ibid.*, **38**, 36 (1966); M. Kirschner and M. B. Lipsett, *J. Clin. Endocrinol. Metab.*, **23**, 255 (1963); R. R. Burtner, E. A. Brown, and R. A. Mikulec, Abstracts, Second International Congress of Hormonal Steroids, Milan, Italy, 1966, p 50; C. J. W. Brooks, E. M. Chambaz, W. L. Gardiner, and E. C. Horning, *ibid.*, p 32; S. Hara, T. Watabe, and Y. Ike, *Chem. Pharm. Bull.* (Tokyo), **14**, 1311 (1966).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, Chapter 14.

(6) P. Eneroth, K. Hellström, and R. Ryhage, *J. Lipid Res.*, **5**, 245 (1964).

(7) J. Diekman and C. Djerassi, *J. Org. Chem.*, **32**, 1005 (1967).

(8) For a complete review, see P. Brown and C. Djerassi, *Angew. Chem. Intern. Ed. Engl.*, **6**, 477 (1967).

(9) A. G. Sharkey, R. A. Friedel, and S. H. Langer, *Anal. Chem.*, **29**, 770 (1957); S. H. Langer, R. A. Friedel, I. Wender, and A. G. Sharkey, *ibid.*, **30**, 1353 (1958).

in developing a convenient method for the analysis of alcohol–hydrocarbon mixtures. Some of their conclusions, however, must be revised in the light of our results obtained by labeling each position of the five-carbon chain with deuterium.

The mass spectrum (Figure 1) of pentan-1-ol trimethylsilyl ether (II) is typical of trimethylsilyl ethers of normal C_1–C_{10} alcohols in that the molecular ion peak (m/e 160, Σ_{40} = 0.14%) is very small whereas the M − CH_3 peak (m/e 145) is very intense (Σ_{40} = 23.61%). Although loss of a methyl radical from the C-5 position (a) of the molecular ion is possible, the most attractive site of methyl cleavage is at the silicon atom (b → c) (Scheme I). This conclusion is substantiated by replacing the three C-5 hydrogen atoms with deuterium atoms as in VII, and noting that no peak corresponding to loss of a CD_3 radical (M − 18) is evident in the mass spectrum.

It is interesting to note that the m/e 145 peak becomes the base peak (Σ_{40} = 29.76%) when the spectrum is recorded on the AEI MS-9 mass spectrometer. As was pointed out in the case of steroid trimethylsilyl ethers,[7] the phenomenon of significant variations in peak intensities when spectra are recorded under slightly different conditions (*i.e.*, different mass spectrometers, variations in source temperature, etc.) appears to be quite common in the mass spectra of trimethylsilyl ether derivatives. All reported spectra involving pentanol trimethylsilyl ethers were recorded on an Atlas CH-4 mass spectrometer.

As in the case of normal aliphatic ethers,[10] α fission can occur in two directions in trimethylsilyl ethers; however, the previously discussed loss of the methyl group from the trimethylsilyl moiety c is greatly preferred over expulsion of a butyl radical to yield the fragment ion d of mass 103 (Σ_{40} = 6.63%). In fact, at 12 ev the m/e 103 peak is absent, while the ion of mass 145 carries the bulk (>85%) of the the total ion current. The composition of the m/e 103 peak is verified by high resolution mass measurements ($C_4H_{11}OSi$) and by a shift from m/e 103 to m/e 105 in the spectrum of 1,1-d_2-pentan-1-ol trimethylsilyl ether (III). The formation of this fragment directly from the moleular ion is supported by a metastable peak at m/e 73.1 (calcd, $103^2/145$ = 73.1).[11]

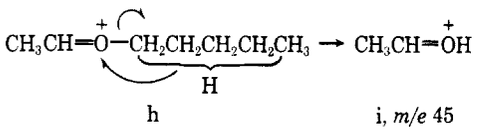
The α-fission product c is the progenitor of the base peak, m/e 75 (Σ_{40} = 26.53%), as shown by the appropriate metastable peak at m/e 38.7 (calcd, $75^2/145$ = 38.7). The fact that the m/e 75 peak is only of 8% relative abundance whereas the m/e 145 peak is the most abundant one when the spectrum is recorded at 15 ev also supports their daughter–parent relationship. High resolution mass measurements show that the fragment of mass 75 has the elemental composition of a dimethylsilanol species, thus suggesting that the fragmentation involves a hydrogen transfer to the charge-retaining moiety accompanied by olefin elimination. By successively labeling each position of the carbon chain with deuterium atoms it is possible to locate the origin of the migrating hydrogen. These results are indicated in Table I; it is evident that the primary α-fission product c undergoes a *non*specific hydrogen transfer with olefin elimination. Djerassi and Fenselau[10] have reported that the α-fission product h of isopropyl *n*-pentyl ether undergoes an analogous fragmentation sequence (h → i) to produce a peak at m/e 45; this fragmentation pattern likewise involves a nonspecific hydrogen transfer. The total hydrogen transfer demonstrated by deuterium labeling accounts for 85%; the difference between this value and 100% must be attributed to an isotope effect, which is of the order of magnitude encountered in many mass spectrometric hydrogen transfer reactions.[12]

TABLE I

ORIGIN OF HYDROGEN TRANSFER IN m/e 75 AND m/e 89 ION PRODUCTION IN PENTAN-1-OL TRIMETHYLSILYL ETHER (II)

Compd	Isotope compn, %	Hydrogen transfer,[a] % m/e 75 → m/e 76	Hydrogen transfer,[a] % m/e 89 → m/e 90
$CH_3CH_2CH_2CH_2CD_2OSiMe_3$ (III)	100% d_2	20.0	...
$CH_3CH_2CH_2CD_2CH_2OSiMe_3$ (IV)	98% d_2 2% d_1	26.7	50.0
$CH_3CH_2CD_2CH_2CH_2OSiMe_3$ (V)	91% d_2 9% d_1	22.9	40.0
$CH_3CD_2CH_2CH_2CH_2OSiMe_3$ (VI)	100% d_2	11.2	6.0
$CD_3CH_2CH_2CH_2CH_2OSiMe_3$ (VII)	89% d_3 7% d_2 6% d_1	3.9	3.8

[a] Corrected for natural isotope abundance and calculated deuterium isotope composition (columns 2 and 3).



The minor α-fission product d is also the precursor of another species which is present in the mass spectra of most alkyl trimethylsilyl ethers (Scheme I). Elimination of formaldehyde from d produces the trimethylsilyl cation, f (m/e 73); this sequence (d → f) is also supported by a metastable peak at m/e 33.1 (calcd, $73^2/103$ = 33.3). Sharkey[9] had previously suggested that this ion of mass 73 was formed directly from the molecular ion by scission of the silicon–oxygen bond (see j in formula II). The m/e 73 peak, like the one at m/e 75, is always observed in the mass spectra of diverse trimethylsilyl ethers and in none of these cases has an appropriate metastable peak been observed for the suggested[9] M^+ → m/e 73 sequence; there is often metastable support, however, for the existence of the fragmentation path d → f. The proposed formaldehyde ejection also has precedent in the behavior of simple dialkyl ethers.[10]

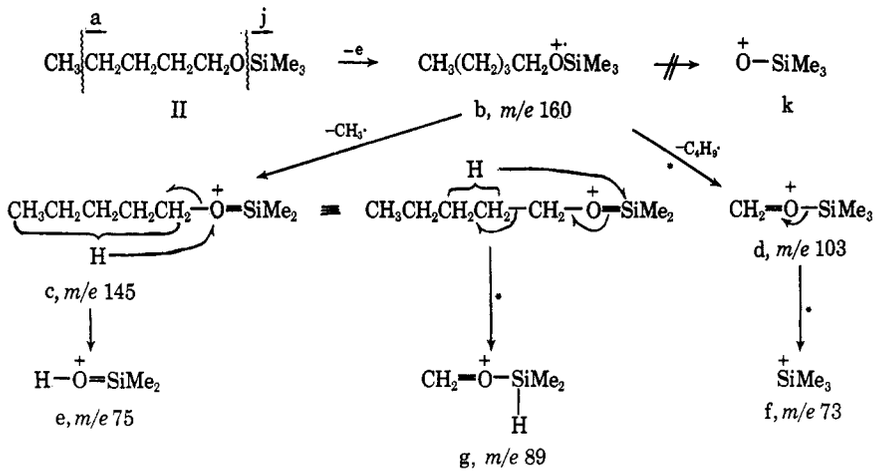
The only remaining important peak in the mass spectrum (Figure 1) of pentan-1-ol trimethylsilyl ether (II) that has not been discussed is the one at m/e 89 (Σ_{40} = 4.24%). Previously, it was assumed[9] that the fragment of mass 89 resulted from fission of the carbon–oxygen bond of the molecular ion (b → k) to produce a trimethylsiloxy species. The observation of a metastable peak at m/e 54.6 (calcd, $89^2/145$ = 54.6) indicated that the M − 15 fragment c and not the molecular ion was in fact the progenitor of the fragment of mass

(10) C. Djerassi and C. Fenselau, *J. Am. Chem. Soc.*, **87**, 5747 (1965); see also Chapter 6 in ref 5.

(11) The presence of a metastable ion for a given process is indicated in this paper by an asterisk (*) over the arrow in the fragmentation scheme.

(12) J. K. MacLeod and C. Djerassi, *Tetrahedron Letters*, 2183 (1966); *J. Am. Chem. Soc.*, **89**, 5182 (1967).

SCHEME I



89 (c → g). This conclusion was verified when the mass spectrum of 1,1-d_2-pentan-1-ol trimethylsilyl ether (III) was recorded and revealed a shift of the *m/e* 89 peak to *m/e* 91. As in the case of the *m/e* 75 fragment, the origin of the migrating hydrogen could be determined by successively labeling each position in the carbon chain. As Table I indicates, the hydrogen transfer involves predominantly (90%) the hydrogen atoms attached to the β and γ positions.

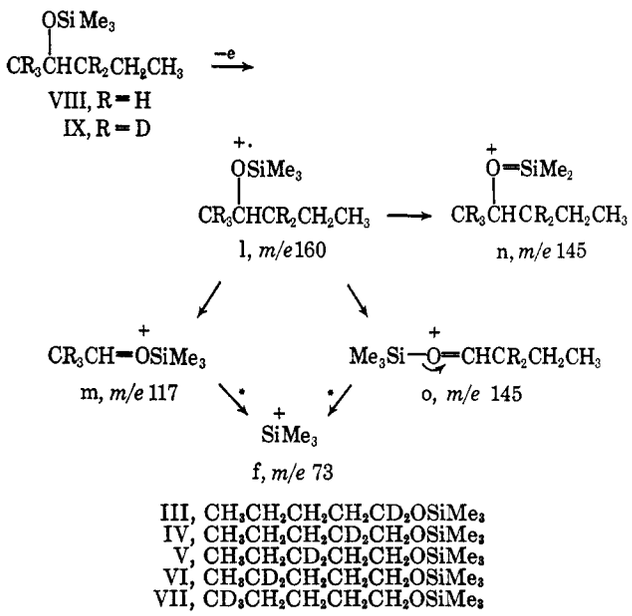
A complete study of the mass spectra of structurally simple trimethylsilyl ethers must include some observations regarding the behavior of a simple branched-chain trimethylsilyl ether upon electron impact; for this reason, the mass spectrum (Figure 2) of pentan-2-ol trimethylsilyl ether (VIII) was recorded. Branching at the α-fission site has a marked effect upon the mode of fragmentation in comparison to the processes observed in the straight-chain trimethylsilyl ether (II).

Ejection of a methyl group from pentan-1-ol trimethylsilyl ether (II) upon electron impact was greatly preferred over expulsion of a butyl radical; this trend, however, is reversed in the case of pentan-2-ol trimethylsilyl ether (VIII) where the peak (*m/e* 117, Σ_{40} = 23.63%) corresponding to loss of a propyl radical (l → m) is four times as intense as the one at *m/e* 145 (M − CH_3, Σ_{40} = 5.45%). The mass spectrum of 1,1,1,3,3-d_5-pentan-2-ol trimethylsilyl ether (IX) indicated that 80% of the *m/e* 145 peak resulted from loss of the methyl group from the silicon atom (M − CH_3), while loss of the C-1 methyl group (M − CD_3) contributed the remaining 20%. Similar results were encountered by Karabatsos, *et al.*,[13] in their work on the deamination of isotopically labeled 1-butylamines in which 2-butanol was an intermediate.

The mass spectrum (Figure 2) of pentan-2-ol trimethylsilyl ether offers a further basis for the questions raised with regard to the previously reported[9] structure of the *m/e* 89 fragment and the previously reported[9] mode of formation of the trimethylsilyl cation (f, *m/e* 73). If the fragment of mass 89 were a siloxy-type species (k) one would expect in VIII a more intense *m/e* 89 peak than in the case of pentan-1-ol trimethylsilyl ether (II) because the expulsion of a more stable secondary pentyl radical is certainly favored over the expulsion of a primary pentyl radical. In fact, an *m/e* 89

(13) G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *ibid.*, **88**, 5651 (1966).

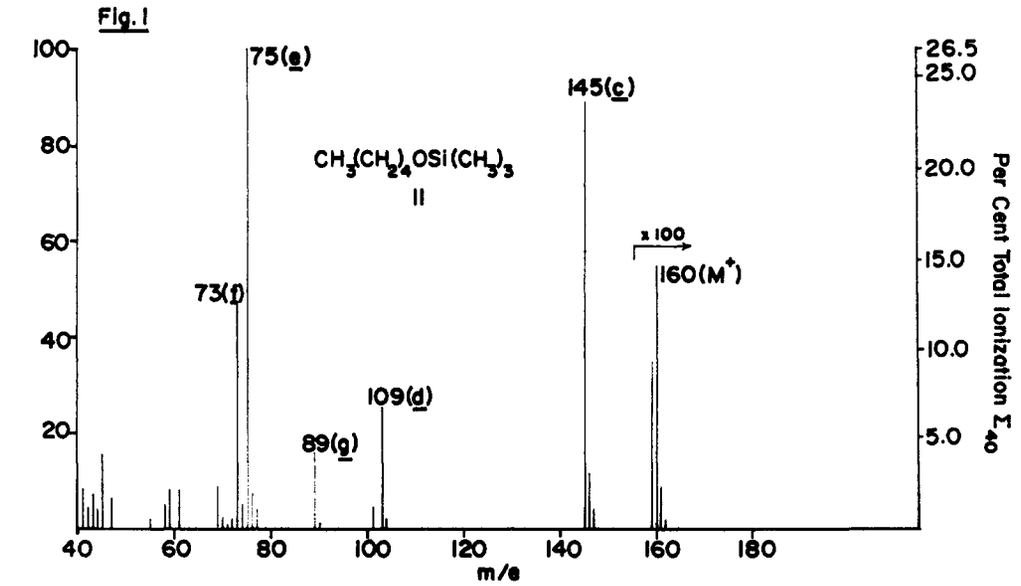
SCHEME II

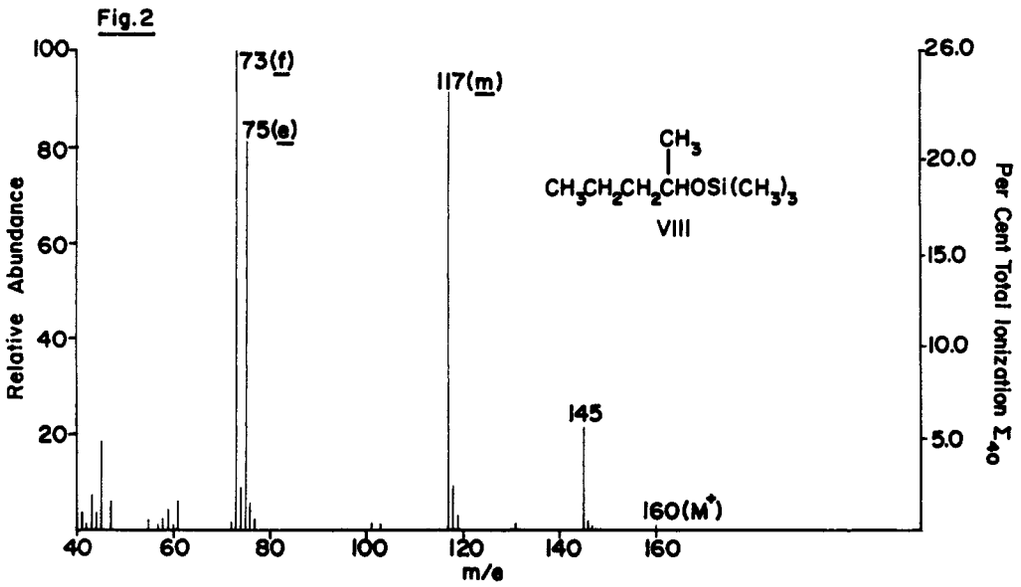


III, $CH_3CH_2CH_2CH_2CD_2OSiMe_3$
IV, $CH_3CH_2CH_2CD_2CH_2OSiMe_3$
V, $CH_3CH_2CD_2CH_2CH_2OSiMe_3$
VI, $CH_3CD_2CH_2CH_2CH_2OSiMe_3$
VII, $CD_3CH_2CH_2CH_2CH_2OSiMe_3$

peak does not even appear in the spectrum (Figure 2) of pentan-2-ol trimethylsilyl ether (VIII); this is to be expected in the light of the structure g proposed in this study, because formation of such a species would necessitate cleavage of both the C-1 or C-2 as well as the C-2 or C-3 bonds accompanied by a hydrogen transfer. Again, no metastable support is found for genesis of the trimethylsilyl cation (f) directly from the molecular ion; however, metastable peaks are observed at *m/e* 36.7 (calcd, $73^2/145$ = 36.8) and *m/e* 45.5 (calcd, $73^2/117$ = 45.5) corresponding to formation from each of the α-fission products, m and o, respectively. Although the *m/e* 73 peak is the base peak (Σ_{40} = 25.97%) at 70 ev, it disappears at 12 ev leaving *m/e* 117 (Σ_{40} = 75.19%) and *m/e* 145 (Σ_{40} = 12.78%) as the only peaks in the spectrum. (See Scheme II.)

The mass spectrum (Figure 3) of pentan-1-ol triethylsilyl ether (X) was recorded in order to ascertain whether the triethylsilyl moiety directed fragmentation sequences in a manner analogous to that of the trimethyl compound. In fact, although of identical mass, the primary fragmentation products (*m/e* 75 and *m/e* 103) of pentan-1-ol triethylsilyl ether (X) (which involve approximately 72% of the total ionization) are associated





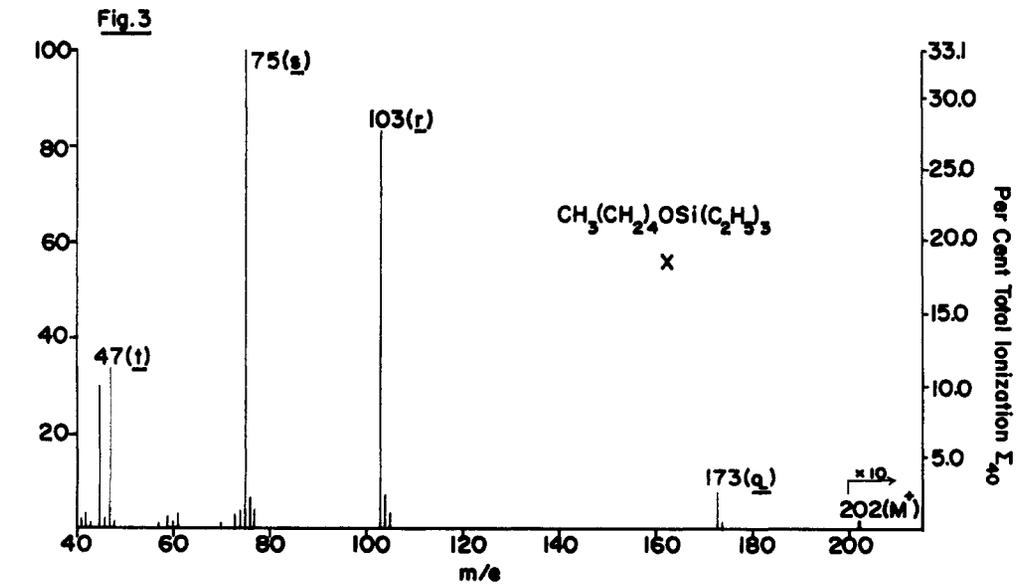
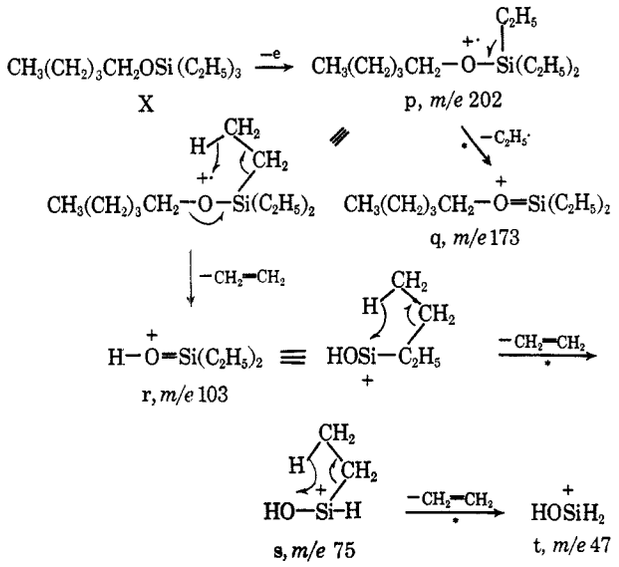


Figure 1.—Mass spectrum (Atlas CH-4) of pentan-1-ol trimethylsilyl ether (II).
Figure 2.—Mass spectrum (Atlas CH-4) of pentan-2-ol trimethylsilyl ether (VIII).
Figure 3.—Mass spectrum (Atlas CH-4) of pentan-1-ol triethylsilyl ether (X).

with fissions and rearrangement processes about the silicon atom which have no analogy in the mass spectrum of pentan-1-ol trimethylsilyl ether (II).

As in the case of pentan-1-ol trimethylsilyl ether (II), there is no loss of a C-5 methyl radical; this is indicated by the absence of an m/e 187 (M − CH_3) peak. Cleavage of an ethyl radical from the silicon atom produces the peak at m/e 173 (q, Σ_{40} = 2.65%); it was shown by labeling the C-4 and C-5 positions with deuterium atoms that there was no loss of an ethyl radical from the carbon chain. (See Scheme III.)

SCHEME III



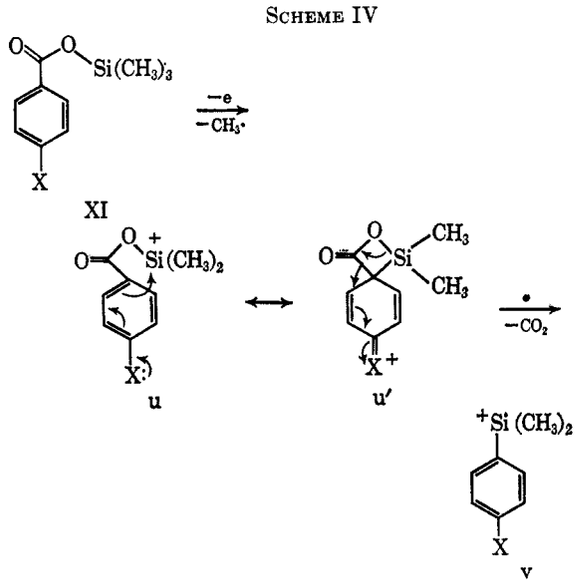
One predominant fragmentation sequence (p → r → s → t) accounts for the other three important peaks (m/e 103, m/e 75 and m/e 47) in the spectrum (Figure 3) of pentan-1-ol triethylsilyl ether. The first distinctive difference in the mass spectra of the trimethylsilyl and triethylsilyl pentanol ethers involves the fragmentation (p → r) of the molecular ion to produce the fragment of mass 103 (Σ_{40} = 27.48%). Although this ion r has an elemental composition [$(C_2H_5)_2SiOH$] analogous to that of the m/e 75 [$(CH_3)_2SiOH$, e] species created in the pentan-1-ol trimethylsilyl ether (II) fragmentation, its formation from the parent ion must involve a completely different genesis. It was shown that in the sequence (c → e) approximately 81% of the transferred hydrogen originated from the carbon chain; deuterium labeling of each position of the triethylsilyl ether (X) indicates that in the production of the m/e 103 ion (p → r), *none* of the transferred hydrogen originates in such a manner. Thus, a scheme (p → r) involving a hydrogen shift from a silicon ethyl group must be envisaged.

Formation of the species of mass 75 (s, Σ_{40} = 33.11%) occurs in triethylsilyl but not trimethylsilyl ethers simply because a larger substituent ($C_2H_5\cdot$) is bonded to the silicon atom. High resolution measurements and a large metastable peak at m/e 54.7 (calcd, $75^2/103$ = 54.7) indicate a hydrogen transfer to the charged silicon-containing moiety with expulsion of a stable neutral ethylene molecule in the formation of the m/e 75 species (s) from the m/e 103 fragment (r). A repetition of this same process, s → t, generates the m/e 47 (Σ_{40} = 11.26%) species; this pathway is again supported by a large metastable peak at m/e 29.6 (calcd, $47^2/75$ = 29.5).

As will become evident in the following discussions, substitution of a triethylsilyl for a trimethylsilyl derivative generally results in a completely different mode of fragmentation which in all cases is identical with the p → t sequence.

Benzyl Trimethylsilyl Ethers.—In a brief, but interesting report by Teeter[14] on the mass spectra of trimethylsilyl esters, it was noted that trimethylsilyl benzoates (XI) show prominent peaks at M − 59. On the basis of appropriate metastable ions, it was suggested that formation of the M − 59 species resulted from elimination of carbon dioxide from the M − CH_3 fragment (u,u′). This M − 59 fragment increases in abundance, with respect to its precursor, u, when the substituent in the *para* position is electron donating and decreases when this substituent is electron attracting. Teeter[14] proposed structure v for the M − 59 ion, formed in the manner indicated in Scheme IV.

SCHEME IV



This important observation, coupled with the intention of investigating the prominent mass spectral fragmentation patterns of compounds more complex than pentanol trimethylsilyl ethers, prompted us to examine in detail the mass spectra of several types of trimethylsilyl derivatives in the expectation of uncovering further examples of skeletal rearrangements. It has been only recently made clear[8] that such skeletal rearrangements are of fairly common occurrence in the electron impact induced fragmentation of many types of compounds.

In this paper, the fragmentations of benzyl trimethylsilyl ethers, substituted on the aromatic ring or on the benzylic carbon atom, together with some benzyl trimethylsilyl amines, sulfides, and their homologs are discussed. Later papers will cover the mass spectra of a variety of trimethylsilyl derivatives of glycols and of trimethylsilyl esters.

The mass spectrum (Figure 4) of benzyl trimethylsilyl ether (XII) at 70 ev is quite simple with only three prominent peaks. The base peak (Σ_{40} = 27.8%) occurs at m/e 91 (C_7H_7) and the M − CH_3 peak (m/e 165) is very strong (Σ_{40} = 22.0%). The most interesting

(14) R. M. Teeter, Abstracts, Tenth Conference on Mass Spectrometry of the American Society for Testing Materials, New Orleans, La., 1962, p 51.

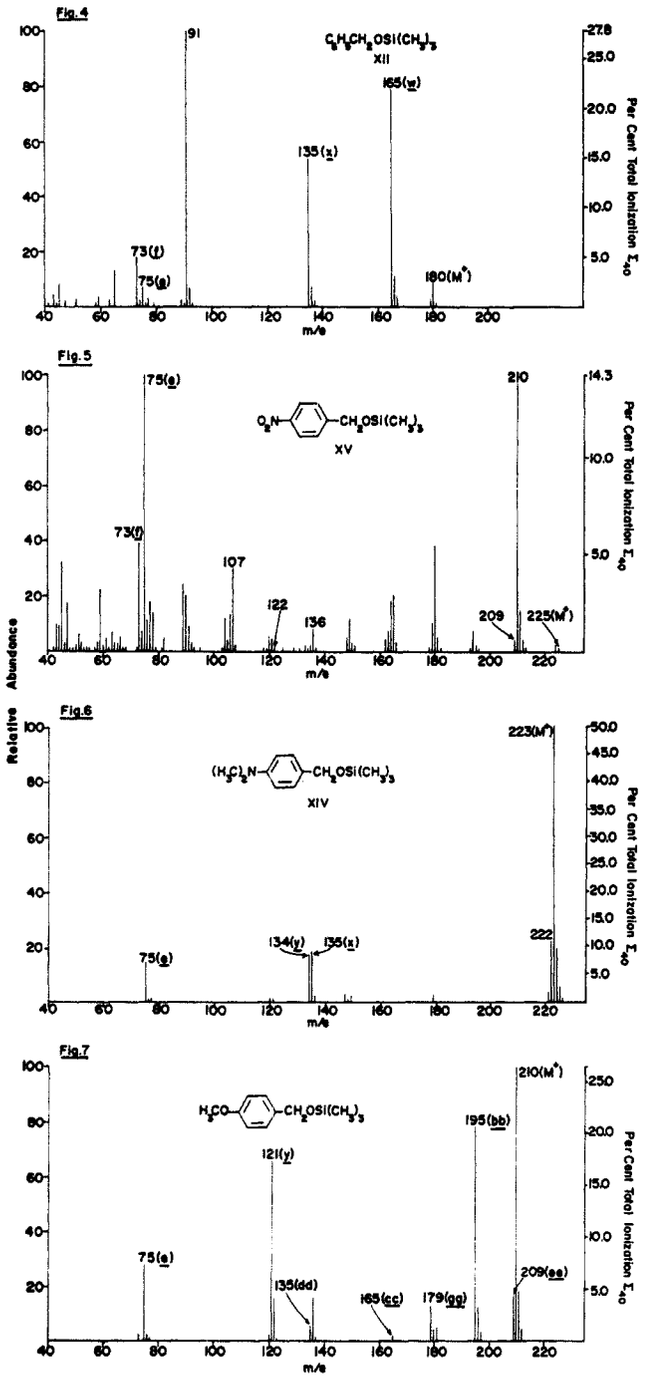


Figure 4.—Mass spectrum (Atlas CH-4) of benzyl trimethylsilyl ether (XII).

Figure 5.—Mass spectrum (Atlas CH-4) of *p*-nitrobenyl trimethylsilyl ether (XV).

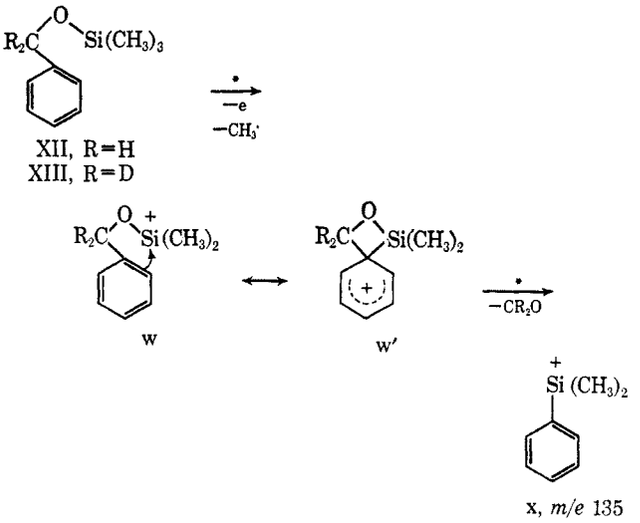
Figure 6.—Mass spectrum (Atlas CH-4) of *p*-dimethylaminobenzyl trimethylsilyl ether (XIV).

Figure 7.—Mass spectrum (Atlas CH-4) of *p*-methoxybenzyl trimethylsilyl ether (XVIII).

feature in the spectrum is an abundant (Σ_{40} = 15.0%) fragment of mass 135 which is formed from M − CH_3 (a metastable ion is observed) by elimination of formaldehyde[15] and for which x is a plausible representation. In the spectrum of the α,α-d_2-benzyl trimethylsilyl ether (XIII), this peak remains at *m/e* 135 while the molecular ion, M − CH_3, and the base peak are shifted quantitatively by two mass units. The elimination of formaldehyde then, is a clean process which does not involve any scrambling between the benzylic and aromatic or Si–CH_3 hydrogen atoms. (See Scheme V.)

(15) The compositions of all fragment ions subsequently discussed were confirmed, when necessary, by high resolution measurements.

SCHEME V



The spectra of a number of *para*-substituted benzyl trimethylsilyl ethers (Table II) all show the M − (CH_3 + CH_2O) peak which, however, is in every case weaker than that from the unsubstituted compound XII. There is no correlation between the the nature of the substituent and the abundance of the rearranged species either at high (70 ev) or low (15 ev) electron beam energies. Note for example the near equality in Table II of the ratios of the rearrangement and the M − CH_3 ions from the *p*-dimethylamino (XIV) and *p*-nitrobenzyl (XV) ethers. The rearrangement ions from the *p*-dimethylamino (XIV) and *p*-methoxybenzyl (XVIII) ethers, however, decompose further, even at low electron voltages (see below), and elimination of formaldehyde from the M − CH_3 species may be a much more favorable process than is indicated by the data in Table II. The data, therefore, do not exclude the possibility that rearrangement is favored by electron-donating groups.

At 15 ev of ionizing energy the benzyl ether (XII) exhibits only four fragments: the molecular ion, a weak M − H species, the M − CH_3 fragment (w), and a weak tropylium ion (*m/e* 91). At 12 ev of ionizing energy only the molecular ion and M − CH_3 (Σ_{40} = 63.3%) peaks appear. For simplicity many of the subsequently reported mass spectra of substituted benzyl trimethylsilyl ethers were recorded at nominal 15 ev rather than the customary 70 ev of ionizing energy.

As was indicated in the conclusion of our previous study,[7] the trimethylsilyl group does *not* consistently direct characteristic mass spectral fragmentation patterns in a variety of compounds. Although it is useful in directing characteristic decomposition modes in the case of Δ^5-3-hydroxy sterol trimethylsilyl ethers, the trimethylsilyl group played only a minor role in the fragmentation of saturated 3-hydroxy sterol derivatives.[7] Likewise the mass spectra of this series of *para*-substituted benzyl trimethylsilyl ethers illustrate the fact that the trimethylsilyl group is not a particularly outstanding fragment director. Except for the fact that all of these derivatives yield to some extent the rearrangement ion x, generally the *para* substituent is responsible for the most characteristic decompositions and this pre-

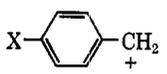
TABLE II

REARRANGEMENT PEAKS IN THE MASS SPECTRA OF *p*-SUBSTITUTED BENZYL TRIMETHYLSILYL ETHERS

	% Σ_{40}[b]				Ratio of	
	M − CH_3		M − (CH_3 + CH_2O)		M − (CH_3 + CH_2O)/M − CH_3	
Compd[a]	70 ev	15 ev	70 ev	15 ev	70 ev	15 ev
$C_6H_5CH_2OTMS$ (XII)	22.0	65.0	15.0	7.1	0.68	0.11
p-$(CH_3)_2NC_6H_4CH_2OTMS$ (XIV)	0.25	≪0.1	0.1	≪0.1	0.40	
p-$O_2NC_6H_4CH_2OTMS$ (XV)	14.0	40.0	5.4	2.0	0.39	0.05
p-$FC_6H_4CH_2OTMS$ (XVI)	23.1	69.0	4.4	2.1	0.19	0.03
p-$ClC_6H_4CH_2OTMS$ (XVII)	17.1	40.0	5.6	2.8	0.33	0.07
p-$CH_3OC_6H_4CH_2OTMS$ (XVIII)	6.8	20.5	0.8	0.5	0.12	0.02

[a] TMS = $Si(CH_3)_3$. [b] The symbol Σ_{40} denotes the percentage of total ionization over the range *m/e* 40 to M^+.

cludes the proposal of a general fragmentation scheme common to the mass spectra of all *para*-substituted benzyl trimethylsilyl ethers. One can generalize to some extent in that, except for the *p*-nitro compound (XV), all of the benzyl ethers (XIV and XVI–XVIII) give quite simple spectra with the benzyl cations, y, or the tropylium ion equivalent, z, being responsible for the base peaks at 70 ev. The only other prominent peaks are due to the M − CH_3 fragment (except in the case of XIV, see Table II), the trimethylsilyl cation (*f*, *m/e* 73), the M − Cl moiety (in the spectrum of XVII), and, in the spectrum of XIV, the molecular ion and M − 1 species.



y

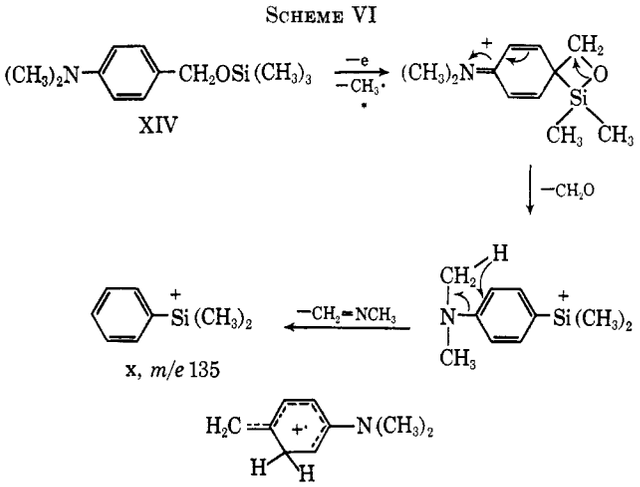
z

The *p*-nitrobenzyl ether (XV) exhibits a much more complex fragmentation pattern (Figure 5) in which the benzyl (y, X = NO_2, *m/e* 136) or tropylium (z) cation is particularly weak (Σ_{40} = 1.14%) and the two silicon-containing species, e (*m/e* 75) and M − CH_3 (*m/e* 210) provide the most abundant peaks. Even at 15 ev, a large number of weak peaks appear with only two intense ones: *m/e* 210 (Σ_{40} = 40.0%) and *m/e* 107 (Σ_{40} = 20.0%). High resolution mass measurements indicate the composition of the fragment of mass 107 to be C_6H_5NO, suggesting loss of the trimethylsiloxy-substituted benzyl carbon atom with hydrogen transfer to the benzene ring and loss of atomic oxygen from the nitro group, a process certainly "atypical" of the previous trimethylsilyl derivatives. Loss of atomic oxygen is a common phenomenon in the mass spectra of nitroarenes;[16] however, loss of both atomic oxygen and the benzyl carbon atom is somewhat unusual in the light of the nature of the *m/e* 107 peak observed in the mass spectrum of *p*-nitrotoluene.[17] In this case the *m/e* 107 peak corresponds to loss of an NO species from the nitro group to yield a fragment of composition $C_7H_7O^+$. It is difficult to speculate as to whether the atomic oxygen is lost prior to cleavage of the benzyl carbon atom, or *vice versa*, because neither the M − 16 peak (*m/e* 209) nor the $C_6H_4NO_2$ peak (*m/e* 122) is particularly intense and no appropriate metastable peaks are observable.

Unlike the *p*-nitro derivative (XV), the halogen analogs, *p*-fluoro and *p*-chlorobenzyl trimethylsilyl ethers exhibit very simple spectra. The 15-ev spectrum of the *p*-fluoro ether (XVI) contains only one abundant fragment (M − CH_3) which, with its isotopic species, carries 80% of the total ion current. The spectrum of the *p*-chloro analog (XVII) at 15 ev is almost as simple with M − CH_3 and M − Cl fragments formed in 60 and 20% ion yield, respectively.

In the spectrum (Figure 6) of *p*-N,N-dimethylaminobenzyl trimethylsilyl ether (XIV) the molecular ion (*m/e* 223), the M − 1 fragment (*m/e* 222), and the benzyl cation (*m/e* 134, y, X = $N(CH_3)_2$) carry over 80% of the total ion current at 15 ev. Approximately 10% of the ion yield is accounted for by the species of mass 135, for which it was very tempting to propose structure *x* produced by a process analogous to the elimination of formaldehyde from aromatic ethers.[18] However, exact mass measurements on the *m/e* 135 peak showed that it corresponded exclusively to $C_9H_{13}N$ rather than to $C_8H_{11}Si$. Its genesis, therefore, results from oxygen–carbon fission with transfer of a hydrogen atom. A plausible representation is x′. (See Scheme VI.)

SCHEME VI



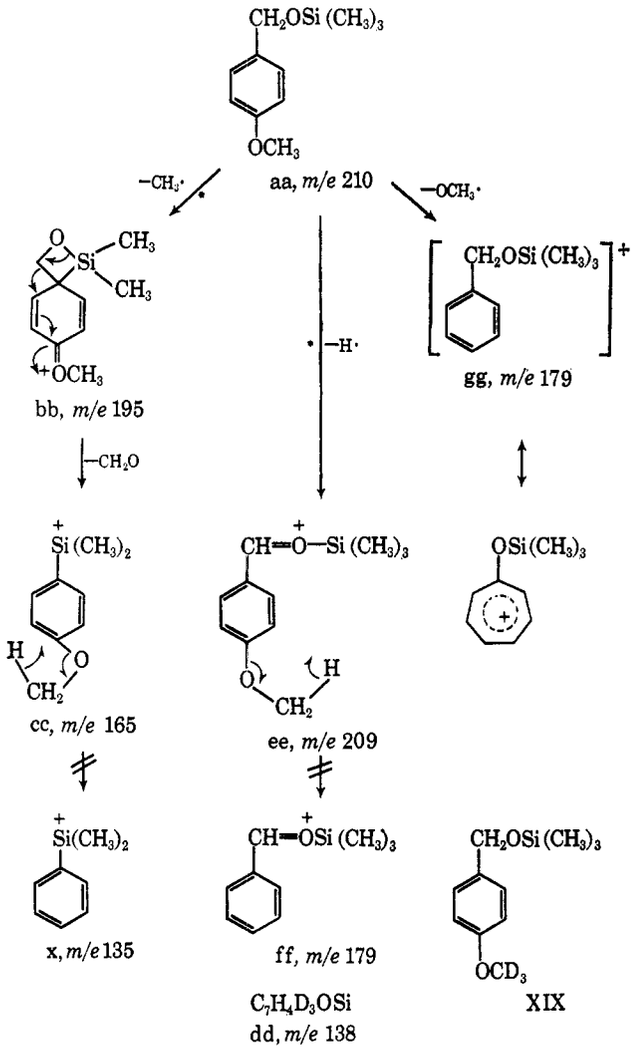
Comparison of the mass spectra of *p*-N,N-dimethylaminobenzyl trimethylsilyl ether (XIV, Figure 6) and of *p*-methoxybenzyl trimethylsilyl ether (XVIII, Figure 7) provides an excellent example of a case in which the trimethylsilyl group does not initiate similar fragmentation patterns despite the similar electron-donating *para* substituents in the two compounds. The only correspondence in the 15-ev spectra is the molecular ion base peaks. The benzyl cation (*m/e* 121) of the *p*-methoxy derivatives (y, X = OCH_3) is much more intense (Σ_{40} = 17.19%) than in the previous case, and also there is a large M − CH_3 peak (bb, *m/e* 195, Σ_{40} = 20.51%) which did not even appear in the dimethylamino derivative. The observation of a weak *m/e* 135 peak (Σ_{40} = 1.58%) as well as a minor one at *m/e* 165 (Σ_{40} = 0.53%) implies a mode of fragmentation

(16) See Chapter 16 in ref 5.

(17) S. Meyerson, I. Puskas, and E. K. Fields, *J. Am. Chem. Soc.*, **88**, 4974 (1966).

(18) See section 6-1B in ref 5.

SCHEME VII



(aa → bb → cc → y) analogous to that suggested originally (but disproved by high resolution measurements) for the genesis of the m/e 135 peak (x) in the dimethylamino derivative. The mass spectrum of p-d_3-methoxybenzyl trimethylsilyl ether (XIX) indicates, however, that here also this fragmentation sequence does not take place. As predicted, there is no loss of the methoxymethyl group (M − 18 in the labeled analog) in the formation of the fragment of mass 195; all methyl radical cleavage thus occurs at the silicon atom (aa → bb) (see Scheme VII). Labeling likewise indicates loss of undeuterated formaldehyde in the formation of the m/e 165 species (bb → cc); however, the subsequent loss of labeled formaldehyde from the *para* position of cc does *not* occur. Instead one retains all three deuterium atoms in this fragment (m/e 135 → m/e 138, dd).

The existence of an M − 1 peak in the spectrum of the deuterated species shows that a benzylic hydrogen atom is lost (aa → ee) to yield the m/e 209 peak (Σ_{40} = 44.47%). Formaldehyde is not ejected from the M − 1 species to produce the fragment (ff) of mass 179. Instead, the presence of an M − OCD_3 peak in the labeled analog indicates direct fission of the methoxyl group (aa → gg) to yield this species (Σ_{40} = 3.15%). Precedent does exist for fragmentation of this type.[19]

(19) Z. Pelah, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *Tetrahedron*, **19**, 2233 (1963); C. S. Barnes and J. L. Occolowitz, *Australian J. Chem.*, **16**, 219 (1963).

Substitution on the benzylic carbon atom of the benzyl ether (XII) results in a marked reduction of the m/e 135 (x) rearrangement peak (Table III). In the

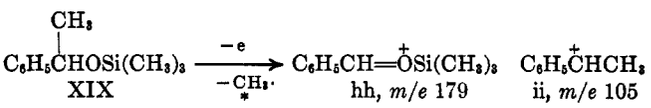
TABLE III

INTENSITY (% Σ_{40}) OF THE REARRANGEMENT PEAK x (m/e 135) IN THE MASS SPECTRA (70 EV) OF α-SUBSTITUTED BENZYL TRIMETHYLSILYL ETHERS AND HIGHER HOMOLOGS

Compd	% Σ_{40}
$C_6H_5CH_2OSi(CH_3)_3$ (XII)	15.0
$C_6H_5CH(CH_3)OSi(CH_3)_3$ (XIX)	0.7
$C_6H_5C(CH_3)_2OSi(CH_3)_3$ (XXI)	0.25
$(C_6H_5)_2CHOSi(CH_3)_3$ (XXII)	0.8
$C_6H_5(CH_2)_2OSi(CH_3)_3$ (XXIII)	0.2[a]
$C_6H_5(CH_2)_3OSi(CH_3)_3$ (XXIV)	0.2[b]

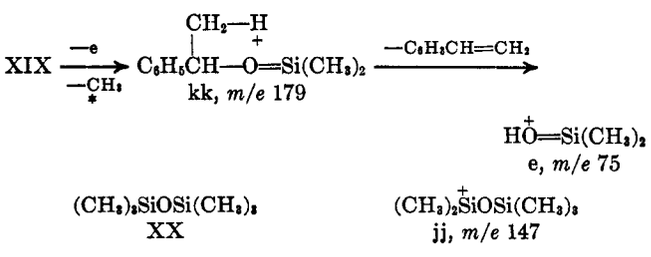
[a] In addition there is present (0.2%) a rearrangement peak at m/e 149 [M − (CH_3 + CH_3O)]. [b] In addition there is present (0.2%) a rearrangement peak at m/e 163 [M − (CH_3 + CH_2O)].

spectrum (Figure 8) of the α-methyl derivative (XIX), the molecular ion is weak (Σ_{40} = 0.99%) and the M − CH_3 base peak is formed in 33% ion yield. The latter species doubtless consists to a large extent of the oxonium ion hh. The rearrangement ion of mass 135 [M − (CH_3 + CH_3CHO)] carries only 0.67% of the total ion current. Besides the α-methylbenzyl cation (ii, m/e 105, Σ_{40} = 3.0%), $C_6H_5^+$ (m/e 77, Σ_{40} = 2.6%), and the trimethylsilyl cation (f, m/e 73, Σ_{40} = 10.0%), the only other fragment formed in over 1% ion yield is that giving rise to the peak at m/e 75, (e, Σ_{40} = 19.00%).



This m/e 75 peak is absent, or weak, in the spectra of freshly prepared benzyl trimethylsilyl ethers that are unsubstituted on the benzylic carbon atom, but appears in the spectra of samples exposed to air. In the latter case a much weaker peak also appears at m/e 147 (jj). It is apparent that trimethylsilyl alcohol, for which m/e 75 represents the M − CH_3 ion, and hexamethyldisiloxane (XX), for which m/e 147 (jj, M − CH_3) is the base peak[9,20] are formed by reaction of the ethers with atmospheric moisture. In the spectrum (Figure 8) of XIX, the peak at m/e 147 is absent; thus in this instance the m/e 75 peak is undoubtedly due entirely to electron impact induced fragmentation (kk → e). (See Scheme VIII.)

SCHEME VIII



The spectrum of α,α-dimethylbenzyl trimethylsilyl ether (XXI) is similar to that of the lower homolog (XIX). The molecular ion is minute and M − CH_3

(20) V. H. Dibeler, F. L. Mohler, and R. M. Reese, *J. Chem. Phys.*, **21**, 180 (1953).

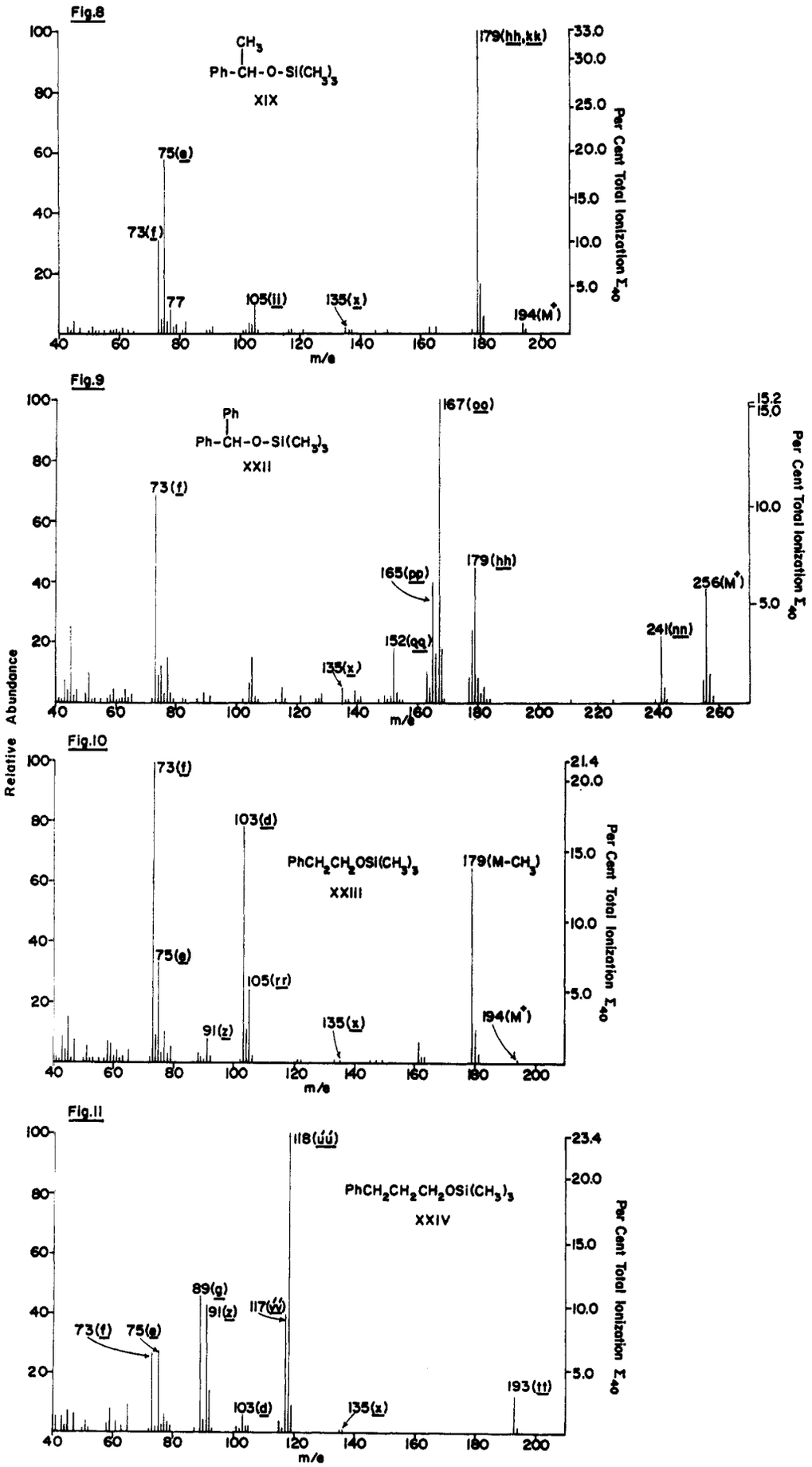
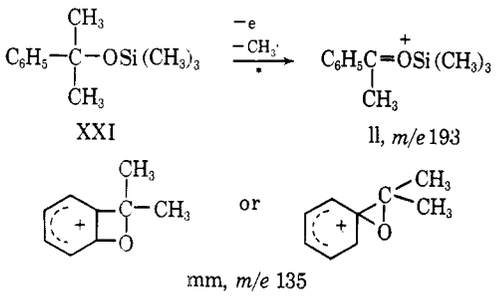
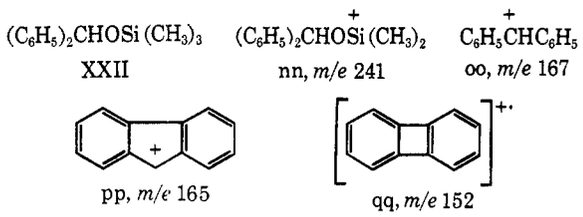


Figure 8.—Mass spectrum (CEC-103C) of α-methylbenzyl trimethylsilyl ether (XIX).
Figure 9.—Mass spectrum (CEC-103C) of α-phenylbenzyl trimethylsilyl ether (XXII).
Figure 10.—Mass spectrum (CEC-103C) of β-phenylethyl trimethylsilyl ether (XXIII).
Figure 11.—Mass spectrum (AEI-MS-9) of dihydrocinnamyl trimethylsilyl ether (XXIV).

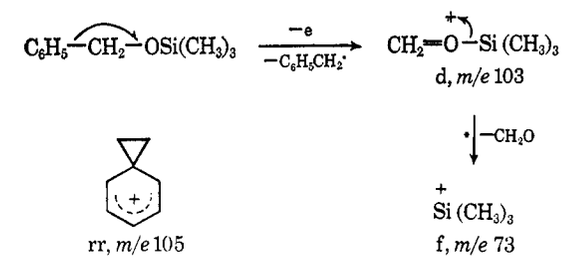
(presumably mostly ll) yields the base peak (Σ_{40} = 23.71%) with the trimethylsilyl cation (f, Σ_{40} = 12.32%) and species e (*m/e* 75, Σ_{40} = 16.45%), being the only other prominent fragments. The species of mass 135 (Σ_{40} = 0.73%) consists of 65% $C_9H_{11}O$ (mm) and 35% rearrangement ion (x, M − [CH_3 + $(CH_3)_2CO$]), as shown by high resolution mass measurements.



In contrast to XIX and XXI, the benzhydryl analog (XXII) exhibits (Figure 9) a complex fragmentation pattern with a moderately strong (Σ_{40} = 5.81%) molecular ion and a relatively weak (Σ_{40} = 3.30%) M − CH_3 peak (nn, *m/e* 241). The rearrangement species x [M − (CH_3 + C_6H_5CHO)] is formed in only 0.8% ion yield. Other prominent peaks are at *m/e* 179 (hh, M − C_6H_5, Σ_{40} = 6.80%), *m/e* 73 (f, Σ_{40} = 10.51%) and the base peak *m/e* 167 (oo, Σ_{40} = 15.23%) which is accompanied by a series of moderate to weak peaks corresponding to the major fragments from diphenylmethane[21] [*e.g.*, *m/e* 165 (pp, Σ_{40} = 6.01%) and *m/e* 152 (qq, Σ_{40} = 2.70%)].



Two examples (XXIII and XXIV) of unbranched homologs of the benzyl ether (XII) have been studied and in neither case is the rearrangement an important feature of the mass spectrum (Table III). The base peak in the spectrum (Figure 10) of β-phenylethyl trimethylsilyl ether (XXIII) occurs at *m/e* 73 (f, Σ_{40} = 21.46%), M − CH_3 is strong (Σ_{40} = 14.00%), and the molecular ion is insignificant (Σ_{40} = 0.21%). The tropylium ion (y or z, *m/e* 91) is not abundant (Σ_{40} = 1.78%) but α cleavage with charge retention on the siloxy fragment (d, *m/e* 103), is an important fragmentation mode for the molecular ion. Indeed, α cleavage is more pronounced than is indicated by the observed ion yield of d (Σ_{40} = 16.91%), since a strong metastable ion at *m/e* 51.5 (calcd, $73^2/103$ = 51.7) demonstrates that,



(21) J. H. D. Eland and C. J. Danby, *J. Chem. Soc.*, 5939 (1965).

at least in part, d decomposes further to yield the most important species (f, *m/e* 73). In the remainder of the spectrum only e, (*m/e* 75, Σ_{40} = 7.09%) and C_8H_9 (*m/e* 105, Σ_{40} = 5.08%), which is perhaps best represented as the spiran rr, are at all prominent.

The spectrum (Figure 11) of dihydrocinnamyl trimethylsilyl ether (XXIV) is quite different from that of its lower homolog (XXIII). The molecular ion (*m/e* 208) is still minute (it does not even appear at 70 ev of ionizing energy) and e (*m/e* 75) is still moderately abundant (Σ_{40} = 6.54%), but the M − CH_3 species (tt, Σ_{40} = 3.04%), the α-cleavage ion (d, *m/e* 103, Σ_{40} = 1.40%), and f (*m/e* 73, Σ_{40} = 6.31%) are much less prominent. The tropylium ion (z), on the other hand, is quite pronounced (*m/e* 91, Σ_{40} = 10.04%).

The most outstanding difference in the spectra of β-phenylethyl trimethylsilyl ether (XXIII) and dihydrocinnamyl trimethylsilyl ether (XXIV) is the nature of the base peak. The genesis of the fragment of mass 118 (Σ_{40} = 23.36%), in Figure 11 has no analogy in the fragmentation pattern observed in the spectrum (Figure 10) of XXIII. High resolution mass measurements indicated that the fragment of mass 118 had the elemental composition C_9H_{10}. By labeling each position of the propyl chain with deuterium (XXV–XXVII, Table IV), it was possible to propose a fragmentation sequence (ss → uu) (Scheme IX) for the formation of this fragment and at the same time to determine also the origin (uu → vv) of the abundant *m/e* 117 (Σ_{40} = 9.34%) species. The proposed fragmentation sequence (ss → uu → vv) suggests that the loss of trimethylsilanol from the molecular ion (ss) involves a *specific* α-transfer of a benzylic hydrogen atom from the charge-retaining moiety to yield the species uu. As Table IV indicates, no deuterium is lost from the C-1 or C-2 positions (*m/e* 118 → *m/e* 120, in XXV and XXVI) in the expulsion of trimethylsilanol; however, one deuterium atom *is* lost from the C-3 position (XXVII) as is shown by the shift of the *m/e* 118 peak by only one mass unit to *m/e* 119.

High resolution mass measurements showed that the species of *m/e* 117 (vv) has the composition C_9H_9; its formation by loss of a hydrogen atom from uu is supported by a large metastable peak at *m/e* 116.2 (calcd, $117^2/118$ = 116.0). If the structue of the *m/e* 118 fragment were truly uu, one would expect a random loss of hydrogen from the C-1, C-2, and C-3 positions to produce the fragment of *m/e* 117. Table IV indicates that the ratio of *m/e* 118:*m/e* 117 in the unlabeled compound (XXIV) is 100:40. Interestingly, the corresponding ratios in the labeled species (XXV–XXVII) are practically identical (100:36; 100:40; 100:30) with the unlabeled case. This suggests that only about 10% of the hydrogen atom loss occurs from the C-1, C-2, and C-3 positions. One could attribute this result to a large kinetic isotope effect, but it is more likely that the fragment of *m/e* 118 is of a tropylium ion type (u′u′). If *m/e* 118 were a tropylium ion derivative, one would expect loss of a hydrogen atom from the ring system; and since only one of the seven ring-carbon atoms has a deuterium atom bonded to it, loss of a hydrogen is more probable than loss of a deuterium. This explanation not only accounts for the fact that no deuterium is lost from the *m/e* 120 fragments of XXV and XXVI, but also for the fact that the

SCHEME IX

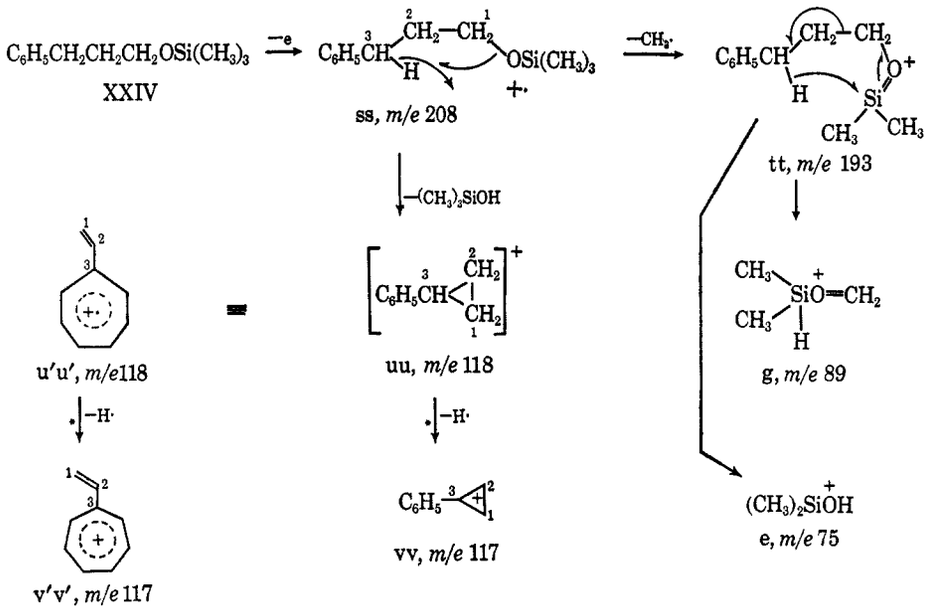


TABLE IV

SHIFTS OF THE m/e 117 AND m/e 118 PEAKS IN THE MASS SPECTRA OF THE DEUTERIUM-LABELED DIHYDROCINNAMYL TRIMETHYLSILYL ETHERS (XXV–XXVII)

Compd	Isotopic compn, %	m/e 116[a,b]	m/e 117[a,b]	m/e 118[a,b]	m/e 119[a,b]	m/e 120[a,b]
$C_6H_5CH_2CH_2CH_2OSi(CH_3)_3$ (XXIV)		6	40	100		
$C_6H_5CH_2CH_2CD_2OSi(CH_3)_3$ (XXV)	100% d_2			7	36	100
$C_6H_5CH_2CD_2CH_2OSi(CH_3)_3$ (XXVI)	100% d_2			8	40	100
$C_6H_5CD_2CH_2CH_2OSi(CH_3)_3$ (XXVII)	98% d_2 2% d_0		8	30	100	

[a] Expressed in relative abundance, %. [b] Corrected for natural isotope abundance and calculated deuterium isotope composition.

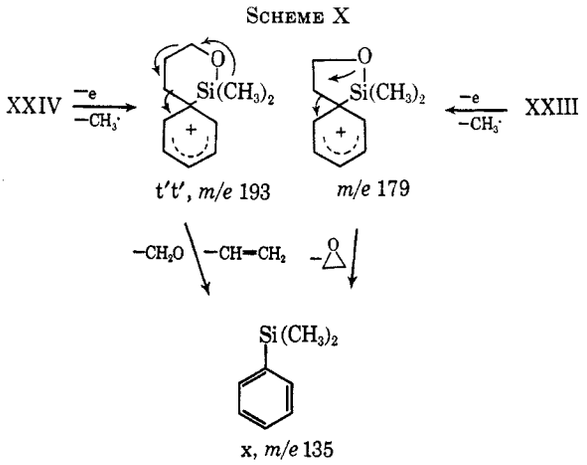
ratio (m/e 119:m/e 118) is slightly lower than that expected in the case of XXVII (indicating that a small amount of deuterium is indeed lost from the ring).

One other prominent peak which appears in the spectrum (Figure 11) of dihydrocinnamyl trimethylsilyl ether (XXIV) and not in the spectrum (Figure 10) of β-phenylethyl trimethylsilyl ether (XXIII) is the one at m/e 89 (Σ_{40} = 10.75%). This fragment is identical in structure to fragment g encountered in the case of pentan-1-ol trimethylsilyl ether (II); as in the previous case, it is formed from the M − CH_3 species as evidenced by a metastable peak at m/e 41.3 (calcd, $89^2/193$ = 41.0). A shift to m/e 91 in the analog labeled in the C-1 position (XXV) verifies that the C-1 carbon atom is retained in this fragment. The hydrogen is transferred specifically from the C-3 position as indicated by a shift from m/e 89 to m/e 90 in the case of XXVII, whereas no such shift is observed in the case of XXVI.

Deuterium labeling also indicates that the hydrogen transfer involved in the formation of species e (m/e 75) from M − CH_3 (tt) is not specific; approximately equal amounts of hydrogen originate from the C-1, C-2, and C-3 positions.

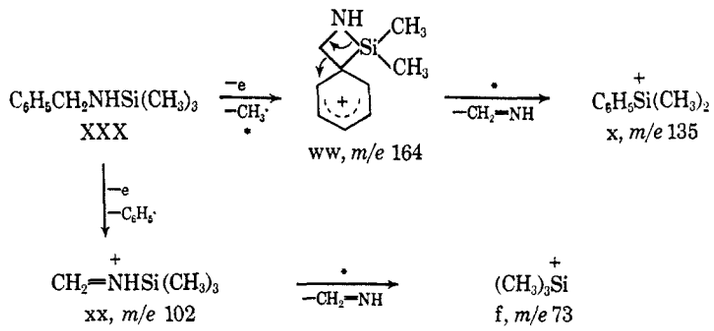
In the spectra of both XXIII and XXIV the m/e 135 rearrangement peak (Table III), corresponding formally to loss of ethylene oxide and trimethylene oxide, respectively, from M − CH_3 is found to be very weak. A plausible rationalization for the formation of the m/e 135 species (x, Σ_{40} = 0.23%) from the dihydrocinnamyl ether (XXIV) molecular ion, involves the spiran form (t't') of the M − CH_3 progenitor. A similar mechanism may be envisaged for the formation of x (Σ_{40} = 0.21%) from the molecular ion of β-phenylethyl trimethylsilyl ether (XXIII). No metastable ions were observed in support of these reaction paths. (See Scheme X.)

SCHEME X



The mass spectra of β-phenylethyl triethylsilyl ether (XXVIII) and dihydrocinnamyl triethylsilyl ether (XXIX) were recorded and, as might be expected (see Figure 1 *vs.* Figure 3), were much more complex than their trimethylsilyl counterparts (XXIII and XXIV, respectively). Both spectra exhibit the characteristic triethylsilyl-directed fragmentation sequence (q → r → s → t) which has been previously discussed. Likewise, both compounds exhibit fragmentations characteristic of the β-phenylethyl and dihydrocinnamyl systems; for instance, m/e 118 and m/e 117 are still

SCHEME XI



prominent peaks in the spectrum of dihydrocinnamyl triethylsilyl ether (XXIX).

$C_6H_5CH_2CH_2OSi(C_2H_5)_3$ XXVIII $C_2H_5CH_2CH_2CH_2OSi(C_2H_5)_3$ XXIX

Benzyl Trimethylsilyl Amines.—In order to delineate further the scope of the previously discussed skeletal rearrangement processes, several benzyl trimethylsilyl derivatives were examined in which the oxygen of XII was replaced by nitrogen or sulfur.

The mass spectrum (Figure 12) of N-(trimethylsilyl)benzylamine (XXX) shows the same major fragments as that of the benzyl trimethylsilyl ether (XII) with the rearrangement ion (x) accounting for the base peak (Σ_{40} = 11.42%) and the M − CH_3 peak (ww) being slightly less abundant (Σ_{40} = 9.90%). The tropylium ion peak (*m/e* 91, Σ_{40} = 3.35%) is reduced considerably, as compared with XII, the trimethylsilyl cation f is increased in relative abundance (Σ_{40} = 7.34%), and there is a great deal more minor fragmentation (see Figure 12). Just as in the benzyl trimethylsilyl ether fragmentation, the α-fission product (xx, *m/e* 102, Σ_{40} = 1.03%) is the progenitor of the trimethylsilyl cation (f). (See Scheme XI.)

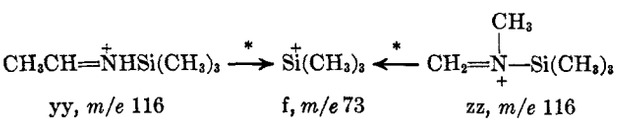
The spectrum of the α-methylbenzylamine (XXXI), like that of its oxygen analog (XIX), is very simple with only three prominent peaks: the rearrangement ion (x) of mass 135 (Σ_{40} = 5.67%), much more abundant (Table V) than in XIX (Table III), the M − CH_3 peak (Σ_{40} = 23.95%), and f (Σ_{40} = 4.31%).

TABLE V

INTENSITY (% Σ_{40}) OF REARRANGEMENT PEAK (x, *m/e* 135) IN MISCELLANEOUS TRIMETHYLSILYL DERIVATIVES

Compd	% Σ_{40}
$C_6H_5CH_2NHSi(CH_3)_3$ (XXX)	11.4
$C_6H_5CH(CH_3)NHSi(CH_3)_3$ (XXXI)	5.7
$C_6H_5CH_2CH_2NHSi(CH_3)_3$ (XXXII)	0.3
$C_6H_5CH_2CH(CH_3)NHSi(CH_3)_3$ (XXXIII)	0
$C_6H_5CH_2N(CH_3)Si(CH_3)_3$ (XXXIV)	6.7
$C_6H_5CH_2N(C_2H_5)Si(CH_3)_3$ (XXXV)	4.1
$C_6H_5CH_2SSi(CH_3)_3$ (XXXVI)	0.6
$C_6H_5CH_2CH_2SSi(CH_3)_3$ (XXXVII)	0
$C_6H_5CH_2OC(CH_3)_3$ (XXXVIII)	0

The unbranched homolog, N-(trimethylsilyl)-β-phenylethylamine (XXXII) also fragments in the same way as the oxygen analog (XXIII) to give a weak (Table V) rearrangement ion. Loss of methyl is not important (Σ_{40} = 3.49%) but the α-cleavage fragment (xx), which gives rise to the base peak (Σ_{40} = 29.29%), and f (Σ_{40} = 20.45%) are abundant. The branched-chain compound (XXXIII) shows no rearrangement peak in its simple spectrum, which is dominated by the benzyl-cleavage species (yy, *m/e* 116, Σ_{40} = 28.67%) and by f (Σ_{40} = 21.65%), the latter being formed, at least in part, from yy, as is indicated by a strong metastable ion at *m/e* 45.8 (calcd, $73^2/116$ = 45.9). The molecular ion is minute; M − CH_3 is formed in only 1.7% and tropylium ion in only 3.1% ion yield.



The mass spectrum of N-methyl-N-(trimethylsilyl)-benzylamine (XXXI) exhibits a much greater prevalence of different fragmentations with the rearrangement ion x accounting for only 6.7% of the ion yield (Table V). As might be expected, the α-fission product (*m/e* 116, zz) produces the base peak Σ_{40} = 9.09%; and similar to the case of XXXIII (yy), it is the progenitor of f. The mass spectrum of N-ethyl-N-(trimethylsilyl)benzylamine (XXXV) seems to follow the trend that increased phenyl side-chain substitution leads to less of the rearrangement ion x, which in this case produces 4.06% of the ion yield. Oddly enough the base peak in this spectrum is the tropylium ion (Σ_{40} = 28.99%).

Benzyl Trimethylsilyl Sulfides.—In contrast to the corresponding ether (XII) and amine (XXX), benzyl trimethylsilyl sulfide (XXXVI) shows (Table V and Figure 13) a very weak (Σ_{40} = 0.68%) rearrangement ion x, of mass 135 [M − (CH_3 + CH_2S)]. The base peak (*m/e* 91, Σ_{40} = 27.75%) is due to the tropylium ion (z), and of the remainder of the spectrum only the trimethylsilyl cation (f) exceeds 20% relative abundance (Σ_{40} = 9.87%). The molecular ion (*m/e* 196, Σ_{40} = 4.12%) and the M − CH_3 peak (*m/e* 181, Σ_{40} = 4.44%) are quite weak. β-Phenylethyl trimethylsilyl sulfide (XXXVII) fragments in a complex manner (Figure 14) and shows no rearrangement peaks in its spectrum. The molecular ion (Σ_{40} = 0.30%) and the M − CH_3 peak (*m/e* 195, Σ_{40} = 0.19%) are weak and the base peak at *m/e* 104 (C_8H_8), corresponding formally to loss of trimethylsilyl thiol from the molecular ion, carries only 9.6% of the total ion current.

Finally, there was examined the spectrum of benzyl *t*-butyl ether (XXXVIII) as the carbon analog of benzyl trimethylsilyl ether (XII), but no rearrangement peak could be discerned. The base peak (*m/e* 91, C_7H_7) is formed in 38% ion yield with the M − CH_3 peak (Σ_{40} = 6.89%) and the tertiary butyl cation (Σ_{40} = 9.11%) being the only other prominent species.

In summary, it may be stated that on the basis of the compounds discussed in this paper two factors appear

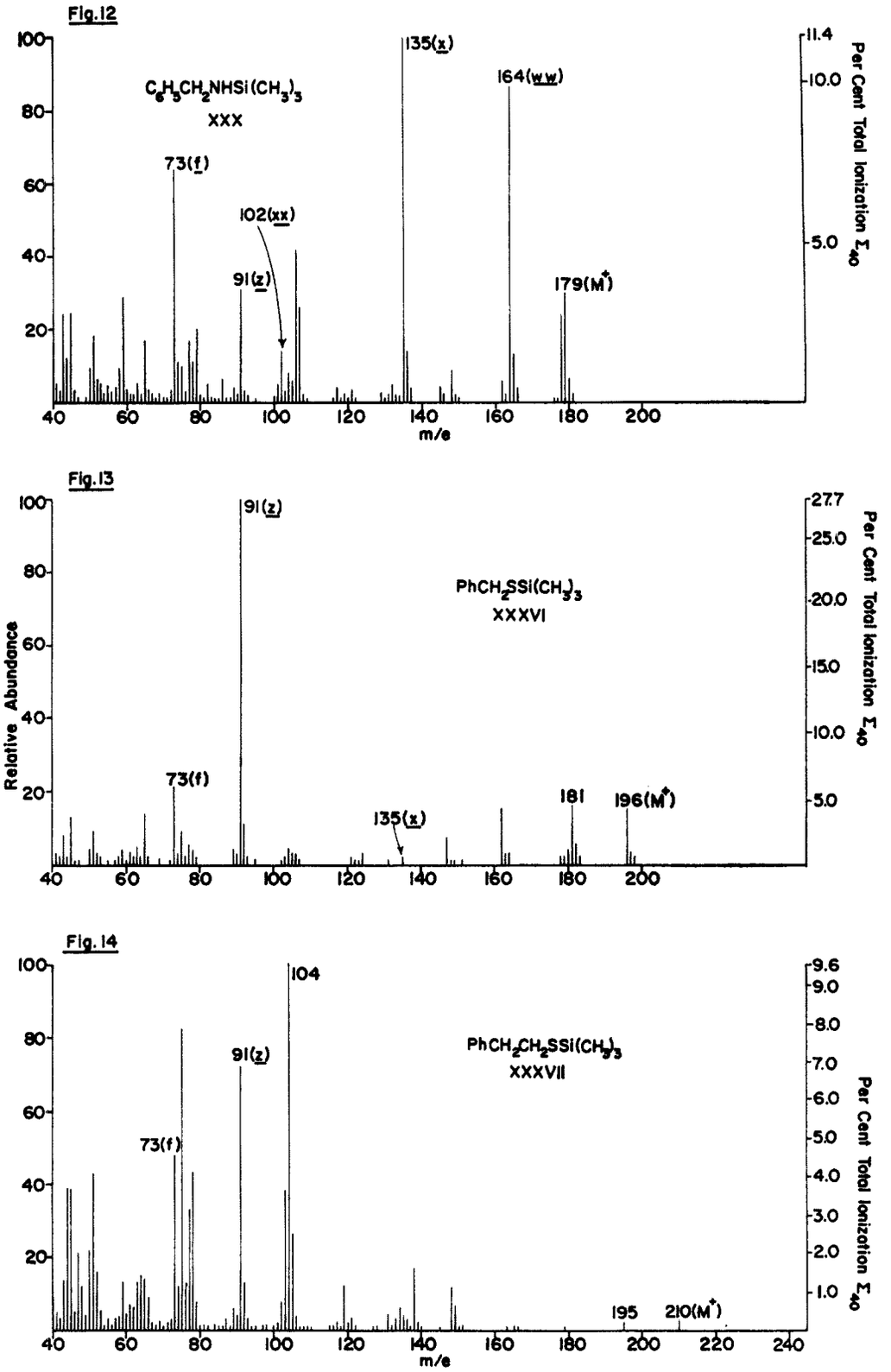
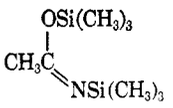


Figure 12.—Mass spectrum (CEC-103C) of N-(trimethylsilyl)benzylamine (XXX).
Figure 13.—Mass spectrum (CEC-103C) of benzyl trimethylsilyl sulfide (XXXVI).
Figure 14.—Mass spectrum (CEC-103C) of β-phenylethyl trimethylsilyl sulfide (XXXVII).

to be of importance for the occurrence of a significant A–B–C → A–C + B rearrangement, which, it should be noted, involves an even rather than an odd electron progenitor (M − CH_3 species in trimethylsilyl derivatives). The first is the nature of the expelled neutral fragment, CH_2O and CH_2NH being favorable and thioformaldehyde (CH_2S) being distinctly undesirable, a conclusion which is consistent with other rearrangement processes (*e.g.*, in esters) in which the nature of the heteroatom has been examined.[8] Second, since the rearrangement does not involve the molecular ion but rather constitutes a further decomposition of a fragment ion (M − CH_3 species), it is not surprising that its abundance drops off rapidly as soon as other attractive primary decomposition modes become available to the molecular ion. The presently studied substances do

not shed any light on the importance of the aromatic nucleus with respect to the occurrence of the rearrangement step, but other studies[22] have shown that considerable latitude is available in this regard.

Preparation of Deuterium-Labeled Compounds.—A description of the synthesis of deuterium-labeled trimethylsilyl ethers needs to cover only the preparations of the parent alcohols because in practically all cases the trimethylsilyl derivatives were generated from the parent alcohol, amine, or sulfide utilizing hexamethyldisilazane as the reagent.[7,23] The one exception to this method involved attempts to silate N-methyl- (XXXIV) and N-ethylbenzylamine (XXXV). Owning to the high degree of substitution of the benzylic nitrogen, these endeavors were unsuccessful when either hexamethyldisilazane or N-(trimethylsilyl)acetamide[24] was employed as the silating agent. Silation was finally accomplished using the recently developed silylating agent, bis(trimethylsilyl)acetamide (XXXIX),[25] which is reported to be much more powerful in silyl donor strength than either hexamethyldisilazane or N-(trimethylsilyl)acetamide. Unfortunately, the yields in this reaction were low: 27% in the case of N-methylbenzylamine and 22% in the case of N-ethylbenzylamine.

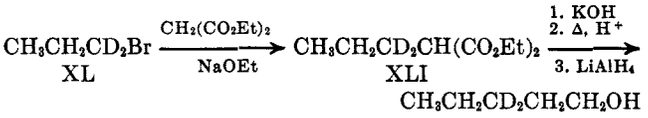


XXXIX

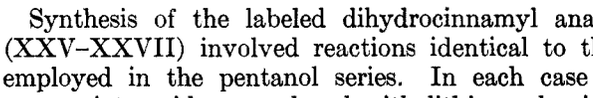
The primary intention of the deuterium-labeling experiments was to synthesize two series of compounds: a series (III–VIII) in which each position of the pentan-1-ol carbon chain is labeled, and a series (XXV–XXVII) in which each position of the propyl chain of dihydrocinnamyl alcohol is labeled.

Synthesis of the pentan-1-ol analogs (III–VIII) was successful from the standpoint of relatively high isotopic purity but occasionally suffered from mediocre yields due to the low molecular weight and high volatility of many of the precursors. Synthesis of the desired deuterated pentanols has been previously described,[10,26] but it was found that higher yields were achieved by revision of various steps in the previous syntheses.

Lithium aluminum deuteride reduction[10] of valeric acid yielded 1,1-d_2-pentan-1-ol in high yield. Reduction of butyric acid with lithium aluminum deuteride likewise gave 1,1-d_2-butan-1-ol, which was easily converted to its bromide. Preparation of 2,2-d_2-valeric acid *via* a Grignard carbonation of 1,1-d_2-butyl bromide was accomplished and the labeled acid was subsequently reduced with lithium aluminum hydride to yield 2,2-d_2-pentan-1-ol. Synthesis of 1,1-d_2-propan-1-ol was achieved by lithium aluminum deuteride reduction of propionic acid; the propyl bromide analog (XL) then underwent a diethyl malonate condensation to give the diester (XLI). Subsequent hydrolysis, decarboxylation, and reduction of XLI yielded 3,3-d_2-pentan-1-ol.



Utilizing a combination of the previously described diethyl malonate condensation and Grignard carbonation, 1,1-d_2-ethyl bromide was converted into 4,4-pentan-1-ol. Synthesis of 5,5-d_2-5-bromopentyl methyl ether (XLII) had been completed in connection with other research in our laboratory;[27] the reaction of this compound (XLII) with lithium aluminum deuteride yielded 5,5,5-d_3-pentyl methyl ether, which was cleaved with hydrogen iodide to give the final pentan-1-ol labeled analog, 5,5,5-d_3-pentan-1-ol.



Synthesis of the labeled dihydrocinnamyl analogs (XXV–XXVII) involved reactions identical to those employed in the pentanol series. In each case the appropriate acid was reduced with lithium aluminum deuteride and elaboration of the labeled alcohols involved a diethyl malonate condensation (in the case of XXVII) or a Grignard carbonation (in the case of XXVI) in order to obtain the propyl carbon chain.

Two other miscellaneous deuterium-labeled compounds were prepared in connection with this work. Exchange of the α-hydrogens of pentan-2-one under acid conditions[28] (so as to avoid base-catalyzed, self-condensation products) yielded 1,1,1,3,3-d_5-pentan-2-one, which was reduced to 1,1,1,3,3-d_5-pentan-2-ol, the parent alcohol of the labeled compound (IX). The final deuterium-labeled analog to be discussed is *p*-d_3-methoxybenzyl trimethylsilyl ether (XIX). Reaction of *p*-hydroxybenzyl alcohol with equimolar amounts of d_3-methyl iodide and potassium carbonate in acetone followed by hexamethyldisilazane silation yielded the desired derivative in high yield.

Experimental Section[29]

Trimethylsilyl Ethers and Amines.[9,23]—A mixture of 1.0 mmole of the appropriate alcohol or amine and 0.5 mmole of hexamethyldisilazane[30] was heated under reflux with 1 drop of trimethylsilyl chloride[30] until evolution of ammonia ceased (1–4 hr for primary and secondary alcohols; 12–20 hr for tertiary alcohols and for the amines). The trimethylsilyl derivatives were isolated from the reaction mixture by preparative gas–liquid partition chromatography; Table VI indicates the retention time and column temperature for each derivative. In most cases the yields of the colorless liquids were essentially quantitative. In each case the accurate molecular weight was

(22) Unpublished data.

(23) S. H. Langer, S. Connell, and I. Wender, *J. Org. Chem.*, **23**, 50 (1958).

(24) L. Birkofer, A. Ritter, and F. Bentz, *Chem. Ber.*, **97**, 2196 (1964).

(25) J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Am. Chem. Soc.*, **88**, 3390 (1966).

(26) A. M. Duffield, R. Beugelmans, H. Budzikiewicz, D. A. Lightner, D. H. Williams, and C. Djerassi, *ibid.*, **87**, 805 (1965).

(27) M. M. Green, unpublished observation.

(28) J. Seibl and T. Gaümann, *Helv. Chim. Acta*, **46**, 2857 (1963).

(29) Melting points (uncorrected) were determined on the Kofler block and the infrared absorption spectra were measured with a Perkin-Elmer Model 137 Infracord spectrophotometer. The mass spectra of most of the compounds discussed in this paper were recorded by Mr. N. S. Garcia on a CEC model 21-103C instrument at 70 ev using a 200° heated, all-glass inlet system. In addition, the spectra of many of the compounds were measured by Dr. J. K. MacLeod at 70 ev on an Atlas CH-4 mass spectrometer with an ion-source temperature of 190°; all 15-ev spectra were recorded on this instrument. High resolution measurements and also low resolution spectra of many of the compounds were carried out by Mr. R. G. Ross using an A.E.I. MS-9 instrument. All of the compounds were prepared on a small scale and purified by gas chromatography on a 6 ft × 0.75 in. stainless steel column packed with 10% GE SF-96 on Chromosorb W with a He flow rate of 250 cc/min.

(30) Hexamethyldisilazane, trimethylchlorosilane, triethylchlorosilane, and bis(trimethylsilyl)acetamide were purchased from Pierce Chemical Co., Rockford, Ill.

TABLE VI

RETENTION TIMES OF TRIMETHYLSILYL AND TRIETHYLSILYL ETHER DERIVATIVES

Compd[a]	Column temp, °C	Retention time, min
$CH_3(CH_2)_3CH_2OTMS$ (II)	85	3.0
$CH_3CH(OTMS)CH_2CH_2CH_3$ (VIII)	70	6.5
$C_6H_5CH_2OTMS$ (XII)	125	2.6
p-$(CH_3)_2NC_6H_4CH_2OTMS$ (XIV)	250	5.1
p-$O_2NC_6H_4CH_2OTMS$ (XV)	240	4.2
p-$FC_6H_4CH_2OTMS$ (XVI)	190	3.4
p-$ClC_6H_4CH_2OTMS$ (XVII)	200	2.9
p-$CH_3OC_6H_4CH_2OTMS$ (XVIII)	205	7.2
$C_6H_5CH(CH_3)OTMS$ (XIX)	176	4.4
$C_6H_5C(CH_3)_2OTMS$ (XXI)	175	5.9
$(C_6H_5)_2CHOTMS$ (XXII)	250	4.2
$C_6H_5CH_2CH_2OTMS$ (XXIII)	167	8.0
$C_6H_5CH_2CH_2CH_2OTMS$ (XXIV)	145	2.8
$C_6H_5CH_2NHTMS$ (XXX)	130	3.6
$C_6H_5CH(CH_3)NHTMS$ (XXXI)	140	1.4
$C_6H_5CH_2CH_2NHTMS$ (XXXII)	135	3.0
$C_6H_5CH_2CH(CH_3)NHTMS$ (XXXIII)	140	2.5
$C_6H_5CH_2N(CH_3)TMS$ (XXXIV)	130	7.2
$C_6H_5CH_2N(C_2H_5)TMS$ (XXXV)	132	5.9
$C_6H_5CH_2STMS$ (XXXVI)	180	4.2
$C_6H_5CH_2CH_2STMS$ (XXXVII)	200	2.0
$C_6H_5CH_2OC(CH_3)_3$ (XXXVIII)	135	1.2
$CH_3(CH_2)_3CH_2OSi(C_2H_5)_3$ (X)	71	4.9
$C_6H_5CH_2CH_2OSi(C_2H_5)_3$ (XXVIII)	182	2.8
$C_6H_5CH_2CH_2CH_2OSi(C_2H_5)_3$ (XXIX)	170	7.1

[a] TMS = $-Si(CH_3)_3$.

determined by mass spectroscopy to assure identity of the product.

N-Methyl-N-(trimethylsilyl)benzylamine (XXXIV).—In 3 ml of acetonitrile, 228 mg of N-methyl benzylamine and 450 mg of bis(trimethylsilyl)acetamide (XXXIX)[25] were heated under reflux for 4 hr and the trimethylsilyl derivative was isolated in 27% yield by preparative gas–liquid partition chromatography (see Table VI). The infrared spectrum indicated typical trimethylsilyl absorptions: λ_{max} 8.1, 11.9 and 13.4 μ (Me_3–Si).

Anal. Calcd for $C_{11}H_{19}NSi$: mol wt, 193. Found: mol wt, (mass spectroscopy), 193.

N-Ethyl-N-(trimethylsilyl)benzylamine (XXXV).—A procedure identical to that utilized in the N-methyl-N-(trimethylsilyl)-benzylamine (XXXIV) case was employed. Using 242 mg of N-ethyl benzylamine, a 22% yield of the trimethylsilyl derivative was obtained.

Anal. Calcd for $C_{12}H_{21}NSi$: mol wt, 207. Found: mol wt, (mass spectroscopy), 207.

Triethylsilyl Ethers (X, XXVIII, and XXIX).—To 2 mmoles of the appropriate alcohol in 10 ml of dry benzene, was added 50 mg of sodium metal. The mixture was heated gently under reflux for 15 hr and cooled, and a solution of 305 mg of triethylchlorosilane[30] in 5 ml of dry benzene was added dropwise. The mixture was again gently heated under reflux for 15 hr, cooled, and filtered, and the benzene removed by means of a rotary evaporator. Isolation by gas–liquid partition chromatography (Table VI) gave the desired triethylsilyl derivatives in 50–70% yields; in each case the mass spectrometrically determined molecular weight verified the identity of the product.

Trimethylsilyl Sulfides (XXXVI and XXXVII).—Sulfide derivatives were prepared by treatment of the sodium salt of the appropriate thiol with trimethylchlorosilane[30] according to the procedure of Langer, *et al.*[23] Isolation of the product was achieved by gas–liquid partition chromatography (Table VI), and in each case the mass spectrometrically determined molecular weight verified the identity of the compound.

Benzyl *t*-Butyl Ether (XXXVIII).—This benzyl ether derivative was prepared according to Frisell and Lawesson[31] and isolated by gas–liquid partition chromatography (Table VI).

1,1-d_2-Pentan-1-ol.—Reduction of valeric acid with lithium aluminum deuteride according to previously published procedures[10,26] yielded the desired labeled analog in 89% yield. The mass spectrum indicated 100% (d_2) deuterium incorporation.

2,2-d_2-Pentan-1-ol.—Reduction of 500 mg of butyric acid with lithium aluminum deuteride according to the procedure used in the 1,1-d_2-pentan-1-ol synthesis yielded an ethereal solution of 1,1-d_2-butan-1-ol. The ether was evaporated on a rotary evaporator and the resulting alcohol was heated on a steam bath with 1 ml of 48% hydrobromic acid and 0.2 ml of concentrated sulfuric acid in a sealed tube for 24 hr. The tube was cooled in an ice bath and then opened, and the mixture was washed twice with water. A clear liquid was distilled from the water through Indicating Drierite using a short-path distillation apparatus operating at reduced (aspirator) pressure. Preparative gas–liquid partition chromatography on a 6 ft × 0.75 in. stainless steel column packed with 15% Carbowax on Chromosorb W with a He flow rate of 100 cc/min yielded 655 mg of 1,1-d_2-butyl bromide.

Under extremely anhydrous conditions and utilizing a system ordinarily used for C^{13} labeling,[32] the butyl bromide underwent a Grignard carbonation with 213 mg of highly purified[32] magnesium and a large excess of carbon dioxide to yield 414 mg of 2,2-d_2-valeric acid after isolation by gas–liquid partition chromatography (using the previously described 10% GE SF-96 column). Reduction of 2,2-d_2-valeric acid to 2,2-d_2-pentan-1-ol was accomplished using conditions identical with those used in the preparation of 1,1-d_2-pentan-1-ol except that lithium aluminum deuteride was replaced with lithium aluminum hydride. This procedure yielded 339 mg of 2,2-d_2-pentan-1-ol, whose mass spectrum indicated the following isotopic composition: 98% d_2, 2% d_1.

3,3-d_2-Pentan-1-ol.—Reduction of 500 mg of propionic acid with lithium aluminum deuteride followed by conversion of the resulting alcohol to 631 mg of 1,1-d_2-propyl bromide was accomplished by procedures discussed above.

In a nitrogen atmosphere, 128 mg of sodium metal was dissolved in 8.0 ml of absolute ethanol and the mixture allowed to stir until it cooled to room temperature; 886 mg (0.84 ml) of diethyl malonate was added dropwise to the mixture, followed by the dropwise addition of the 1,1-d_2-propyl bromide. The reaction mixture was heated gently under reflux for 2 hr and then stirred at room temperature an additional hour. The ethanol was distilled from the reaction mixture and 840 mg of potassium hydroxide, dissolved in 0.84 ml of water, was slowly added. The mixture was again heated under reflux for 2 hr, diluted with 1 ml of water, and the remaining ethanol was distilled from the mixture until the reaction temperature reached 100°. After cooling the mixture in an ice bath, 0.84 ml of concentrated sulfuric acid in 2.1 ml of water was added and the reaction heated overnight. After a twofold extraction with ether, drying over anhydrous magnesium sulfate, filtering, and stripping the ether on a rotary evaporator, 388 mg of 3,3-d_2-valeric acid was isolated by preparative gas–liquid partition chromatography according to the conditions used for 2,2-d_2-valeric acid. Reduction of the labeled valeric acid with lithium aluminum hydride yielded 298 mg of 3,3-d_2-pentan-1-ol whose mass spectrum showed the following isotopic composition: 91% d_2 and 9% d_1.

4,4-d_2-Pentan-1-ol.—Using previously described reactions, 750 mg of acetic acid was reduced with lithium aluminum deuteride, and the resulting 1,1-d_2-ethanol, after purification on a spinning band distillation column, was converted to 1,1-d_2-ethyl bromide. A malonic ester condensation of the labeled ethyl bromide yielded 3,3-d_2-butyric acid which was reduced with lithium aluminum hydride to 3,3-d_2-butan-1-ol. Conversion of this alcohol to its bromide, followed by a Grignard carbonation and further reduction with lithium aluminum hydride yielded 492 mg of 4,4-d_2-pentan-1-ol whose mass spectrum showed the isotopic composition to be 100% d_2.

5,5,5-d_3-Pentan-1-ol Trimethylsilyl Ether.—In a dry nitrogen atmosphere, 210 mg of lithium aluminum deuteride was added to 25 ml of ether (freshly dried over sodium wire). To the resulting slurry was added 173.5 mg of 5,5-d_2-5-bromopentyl methyl ether[27] and the mixture was heated under reflux for 24 hr. Excess lithium aluminum deuteride was decomposed with saturated sodium sulfate, and the mixture was filtered and dried over anhydrous magnesium sulfate. The mixture was again filtered and most of the solvent was removed by careful distillation (6 hr) through a 15-cm Vigreux column. Purification by gas–liquid partition chromatography on a 15% Carbowax

(31) C. Frisell and S.-O. Lawesson, *Org. Syn.*, **41**, 91 (1961).

(32) J. Trudell and C. Djerassi, to be published.

column (20°, 70 cc/min) yielded 62.1 mg of 5,5,5-d_3-pentyl methyl ether. The labeled pentyl methyl ether was placed with an excess of anhydrous hydrogen iodide in a 1-ml sealed tube and allowed to stand for 24 hr at 0°. Due to the small amount of product, the reaction mixture was refluxed with an excess (0.5 ml) of hexamethyldisilazane and one drop of chlorotrimethylsilane until no more ammonia was evolved. The 5,5,5-d_3-pentan-1-ol trimethylsilyl ether was collected by gas–liquid partition chromatography (10% GE SF-96 column) and the mass spectrum revealed the following isotopic composition: 87% d_3, 7% d_2, 6% d_1.

1,1-d_2-Dihydrocinnamyl Alcohol.—Reduction of 100 mg of dihydrocinnamic acid with lithium aluminum deuteride yielded 85.0 mg of 1,1-d_2-dihydrocinnamyl alcohol whose mass spectrum revealed an isotopic composition of 100% d_2.

2,2-d_2-Dihydrocinnamyl Alcohol.—Using the above-described procedures, 2.3 g of phenylacetic acid was reduced with lithium aluminum deuteride and the resulting 1,1-d_2-β-phenylethanol converted to its bromide. The bromide was subjected to a Grignard carbonation, followed by a lithium aluminum hydride reduction to yield 697 mg of 2,2-d_2-dihydrocinnamyl alcohol whose mass spectrum revealed an isotopic composition of 100% d_2.

3,3-d_2-Dihydrocinnamyl Alcohol.—Reduction of 500 mg of benzoic acid with lithium aluminum deuteride and conversion of the resulting 1,1-d_2-benzyl alcohol to its bromide were carried out by previously described procedures. A malonic ester condensation, followed by hydrolysis, decarboxylation, and reduction with lithium aluminum hydride yielded 339 mg of 3,3-d_2-dihydrocinnamyl alcohol whose mass spectrum indicated the following isotopic composition: 98% d_2, 2% d_0.

1,1,1,3,3-d_5-Pentan-2-ol.—Utilizing a procedure similar to that of Seibl and Gaümann,[28] pentan-2-one was exchanged under acid-catalyzed conditions. Preparation of the labeled acid catalyst was accomplished by slowly dissolving 4.0 g of dry phosphorus pentachloride in 16 ml of deuterium oxide in a nitrogen atmosphere. The solution was then diluted with another 16 ml of deuterium oxide and stored in a tightly stoppered flask.

A mixture of 1.0 g of pentan-2-one and 10 ml of 10% deuteriophosphoric acid in deuteriochloric acid solution was heated under reflux for 12 hr. Extraction with deuterium oxide washed ether was followed by neutralization of the combined aqueous–ethereal layers with potassium carbonate. After extracting three more times with ether, the solvent was stripped on a rotary evaporator. The exchange procedure was repeated three more times and the final ethereal extract dried over anhydrous magnesium sulfate. After filtration, a lithium aluminum hydride reduction of the ethereal solution yielded 247 mg of 1,1,1,3,3-d_5-pentan-2-ol whose mass spectrum indicated the following isotopic composition: 73% d_5, 24% d_4, 2% d_3 and 1% d_2.

p-d_3-Methoxybenzyl Alcohol.—In 5 ml of acetone was placed 270 mg of p-hydroxybenzyl alcohol and 276 mg of potassium carbonate. To the mixture 284 mg (0.14 ml) of d_3-methyl iodide was rapidly added and the mixture heated under reflux for 8 hr using a Dry Ice condenser. The solution was cooled, diluted with 5 ml of water, and extracted twice with ether. The ethereal extracts were washed twice with water and dried over anhydrous magnesium sulfate. Filtration followed by evaporation of the ether on a rotary evaporator yielded 267 mg of p-d_3-methoxybenzyl alcohol whose mass spectrum showed the isotopic composition to be 100% d_3.

Registry No.—II, 14629-45-9; III, 14629-46-0; IV, 14629-47-1; V, 14629-48-2; VI, 14629-49-3; VII, 14629-50-6; VIII, 1825-67-8; IX, 14629-51-7; X, 14629-52-8; XII, 14642-79-6; XIII, 14629-53-9; XIV, 14629-54-0; XV, 14856-73-6; XVI, 14629-55-1; XVII, 14856-74-7; XVIII, 14629-56-2; XIX, 14856-75-8; XXI, 14629-57-3; XXII, 14629-59-5; XXIII, 14629-58-4; XXIV, 14629-60-8; XXV, 14856-76-9; XXVI, 14629-61-9; XXVII, 14856-77-0; XXVIII, 14629-62-0; XXIX, 2290-40-6; XXX, 14856-79-2; XXXI, 14629-63-1; XXXII, 10433-33-7; XXXIII, 14629-65-3; XXXIV, 14884-70-9; XXXV, 14629-66-4; XXXVI, 14629-67-5; XXXVII, 14856-80-5; XXXVIII, 3459-80-1; 2,2-d_2-pentan-1-ol, 14856-81-6; 3,3-d_2-pentan-1-ol, 14629-68-6; 4,4-d_2-pentan-1-ol, 14629-69-7; 1,1,1,3,3-d_5-pentan-2-ol, 14629-70-0; p-d_3-methoxybenzyl alcohol, 14629-71-1.

Control of Lithium Aluminum Hydride Reduction of Cyclic Dicarboxylic Acid Anhydrides to Produce γ-Lactones or Diols[1]

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The reduction of *cis*- and *trans*-1-methylcyclohex-4-ene-1,2-dicarboxylic acid anhydride, **1** and **3**, and of their saturated derivatives, **5** and **7**, by lithium aluminum hydride in tetrahydrofuran at −55° produced γ-lactones with reduction at the more hindered carbonyl as the sole product in yields of 89, 75, 78–82, and 85%, respectively. Similar treatment of methyl and phenyl succinic anhydride, **14** and **15**, produced mixtures of lactones in 69 and 72% yields. Five other symmetrical anhydrides also gave lactones in 70–80% yields. A mechanism involving 1,4-hydride addition is invoked to account for the high stereoselectivity observed in these reductions. Diols are produced in excellent yield when anhydrides are reduced with excess lithium aluminum hydride in refluxing tetrahydrofuran.

The reduction of mono- or dicarboxylic acid anhydrides by lithium aluminum hydride has been very infrequently used for the production of alcohols.[3] If a cyclic anhydride is reduced, the expected product is a diol. Our main interest in this area has been in the synthesis of 1,4-diols as intermediates in a broader program.[4–6] When reductions were carried out in diethyl ether, besides the expected diol, a frequently encountered product was a γ-lactone. This result is annoying when diols are desired, but there is a precedent for it.[3b,7,8]

Our interest in developing a lactone synthesis, without concurrent formation of diol, was spurred by several

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