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MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS—CLVIII* ELECTRON IMPACT PROMOTED FRAGMENTATION OF TRIPHENYLMETHYL ETHERS†

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Abstract—The triphenylmethyl (trityl) moiety is frequently used for the protection of alcohols but the mass spectra of such trityl ethers have hitherto escaped scrutiny. It has now been found that triphenylmethyl derivatives of primary alcohols yield abundant molecular ions which permit the determination of the isotopic purity of the parent alcohol. Upon electron impact the triphenylmethyl entity directs the fragmentation of trityl ethers as demonstrated by a detailed study of *n*-pentyl trityl ether and its deuterated analogs. Ions formed by migration of phenyl groups were observed in the mass spectra of the trityl ethers investigated as well as in the spectrum of triphenylmethane itself.

TRIPHENYLMETHYL ether (trityl) derivatives of alcohols have been widely used in organic chemistry for the protection of hydroxylic functions present in sugars,[1] nucleosides[5] and nucleotides[2] because of their crystalline nature, base stability and facile removal under acidic conditions.

Quantitative calculations of the isotopic purity of alcohols is often made extremely difficult due to the absence or low intensity of the molecular ion peak of these compounds.[3] Several derivatives of alcohols, notably N-methylaminobenzoates[4] and phenyl urethanes yield strong molecular ion peaks while in other derivatives fragment ions (M $-$ NO of 3,5-dinitrobenzoates,[5] M $-$ CH_3 of trimethylsilyl ethers[6] and acetonides[7] and M $-$ C_6H_5NCO of bis-phenylurethanes §) may be used for molecular weight determination and the calculation of isotopic composition (D or ^{18}O) of alcohols. We now wish to report that the mass spectra (Figs. 1–4) of triphenylmethyl ethers of 1-propanol (I), 1-butanol (II), *n*-pentanol (III) and 1-heptanol (IV) contain molecular ions of appreciable intensity and are thus suitable for the determination of molecular weights and isotopic purity, in marked contrast to the spectra of the parent alcohols. This result prompted us to examine the mass spectra of triphenylmethyl ether derivatives of primary alcohols using deuterium labeling techniques to clarify the origin of the fragments observed.

Discussion of mass spectra. The mass spectra of the triphenylmethyl derivatives of *n*-propanol (I), 1-butanol (II), 1-pentanol (III) and 1-heptanol (IV) are reproduced in Figs. 1–4. Each contains a molecular ion of appreciable intensity and an abundant

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* For part CLVII see O. Buchardt, A. M. Duffield and C. Djerassi, *Acta Chem. Scand.*, submitted for publication.

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‡ Visiting Investigator from the East-West Center, University of Hawaii.

§ J. Seibl (E. T. H, Zürich), private communication.

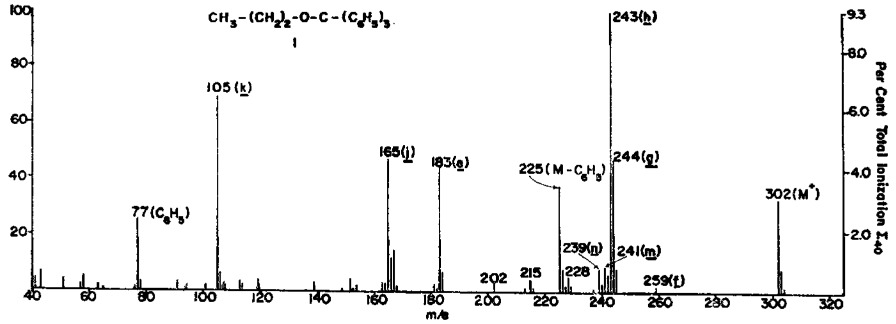


FIG. 1. Mass spectrum (70 eV) of *n*-propyltriphenylmethyl ether.

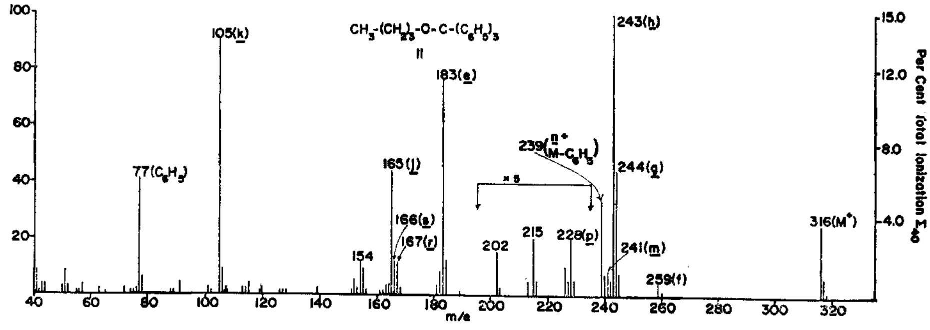


FIG. 2. Mass spectrum (70 eV) of *n*-butyltriphenylmethyl ether.

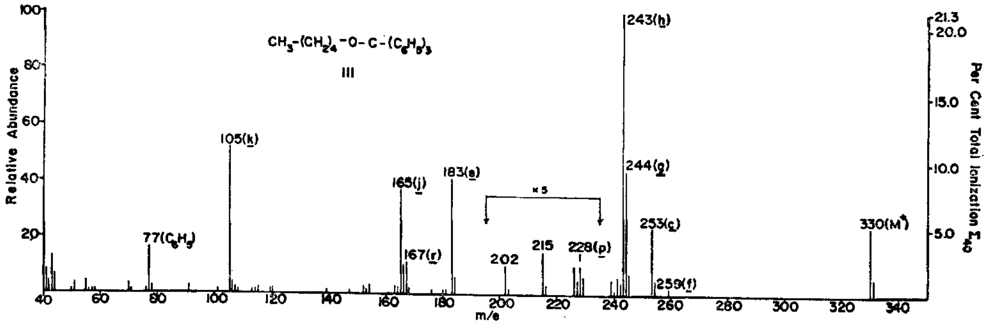


FIG. 3a. Mass spectrum (70 eV) of *n*-phenyltriphenylmethyl ether.

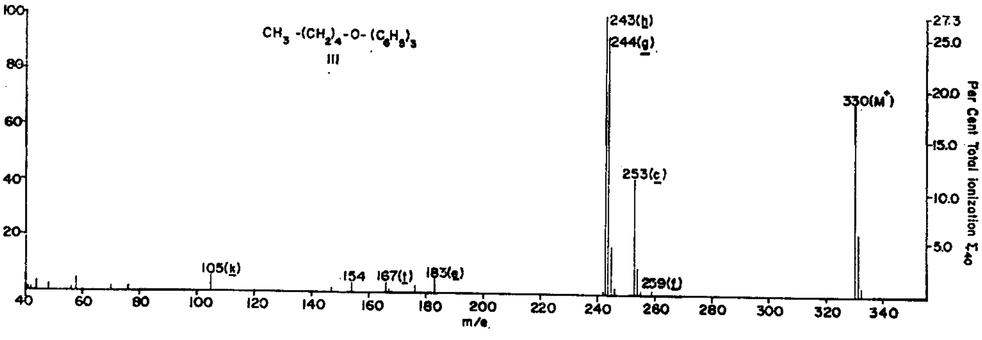


FIG. 3b. Mass spectrum (12 eV) of *n*-pentyltriphenylmethyl ether.

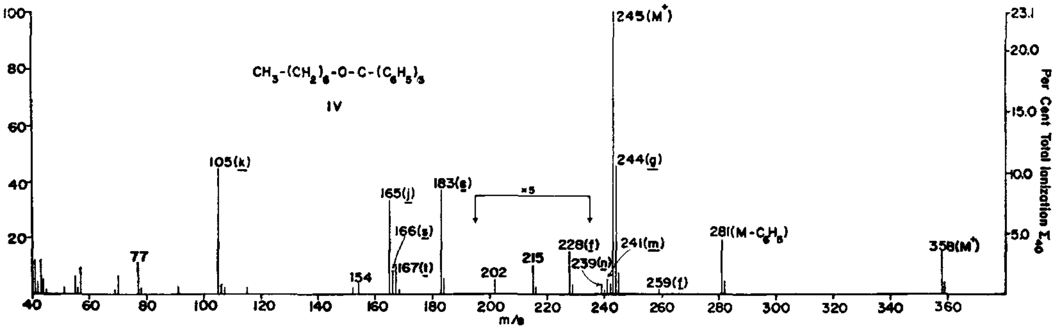


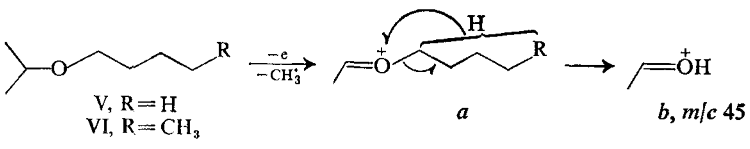
FIG. 4. Mass spectrum (70 eV) of *n*-heptyltriphenylmethyl ether.

peak due to the elimination of a phenyl radical from the parent ion. Both of these peaks increase at low voltage (see Fig. 3b) and are suitable for the calculation of the isotopic purity of the parent alcohols.

$$CH_3—(CH_2)_n—O—C—(C_6H_5)_3$$

$$\text{I}, n = 2$$
$$\text{II}, n = 3$$
$$\text{III}, n = 4$$
$$\text{IV}, n = 6$$

The behavior of aliphatic ethers subsequent to electron impact has been extensively investigated and many of the fundamental processes have been elucidated.[8,9] Much of our present knowledge was gained from a study employing extensive isotopic labeling of two typical aliphatic ethers *iso*-propyl *n*-butyl and *iso*-propyl *n*-pentyl ether (V and VI).[10] A favored decomposition mode of aliphatic ethers is α-cleavage (V and VI → *a*),* the product *a* of which then eliminates the alkyl chain less one hydrogen atom with the formation of *b*. In the case of V and VI the site of the itinerant hydrogen atom was demonstrated to involve to a significant degree all the carbon atoms of the alkyl chain.[10] In our study of the mass spectra of triphenylmethyl ethers of primary alcohols we have labeled the alkyl chain of *n*-pentyl trityl ether (III) in order to determine the site specificity of the hydrogen rearrangement processes occurring in this class of compounds and to compare it with that of typical dialkyl ethers.[8]



V, R=H
VI, R=CH3

a

b, *m/e* 45

An important high-mass fragment ion in the spectra (Figs. 1–4) of the *n*-alkyl trityl ethers (I–IV) is due to the loss of a phenyl radical from the molecular ion and for the pentyl homolog this can be rationalized by III → *c*, *m/e* 253.† A most striking observation is the complete absence at both 70 and 12 eV (Figs. 1–4) of the

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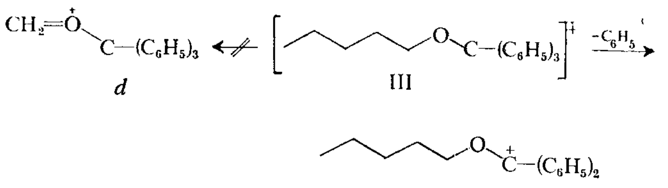
* The alternative α-cleavage process, loss of C_3H_7 and C_4H_9 from V and VI is observed in equal abundance, although the species a predominates at low ionizing voltage (15 eV).[14]

† This fragment may well exist either partially or completely as a tropylium species.

corresponding α-cleavage product *d*, (M − C_4H_9 in the case of III). Although the larger alkyl group is invariably eliminated at 70 eV in the α-cleavage fragmentation of dialkyl ethers, provided identical degrees of substitution are present on the respective α carbon atoms, this is not the situation at low ionizing voltages.[11] In the case of trityl ethers the complete preference for elimination of a phenyl, as compared to a primary alkyl radical, may be attributed to greater resonance stabilization of *c* relative to *d*. In addition one would expect a considerable proportion of the molecular ion to bear the positive charge in the aromatic rings in which case loss of a phenyl radical would correspond to the energetically favored rupture of a benzylic bond. One of the characteristic features of the mass spectra of trityl ethers is the dominant role of the triphenylmethyl moiety in the fragmentation processes since this group controls the mode of fission of these compounds to a remarkable degree. This represents compelling evidence for charge localization principally within the trityl group of these ethers.

An ion of substantial abundance is found at mass 183 in the spectra (Figs. 1–4) of all the *n*-alkyl trityl ethers (I–IV) examined. A metastable ion in the spectrum of



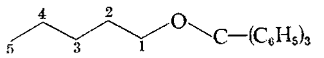
d

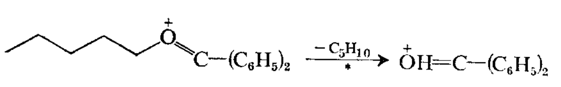
III

c, *m*/*e* 253

the *n*-pentyl homolog established that at least a portion of the ion yield at mass 183 arose from a decomposition of the species *c* by expulsion of the alkyl group less one hydrogen atom (*e*, *m*/*e* 183). This process is thus analogous to the decomposition *a* → *b* previously studied[10] in *iso*propyl *n*-alkyl ethers. Deuterium transfer in the deuterated derivatives of III (Table 1) established that no specific carbon atom was associated with this hydrogen transfer process, thus being in agreement with the results previously encountered with *iso*propyl *n*-alkyl ethers.[10]

TABLE 1. SPECIFICITY OF HYDROGEN TRANSFER IN REARRANGEMENT ION FORMATION IN *n*-PENTYL TRIPHENYLMETHYL ETHER (III).

Compound 	Isotopic Purity	*m*/*e* 183 (*e*) % transfer	*m*/*e* 244 (*g*) % transfer
1,1-d_2	98% d_2	12%	70%
2,2-d_2	95% d_2	20%	10%
3,3-d_2	98% d_2	21%	10%
4,4-d_2	95% d_2	14%	10%



c

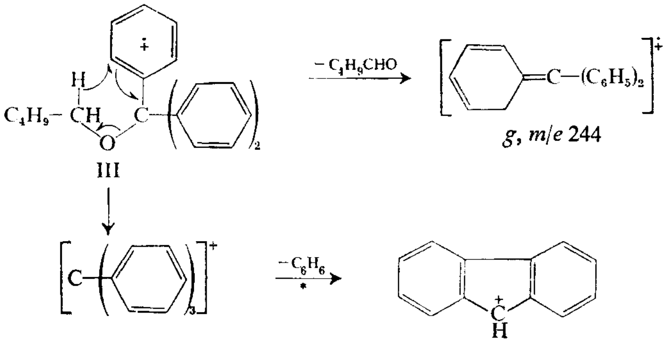
e, *m*/*e* 183

In view of the large percentage (33%—Table 1) of hydrogen whose origin was undetected by deuterium labeling for the process $c \rightarrow e$ it is likely, since the primary carbon atoms (C-5) would not be expected to contribute the entire amount nor would such a large isotope effect[12] discriminating against deuterium transfer be anticipated, that a second mode of formation exists for the species *e*. One such possibility would be the elimination of benzyne from *f*(*m*/*e* 259), the species associated with the loss of the complete alkyl chain from the molecular ion of all the *n*-alkyl trityl ethers investigated. No metastable ion could be found to substantiate this hypothesis which would, however, explain the large amount of hydrogen undetected by deuterium labeling for the process $c \rightarrow e$, *m*/*e* 183.

$$[R—O—C—(C_6H_5)_3]^{+\cdot} \xrightarrow{-R\cdot} [\dot{O}—C—(C_6H_5)_3]^{+\cdot} \xrightarrow{-C_6H_4} H\overset{+}{O}=C—(C_6H_5)_2$$

III, R = *n*-C_5H_{11} *f*, *m*/*e* 259 *e*, *m*/*e* 183

The base peak (100% relative abundance) in all the *n*-alkyl trityl ether spectra (Figs. 1–4) examined occurs at *m*/*e* 243 and can be ascribed to the species *h*,* the product formed by the loss of an alkoxy radical from the molecular ion. The ion of mass 244 corresponds to *h* plus an additional hydrogen atom from the alkyl chain. The principal donor of hydrogen in this rearrangement process for the *n*-pentyl homolog III is C-1 of the alkyl chain (Table 1) with smaller but equal contributions from C-2, C-3 and C-4. The following rationalization invoking hydrogen transfer from C-1 through a six-membered intermediate to the *ortho* position of a benzene ring is thus consistent with the origin of 70% of the ion current at mass 244 in the spectrum (Fig. 3a) of the *n*-pentyl analog III.



III

g, *m*/*e* 244

h, *m*/*e* 234

j, *m*/*e* 165

A metastable ion in the mass spectra (Figs. 1–4) of the *n*-alkyl trityl ethers I–IV demonstrated that at least some of the ion current at mass 165 arose from the elimination of benzene from the fragment *h*, *m*/*e* 243 and a stable representation for this species is the cation *j*, *m*/*e* 165. The two weaker adjacent peaks at *m*/*e* 166 and 167 may have their genesis by the loss of a phenyl radical from *h* and *g* respectively.

The prominent ion of mass 105 occurs in all the spectra (Figs. 1–4) of the *n*-alkyl trityl ethers (I–IV) investigated but this fragment is less abundant at low (12 eV,

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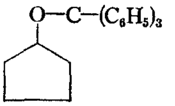
* This fragment may well exist either partially or completely as a tropylium species.

see Fig. 3b) ionizing voltages. The occurrence of an intense peak at mass 77 and a metastable ion correlating it with the elimination of 28 mass units from the ion of mass 105 suggests evidence for the latter species being assigned the benzoyl structure (*k*, *m/e* 105) in view of the ubiquitous decomposition 105 → 77 present in all mass spectra containing the benzoyl cation. Furthermore, the ion of mass 105 is itself derived, at least in part, by the loss of 78 mass units from *e* (*m/e* 183) since the appropriate metastable ion was recognized.

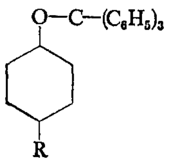
$$H\overset{+}{O}{=}C{-}(C_6H_5)_2 \xrightarrow[*]{-C_6H_6} C_6H_5{-}C{\equiv}\overset{+}{O} \xrightarrow[*]{-CO} C_6H_5^+$$

e, *m/e* 183 *k*, *m/e* 105 *m/e* 77

The mass spectra (Figs. 5, 6 and 7) of cyclopentanol, cyclohexanol and 4-methylcyclohexanol trimethylphenyl ethers (VII, VIII and IX) display a close resemblance to the spectra (Figs. 1–4) of the *n*-alkyl trityl ethers examined. Thus all the principal ions in the cyclanol derivatives studied arise from charge retention within the triphenylmethyl moiety and their origin would be similar to those presented for compounds I–IV. However, the molecular ion and [M − C_6H_5] peaks in the cycloalkanol trityl ether spectra are considerably weaker as compared to the *n*-alkyl derivatives; nevertheless they should be suitable for the calculation of isotopic composition provided high recorder sensitivities are employed.



VII



VIII, R = H
IX, R = CH_3

The peak at *m/e* 183 in the mass spectra (Figs. 5–7) of cycloalkyl trityl ethers is again associated with ion *e* and has the origin as depicted above (*c* → *e*) for this ion in the mass spectrum (Fig. 3a) of *n*-pentyl trityl ether III. In the case of IX, deuterium labeling (4-methylcyclohexyl-2,2,6,6-d_4 trityl ether) indicated that 55% of the hydrogen transferred in this decomposition arose from C-2 and C-6 of the ring.

In conjunction with our study of the fragmentation of triphenylmethyl ethers we have subjected *n*-pentyl and *n*-hexyl triphenylmethyl thioethers X and XI to mass spectral scrutiny (see for instance Fig. 8). In these latter compounds no molecular ion was visible, the fragments of highest mass being the ions *g* (*m/e* 244) and *h* (*m/e* 243). The only other species of abundance greater than 10% is that of mass 165 (*j*) while the alkyl chains of X and XI are responsible for the low abundance ions of mass 70, 71 and 84, 85 respectively. It is also noteworthy that no carbon-sulfur bond fission with charge retention on sulfur occurs in the spectra of the two trityl thioethers studied or in tetrahydropyranyl thioethers[13] in marked contrast to the behavior of alkyl thioethers.[14]

Benzyl and *p*-methoxyphenyl triyl ethers (XII and XIII) lack a molecular ion peak in their mass spectra (see Fig. 9 for the spectrum of XII). The instability of the

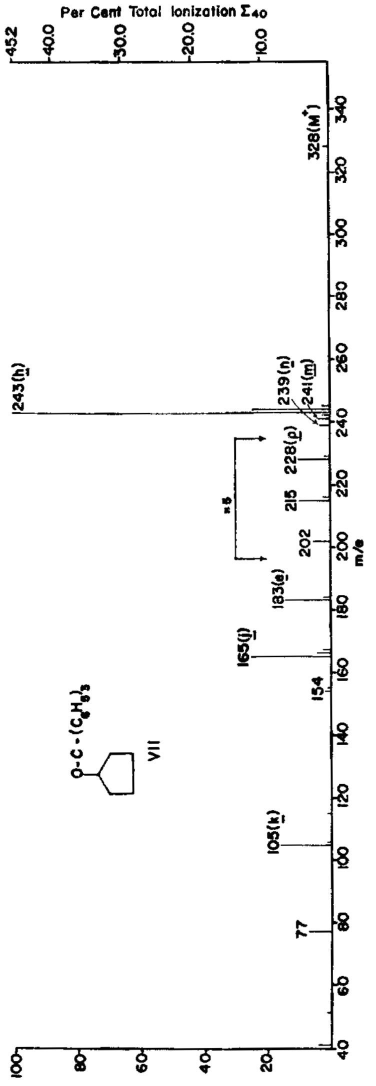


FIG. 5. Mass spectrum (70 eV) of cyclopentyltriphenylmethyl ether.

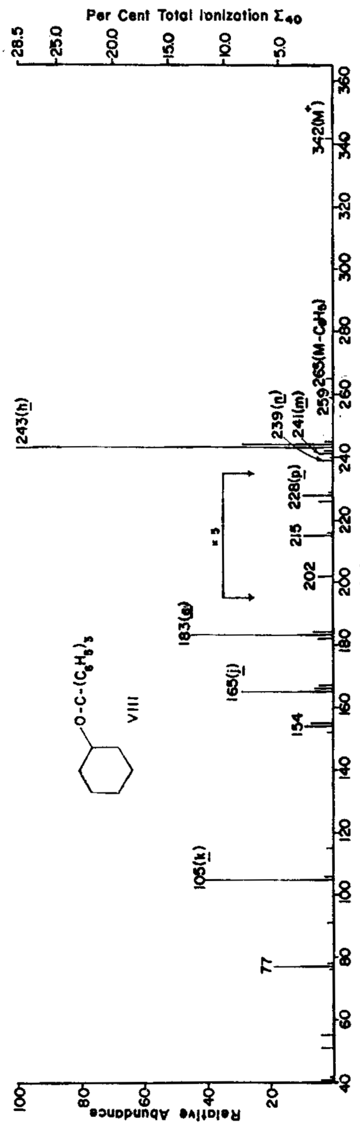


FIG. 6. Mass spectrum (70 eV) of cyclohexyltriphenylmethyl ether.

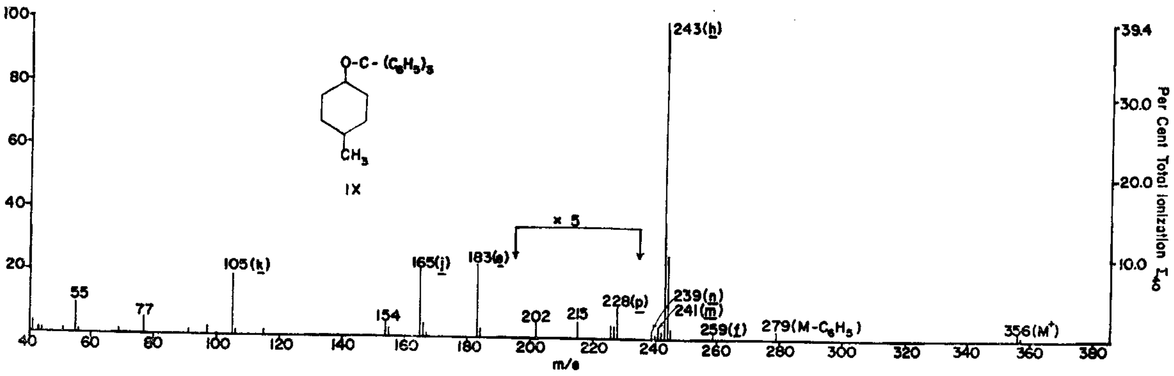


FIG. 7. Mass spectrum (70 eV) of 4-methylcyclohexyl triphenylmethyl ether.

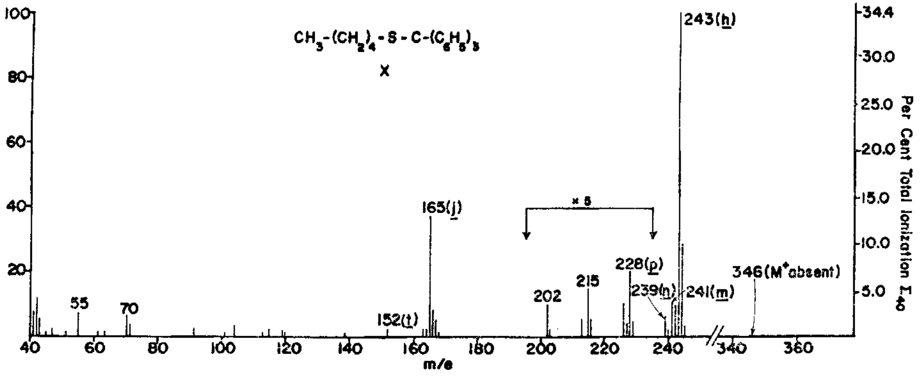


FIG. 8. Mass spectrum (70 eV) of *n*-pentyltriphenylmethyl thioether.

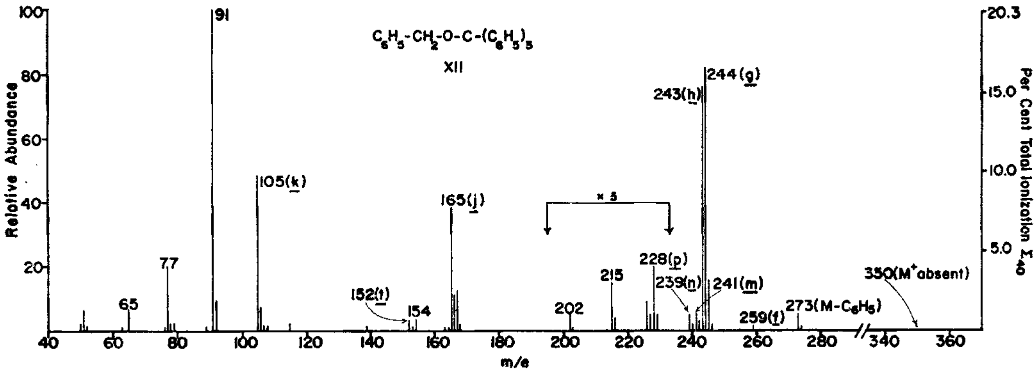
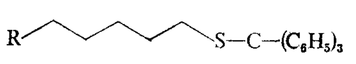
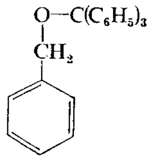


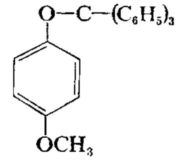
FIG. 9. Mass spectrum (70 eV) of benzyltriphenylmethyl ether.



X, R = H
XI, R = CH3



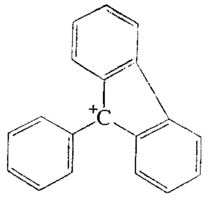
XII



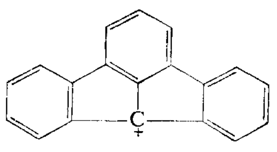
XIII

molecular ion of the trityl ethers and thioethers (X–XIII), in contrast to the situation existing in the *n*-alkyl trityl ethers (I–IV; VII–IX) studied, can be rationalized by the more facile elimination of a thioalkyl, benzyl and *p*-methoxyphenyl radical (X–XIII) than an alkoxyl radical (I–IV; VII–IX).

A series of low-abundance but mechanistically interesting peaks (see for instance *m/e* 229, 215 and 202) occur in the mass spectra (Figs. 1–9) of all the trityl ethers and thioethers examined and these ions must arise from the common triphenylmethyl group. The mass spectrum (Fig. 10) of triphenylmethane (XIV) is dominated by the molecular ion peak (*m/e* 244) while a relatively abundant [M − 1] species is also present. An interesting feature of the mass spectrum of XIV is the elimination of from one to five hydrogen atoms from the molecular ion—an observation made also in the spectra (Figs. 1–9) of the trityl ethers studied. The two most abundant ions of this group, excluding the [M − 1] species h, are of mass 241 and 239 and can be represented by *m* and *n* respectively.



m, *m/e* 241



n, *m/e* 239

Loss of a methyl radical from the molecular ion of triphenylmethane (XIV) can be rationalized by the following sequence while the odd electron species of mass 228

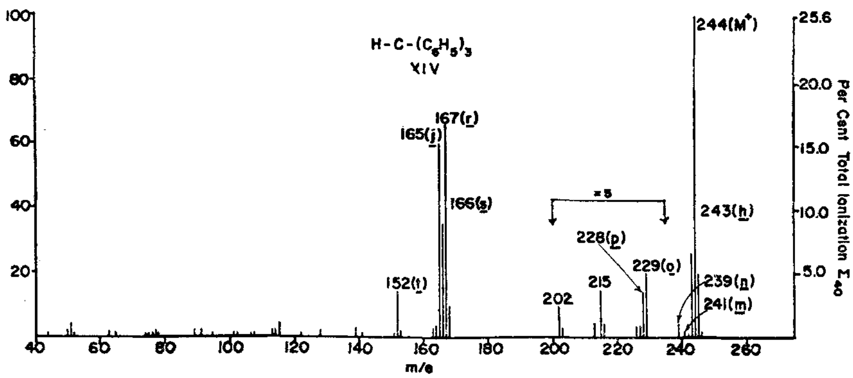
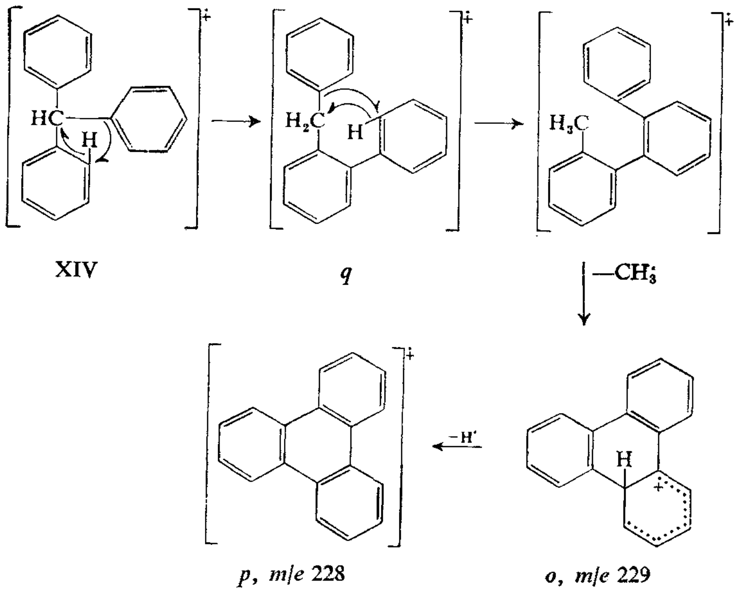


Fig. 10. Mass spectrum (70 eV) of triphenylmethane.

could be generated from the further loss from *o* of a hydrogen atom. It is pertinent to note that the intermediate *q* is a substituted diphenylmethane and this class of compound is known[15] to undergo loss of a methyl radical upon electron impact. The mass spectrum of tri-(phenyl-2,4,6-d_3) methane* indicated that the deuterium atoms were eliminated (*m/e* 229 located in 75% yield at *m/e* 236) in this rearrangement process thus offering support for the presented origin for the species *o*.



XIV

q

p, *m/e* 228

o, *m/e* 229

The subsequent elimination of acetylene from *m* (*m/e* 241) and from *p* (*m/e* 228) would rationalize the formation of the fragments of mass 215 and 202 in the spectrum (Fig. 10) of triphenylmethane (XIV).

The prominent peak at *m/e* 167 in the mass spectrum (Fig. 10) of triphenylmethane (XIV) arises by the elimination of a phenyl radical from the molecular ion and can be

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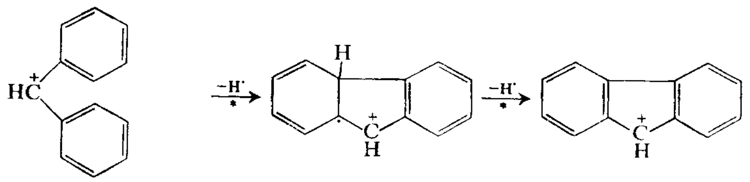
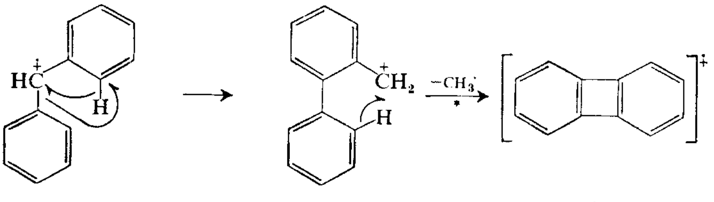
* We thank Mr T. M. Cole of Stanford University for providing us with this compound.

ascribed structure *r* (*m*/*e* 167).* It is pertinent to note that while this ion is found in the spectra of all the trityl ethers examined (Figs. 1–9), it is usually much less intense. The ion of mass 165 (*j*) has been completely erased from the mass spectrum (Fig. 10) of XIV at 12 eV (*m*/*e* 166 and 167 = 1% relative abundance respectively) while using 20 eV electrons it attained 5% relative abundance (*m*/*e* 166 = 13% and 167 = 27%). The ions of mass 166 and 165 are derived from multiple pathways as shown by recognition of metastable ions. Thus both arise by the respective loss of benzene from the molecular ion and from the [M − 1] species (*h*) of XIV. A second mode of origin is by the loss of a hydrogen atom from *r* (*m*/*e* 167) generating *s* (*m*/*e* 166) which in turn ejects a second hydrogen atom to yield *j* (*m*/*e* 165).



r, *m*/*e* 167 *s*, *m*/*e* 166 *j*, *m*/*e* 165

The ion of mass 152 in the spectrum (Fig. 10) of triphenylmethane is generated, at least in part, by the loss of a methyl radical from *r* (*m*/*e* 167) and formally its genesis is analogous to that of *o* (*m*/*e* 229). The biphenylene ion *t* (*m*/*e* 152) may be a convenient formulation.



r, *m*/*e* 167 *t*, *m*/*e* 152

A peak of low intensity at *m*/*e* 154 is found in the mass spectra of all the trityl ethers investigated. This fragment must correspond to ionized biphenyl and it is interesting that it is absent from the spectrum (Fig. 10) of triphenylmethane (XIV) itself.

EXPERIMENTAL

Low resolution spectra were obtained with an A.E.I. MS 9 mass spectrometer using direct sample insertion into the ion source whose temperature was 165°. Low voltage refers to nominal eV values only. Triphenylmethane was obtained from Aldrich Chemical Co., Milwaukee, Wis.

n-Alkyl triphenylmethyl ethers and thioethers (I–IV, VII–XI). These compounds were prepared by a general method[16] as follows: Triphenylmethyl chloride (0.5 g, 1.8 mmole) was added to a solution of the required alcohol or mercaptan (5 mmoles) in anhydrous pyridine (2 ml). The reaction mixture was warmed to 70° for a few minutes, allowed to stand at room temperature for 72 hr and then poured onto ice. Extraction with ether followed by washing the organic phase with 0.1 N hydrochloric acid, saturated sodium carbonate, water and drying over sodium sulfate yielded the crude triphenylmethyl ether derivatives. Those compounds which were solids were recrystallized to constant m.p. (see Table 2) while the remainder were purified by preparative thin-layer chromatography over silica gel H.F. using cyclohexane or cyclohexane:ether (99:1) as developer.

Benzyl and p-methoxyphenyl triphenylmethyl ethers (XII and XIII). Triphenylmethyl chloride and an excess of the alcohol were heated in pyridine solution at 100° for 3–4 hr and then the reaction

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* This fragment may well exist either partially or completely as a tropylium species.

TABLE 2. MELTING POINTS OF TRIPHENYLMETHYL ETHER EXAMINED

Compound	m.p.[a]
I	54°
II	33.5°
III	oil[b]
IV	oil[b]
VII	61.5°
VIII	103°
IX	133–134°
X	78°
XI	55.5–56°
XII	105°
XIII	91°

[a] Recrystallized to constant m.p.
[b] Purified by preparative T.L.C.

mixture allowed to stand at room temperature for 72 hr. The products were processed as above and recrystallized to constant m.p.

Deuterated n-pentyl triphenylmethyl ethers. These compounds were prepared from the deuterated pentanols[17] by the general method described above and purified by preparative thin-layer chromatography. Their isotopic purity is listed in Table 1. (p. 254)

4-*Methylcyclohexyl*-2,2,6,6,-d_4 *triphenylmethyl ether.* 4-Methylcyclohexanone was exchanged twice in deuterium oxide containing NaOD to yield the 2,2,6,6,-d_4 analog (>95% d_4, mass spectrometry). Lithium aluminum hydride reduction in ether solution yielded 4-methyl-cyclohexanol-2,2,6,6-d_4 which was converted into the corresponding trityl ether by the general method[17] outlined above.

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