in melting point with the nondeuterated analog XXII described in Table III.

2α-Bromocholestan-7β-ol-3-one[24] was converted into 1α-d_1-cholestan-7β-ol-3-one by standard chemical procedures.[25]

1α-d_1-Cholestan-7-one Ethylene Ketal (XXV).—1α-d_1-Cholestan-7β-ol-3-one (145 mg.) in triethylene glycol (4 ml.), *n*-butyl alcohol (1.5 ml.), and 95% anhydrous hydrazine (1 ml.) was heated under reflux for 2 hr. After cooling the mixture, potassium hydroxide (0.5 g.) was added. Solvent was then removed by distillation until the temperature of the solution reached 200°. Heating was continued for 4 hr. at 200–210°, after which time the organic material was isolated in the conventional manner. The crude product (121 mg.) in acetone (3 cc.) was treated with a slight excess (10%) of 8 *N* chromic acid solution.[26] This solution was diluted with water and ether, and the ether phase washed twice with water, dried, and evaporated. The residue (110 mg.) so obtained was crystallized from methanol affording 1α-d_1-cholestan-7-one (75 mg.), m.p. 117–118°. This material was converted to 1α-d_1-cholestan-7-one ethylene ketal (XXV), m.p. 122–123°, by the standard method outlined above. The unlabeled ethylene ketal XXIV derived directly from cholestan-7-one had an identical melting point.

(24) We wish to thank Dr. T. Nakano (University of Kyoto) for a generous gift of this material. We are also indebted to Syntex S.A., Mexico City, for samples of compounds V and XIII and to Dr. S. Bernstein and L. H. Sarett for samples of the cortisone derivatives XX and XXI.

(25) See, for example, D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2091 (1963).

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

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STEVENS INSTITUTE OF TECHNOLOGY, HOBOKEN, N. J.]

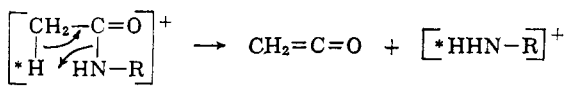
Mass Spectral Studies. III. Fragmentation of Aromatic Amides[1]

BY K. G. DAS, PHILLIP T. FUNKE, AND AJAY K. BOSE

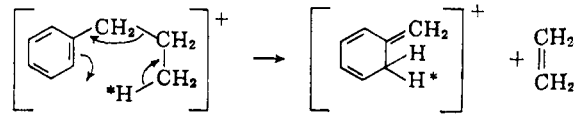
RECEIVED MARCH 18, 1964

A study of the mass spectra of several aromatic amides, their deuterated forms, and analogs has been made. The major fragmentation in N,N-diphenylphenylacetamide (Ia) and analogs involves the transfer of a proton from the acyl group to the nitrogen. In diphenylacetanilide (IIa) and analogs the base peak is formed by the transfer of a proton from the nitrogen to the acyl group. Deuteration studies and direct comparison with the spectra of diphenylamine and diphenylmethane indicate that a four-membered ring transition state is favored over a six-membered one. Carbazole and fluorene seem to be possible intermediates in the stepwise fragmentation of Ia and IIa. A simple cleavage of the type (>C–C(=O)–N–) was observed in aromatic amides when stable carbonium ions are formed as a result of this cleavage. A new type of rearrangement involving the migration of an aryl group from nitrogen to the carbon atom α to the carbonyl group was noticed in the spectrum of N,N-diphenylphenylacetamide (Ia) and its analogs. Dideuteration was observed to reduce markedly the aryl migration caused by deuterium isotope effect. No migration of an aryl group from carbon to nitrogen was observed in the spectrum of diphenylacetanilide (IIa) and its analogs.

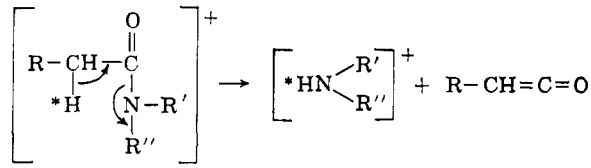
The mass spectral fragmentation patterns for a variety of aliphatic amides have been discussed recently.[2] Lately it has been shown[3] by deuteration studies that one of the major fragmentation modes in aliphatic amides is the transfer[4] of a proton from the acyl group to the amino nitrogen. We present here our findings on aromatic amides.



N,N-Diphenylphenylacetamide and Its Analogs (Fig. 1 and 2).—As expected from the analogy with aliphatic amides, we observed the fragments formed by the scission of the amide bond and from the transfer of a proton from the acyl group to the amine fragment. The latter fragment gave the base peak in the spectra of N,N-diphenylphenylacetamide, its deuterated form,[4] and analogs (such as Ib and Ic). The metastable peak at *m/e* 100.5 supports this rearrangement (calcd. 100.2 for *m/e* 298 → *m/e* 169). In aliphatic amides this proton transfer can take place only through a four-membered ring transition state as shown by Djerassi.[3] But McLafferty[5] has shown, also by deuteration studies, that a six-membered ring transition state and the transfer of a proton to the phenyl group are involved in rearrangements of the type



We can write a four-membered ring transition state and/or a six-membered ring transition state to explain the proton transfer in the amide Ia.



Ia, R = R′ = R″ = C_6H_5 (metastable peak at 100.5; calcd. 100.2 for *m/e* 287 → 169)

b, R = *p*-tolyl, R′ = R″ = C_6H_5 (metastable peak at 95.5; calcd. 94.9 for *m/e* 301 → 169)

c, R = C_6H_5, R′ = R″ = *p*-tolyl (metastable peak at 124; calcd. 123.2 for *m/e* 315 → 197)

(1) Part II: P. Funke, K. G. Das, and A. K. Bose, *J. Am. Chem. Soc.*, **86**, 2527 (1964).

(2) J. A. Gilpin, *Anal. Chem.*, **31**, 935 (1959); see also F. W. McLafferty, *ibid.*, **28**, 306 (1956).

(3) Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2470 (1963).

(4) Protons exchangeable with deuterium are marked with an asterisk.

(5) F. W. McLafferty, "Mass Spectrometry of Organic Ions," Academic Press, Inc., New York, N. Y., 1963, p. 337; see also K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 122–124.

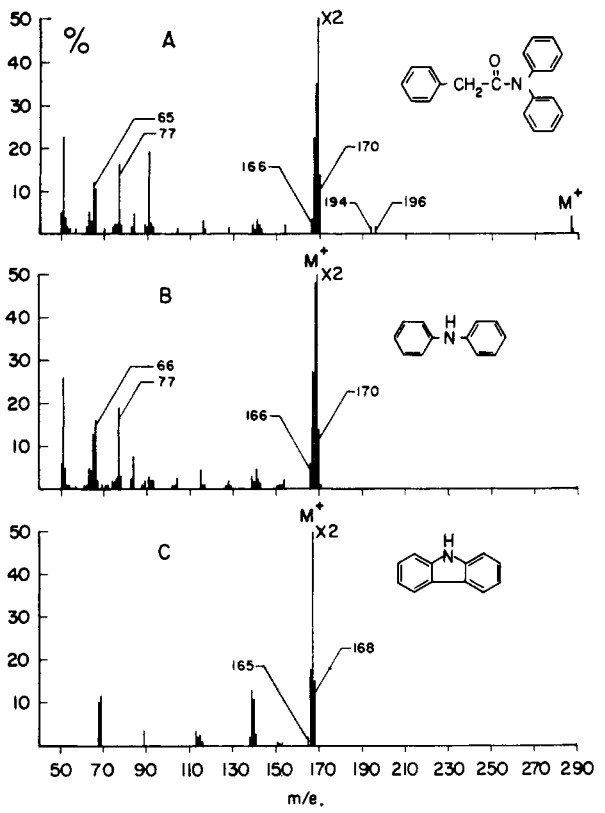
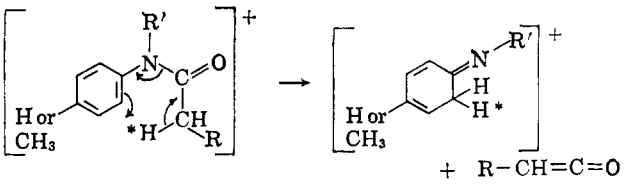


Fig. 1.—Mass spectra of: A, N,N-diphenylphenylacetamide; B, diphenylamine; C, carbazole.

and/or



The proton transfer involving a four-centered transition state would give diphenylamine; that involving a six-centered transition state would give an isomer of diphenylamine as one of the primary intermediates in the fragmentation of Ia. The deuterated form and analogs Ia and Ib would give deuterated diphenylamine and its analogs. A comparison of the spectra (see Table I) of diphenylamine and its N-deuterated forms with the spectra of both the N,N-diphenylphenylacetamide (Ia) and its deuterated form showed very close similarity.

TABLE I

m/e	Diphenylamine	N,N-Diphenylphenylacetamide	Diphenylamine (50% monodeuterated)	N,N-Diphenylphenylacetamide (70% dideuterated)
165	0.2	0.2	0.1	0.3
166	5.0	3.5	4.0	4.5
167	27.3	21.6	23.5	25.8
168	48.5	35.0	49.0	50.5
169	100.0	100.0	100.0	100.0
170	13.1	13.4	71.5	58.5
171	1.0	0.8	9.0	7.2
172	...	...	0.1	0.5

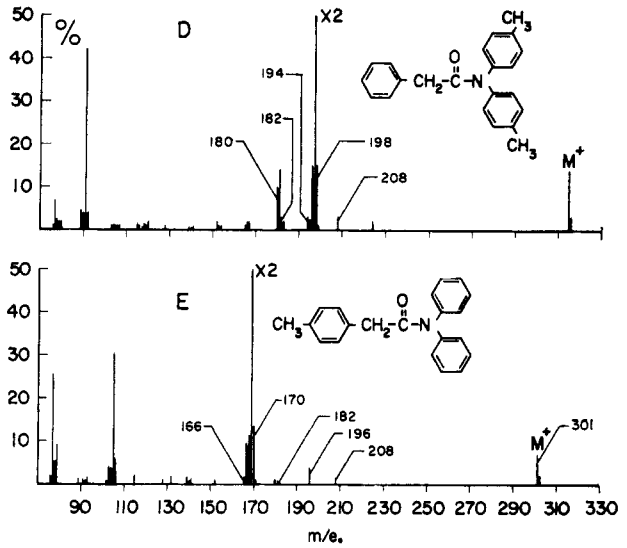
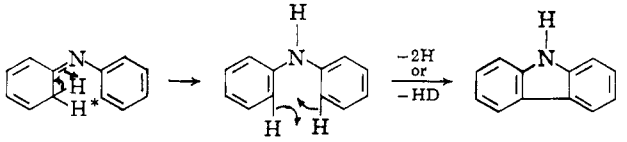


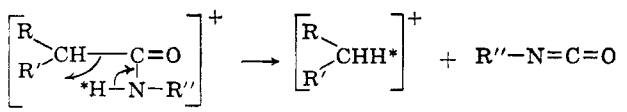
Fig. 2.—Mass spectra of: D, N,N-ditolylphenylacetamide; E, N,N-diphenyl-*p*-tolylacetamide.

All the peaks in the spectrum of carbazole were also found in the spectra of the amide and diphenylamine. This observation suggests the sequence amide Ia → diphenylamine → carbazole represents a possible route for the stepwise fragmentation of Ia. In support of such a route it can be cited[6] that on photolysis diphenylamine is converted to carbazole. On the basis of this evidence we favor a four-membered transition state over a six-membered transition state, although both may be operating simultaneously. In the case of the six-membered rearrangement a mechanism such as that postulated below might be possible. Another alternative is that both A and B can rearrange to some common ionic intermediate which is isomeric with carbazole C.



A B C

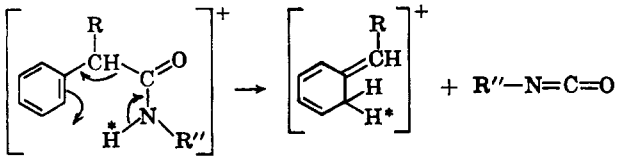
Diphenylacetanilide and Its Analogs (Fig. 3).—More definitive evidence for the four-centered mechanism was obtained from a study of the mass spectrum of diphenylacetanilide (IIa). The base peak in the spectrum of IIa can only be explained by a rearrangement involving a transfer of a proton from the nitrogen to the carbon adjacent to the carbonyl group. This was supported by the presence of a metastable peak at *m/e* 99.0 (calcd. 98.3 for *m/e* 287 → *m/e* 168). This type of proton transfer does not appear to have been noticed previously. Both a four-centered and/or a six-centered mechanism can be written to represent this rearrangement.



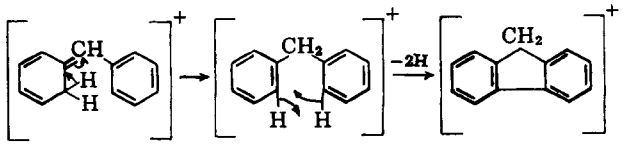
IIa, R = R′ = R″ = C_6H_5
b, R = R′ = *p*-tolyl, R″ = C_6H_5
c, R = R′ = C_6H_5, R″ = *p*-tolyl

(6) K. H. Grellmann, G. M. Sherman, and H. Linschitz, *J. Am. Chem. Soc.*, **85**, 1881 (1963).

and/or

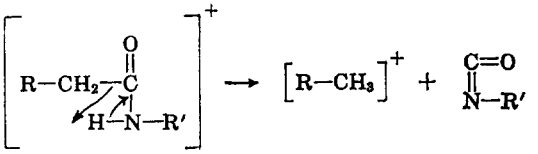


A comparison of the spectra (see Fig. 3) of the amide IIa with those of diphenylmethane and fluorene showed very close similarity indicating that the sequence the amide IIa → diphenylmethane → fluorene represents one of the routes for the stepwise fragmentation of the amide IIa. We favor a four-centered mechanism over a six-centered one in this case also, although both may be operating simultaneously. If a six-centered mechanism is in operation, the fragment D is rearranging to F. It is also possible that both D and E rearrange to some common ionic intermediate which is isomeric with fluorene F.



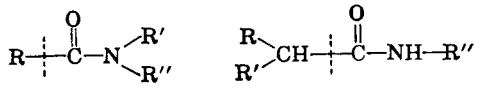
D E F

We have also observed this type of rearrangement involving the transfer of a proton from the nitrogen to the carbon α to the carbonyl group, in the following type of amide (III).



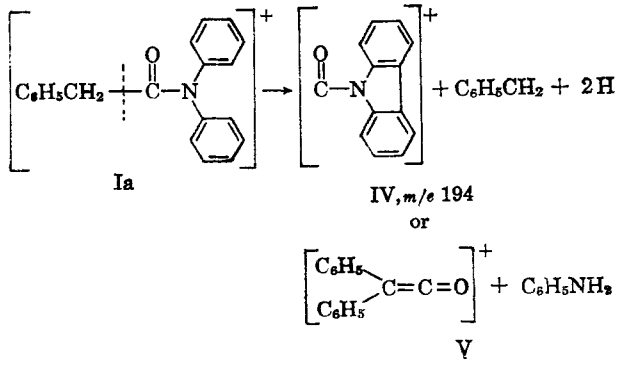
IIIa, R = H, R′ = C_6H_5
b, R = R′ = C_6H_5
c, R = benzyl, R′ = C_2H_5

In the aromatic amides of type I and II the scission of the carbon–carbonyl bond was observed to be a significant mode of fragmentation. This simple cleavage is presumably favored when very stable carbonium ions are formed as fragments. This mode of cleavage has been reported[2] before for aliphatic amides.



I II

The peak at *m/e* 194 in the spectrum of N,N-diphenylphenylacetamide (Ia) gave us a clue to a rearrangement not previously described which takes place under electron impact. It is possible to assign a carbazole type of structure IV to this fragment which can be formed by the loss of two protons from one of the simple cleavage products. We can also assign the diphenylketene structure V if we assume that a phenyl group has migrated from the nitrogen to the carbon atom α to the carbonyl group.



Ia IV, *m/e* 194

or

V

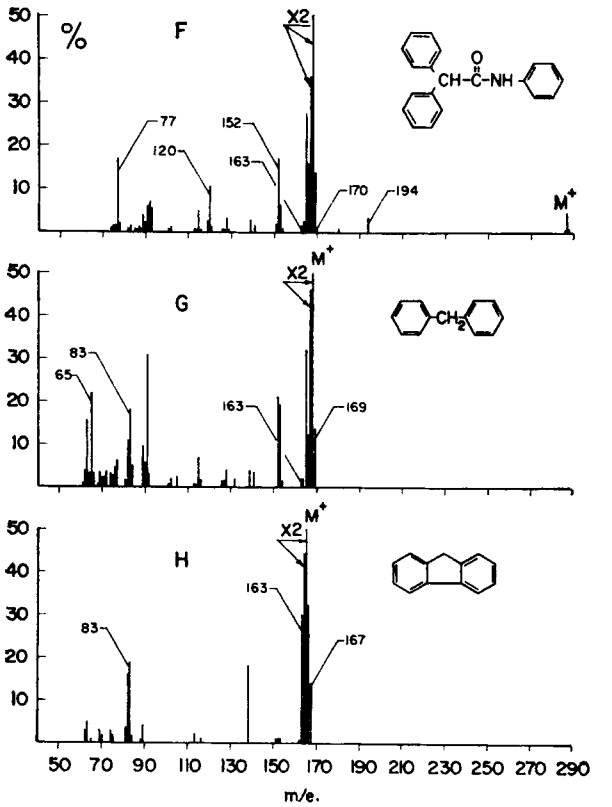


Fig. 3.—Mass spectra of: F, diphenylacetanilide; G, diphenylmethane; H, fluorene.

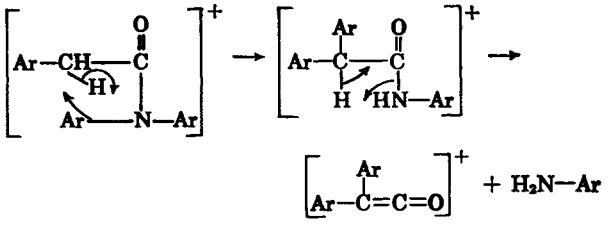
To get more information on this rearrangement the spectra of N,N-ditolylphenylacetamide (Ic) was examined. As expected for tolyl migration we observed a peak at *m/e* 208 and not at *m/e* 194 (see Fig. 2). If we assign a carbazole type of structure to this fragment then we have to make the unlikely assumption that it is formed as a result of a loss of one methyl group and one hydrogen atom from a simple cleavage product.

Definitive evidence for aryl migration was obtained in different ways. When the spectrum of N,N-diphenyl-*p*-tolylacetamide (Ib) was examined there was no peak at *m/e* 194, but we noticed a peak at *m/e* 208 (see Fig. 2). This was indeed expected for phenyl migration. This rearrangement was supported by a metastable peak at *m/e* 144 (calcd. 143.7 for *m/e* 301 → *m/e* 208). It is not possible to conceive how a carbazole type of structure could be assigned to this fragment.

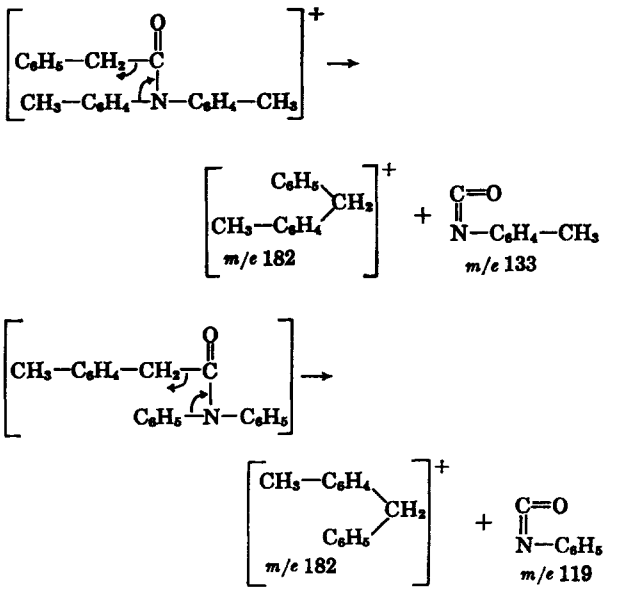
An indirect evidence for aryl migration was obtained by deuteration studies. In the spectrum of the dideuterated form of Ia the peak at *m/e* 194 was practically absent. It is very difficult to conceive how the incorporation of two deuterium atoms on the methylene group can prevent the formation of a carbazole type of structure. On the other hand, if aryl migration were the normal mode of rearrangement in the nondeu-

terated amide, then the deuterium isotope effect must have slowed down the aryl migration to a significant extent. Deuterium isotope effect in hydrogen rearrangement processes[7] and in reducing the rate of reactions is well known.

Significant peaks were observed at *m/e* 93 (C_6H_5–NH_2) and at *m/e* 107 (CH_3–C_6H_4–NH_2) in the mass spectra of N,N-diphenylphenylacetamide (Ia) and N,N-ditolylphenylacetamide (Ic), respectively. These fragments can only be formed by a double proton transfer from the methylene group to the nitrogen atom in two stages as shown below. Double proton transfers have been postulated before by other workers.[8] We propose the following mechanism for aryl migration and double proton transfer.



Another line of evidence for aryl migration is the identification of significant peaks at *m/e* 182 and 181 in the mass spectra of N,N-ditolylphenylacetamide (Ic) and N,N-diphenyl-*p*-tolylacetamide (Ib). These fragments must have been formed by the migration of *p*-tolyl and phenyl groups, respectively, from the nitrogen to carbon. No peaks corresponding to the fragments formed by the migration of an aryl group from



the carbon to nitrogen were observed in the mass spectra of the amides that were examined.

Experimental[9]

All the amides studied were prepared from the corresponding acid chlorides and amines in dry benzene solution. Their authenticity was established by comparison with the physical data cited in literature. The deuterated analogs of these amides were prepared by repeated equilibration of the amides in a 1:1 mixture of deuterated methanol and deuterated water with a trace of sodium methoxide. N-Deuterated diphenylacetanilide was prepared by first deuterating aniline and then treating it with diphenylacetyl chloride.

Acknowledgment.—This work was supported by a grant (MH-03930) from the U. S. Public Health Service.

(7) D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 284 (1964).

(8) See C. Beard, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *ibid.*, **86**, 269 (1964), and F. W. McLafferty and M. C. Hamming, *Chem. Ind.* (London), 1366 (1958).

(9) All mass spectra were obtained with a Consolidated Electrodynamic Corporation mass spectrometer Model No. 21-103C using an all-glass inlet system heated to temperatures well below the melting points of the samples. The ionizing energy was kept at 70 e.v. and the ionizing current at 50 μa.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA 4, PENNSYLVANIA]

Mass Spectral Mechanisms. Homoallylic Participation in Fragmentation of Butadiene–Maleic Anhydride Adduct[1]

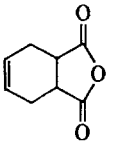
BY STEPHEN J. WEININGER,[2] VU THI MAI, AND EDWARD R. THORNTON

RECEIVED MARCH 14, 1964

The mechanistic path of the mass spectral fragmentation of 1,2,3,6-tetrahydrophthalic anhydride has been investigated by comparison with several model compounds, including the 3,3,6,6-tetradeuterated derivative. The fragmentation appears to derive some driving force from loss of CO from the molecular ion leading to a homoallylic carbonium ion.

The behavior of ions formed by electron bombardment promises to provide information about reactions of ions in the gas phase, for comparison with reactions of ions in solution. Also, structures which have not been identified in solution may easily be formed and studied under the high energy conditions of the mass spectrometer.

We have observed an unexpected fragmentation pattern in the mass spectrum of the Diels–Alder adduct, 1, of butadiene with maleic anhydride. This compound exhibits *no* molecular ion peak (M) and exhibits intense peaks at M − 28 (M − CO) and M −



1

73 (M − C_2O_3H)[3], using 76-v. electrons.

(1) Supported in part by a PHS research grant, GM 10693, from the National Institutes of Health, Public Health Service.

(2) Socony-Mobil Fellow, 1962–1964.

(3) Since it is confusing to list only masses, we include in parentheses probable assignments of the fragments. In many cases only one assignment is possible, but assignments are checked by isotopic natural abundance peak intensities wherever possible. In principle, all assignments could be made with certainty by using a double-focusing mass spectrometer.