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MASS SPECTRA OF BENZOFURANS

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Abstract—The mass spectra of a number of substituted benzofurans are reported. Ring fragmentation as opposed to substituent fragmentation was observed in halogenated benzofurans. Initial loss of carbon monoxide was found without any evidence for loss of formyl radical (HCO). Benzocyclopropenecarboxaldehyde is proposed as a possible intermediate ion. Hydrogen scrambling observed with deuterated substrates occurred in either the molecular ion, the carboxaldehyde radical ion or the CO elimination product, the benzocyclopropene radical ion. The chlorobenzofurans and, in part, bromobenzofuran fragmented by successive loss of CO and halogen atom. The bromobenzfuran molecular ion also showed the inverted sequence of initial loss of bromine followed by loss of CO. This process was examined by use of the spectra of nitro- and methoxy-benzofurans. Fluorobenzofurans showed little fluorine loss in the early stages of the fragmentation process.

RING systems commonly fragment with loss of neutral molecules on electron impact, especially in heterocyclic ring systems containing oxygen.[1,2] These processes are referred to generally as *expulsion reactions*.[3] Benzofurans on electron impact have been reported to expel either carbon monoxide to give ion **2a** (M—CO, *m/e* 90) or formyl radical to give ion **3** (M—CHO, *m/e* 89).[4,5] The ion fragment corresponding to loss of formyl radical has also been reported to form by consecutive loss of carbon monoxide (M—CO, *m/e* 90) and a hydrogen radical (M—CO—H, *m/e* 89).[6–9] Metastable peaks,[4,10] offered as support for combined loss of carbon monoxide and hydrogen radical (*m** 68·6), do not exclude direct loss of formyl radical (*m** 67·1) since their close proximity requires good resolution to adequately distinguish these already broad peaks.

Substituent fragmentation is a problem in attempting to examine ring collapse on electron impact. Almost all of the substituted benzofurans for which mass spectra are known[2–4,6,7,11] are compounds with structural features which permit ionization via routes which complicate direct ring fragmentation. Alkyl substituted benzofurans, for example, ionize almost exclusively to benzyl cations and their equivalent, substituted tropylium ions. This is true regardless of the substituent position whether on the benzene or furan ring.[5] Spectra of several alkylbenzofurans not heretofore reported illustrate this type of fragmentation (Table 1). Alkyl substituents also add complexity to these spectra by the possible interconversion of different ring systems. The similarity of the mass spectra of the two isomeric oxygen heterocycles, chrom-3-ene and 2-methylbenzofuran,[6] suggests a rapid interconversion to common ions.

Nitrobenzofuran is another example where the ring does not fragment but the nitro group attached to it breaks up by loss of NO or NO_2.[5] The spectra of methoxybenzofurans illustrate another non-ring fragmentation process. These spectra are in substantial agreement with the fragments of the M—CO ion in the spectrum of

TABLE 1. MASS SPECTRA OF ALKYLBENZOFURANS

Ion fragment	Methylbenzofuran isomer				Dimethylbenzofuran isomer				5-Ethyl-benzofuran*
	m/e	2-†	5-	6-	*m/e*	3,6-	2,6-	5,6-	
M^+‡	132	79	97	95	146	100	100	100	32
M—1	131	100	100	100	145	94	84	68	3
M—CH_3	121	—	—	—	131	24	20	90	100
M—CO	104	6	21	21	118	4	4	10	3
M—HCO	103	13	18	16	117	19	23	14	4
M—31	101	1	1	1	115	20	22	21	6
$C_7H_7^+$	91	—	—	—	91	14	18	14	4
$C_6H_6^+$	78	10	14	13	78	3	4	3	1
$C_6H_5^+$	77	17	24	25	77	7	10	11	11
$C_5H_3^+$	63	11	12	13	63	12	13	13	9
	51	22	32	30	51	14	17	21	10
$C_3H_3^+$	39	13	10	12	39	18	20	22	8

* *m/e* Values are identical with the dimethylbenzofurans.
† MCA Spectra No. 89.
‡ Molecular ion.

7-methoxycoumarin.[8,12] In these, methyl, formyl, or other fragments, which are either a substituent or a part of one, are lost initially. In all of these cases carbon monoxide or formyl radical from the ring is expelled only via a minor or secondary ionization route, except, of course, for benzofuran itself.

We have found in an extensive study of the mass spectral behavior of numerous simply substituted benzofurans that the ring system of some halogenated benzofurans, like benzofuran itself, fragments in the initial decomposition of the molecular ion. The results show these compounds lose carbon monoxide exclusively without any evidence for formyl radical loss.

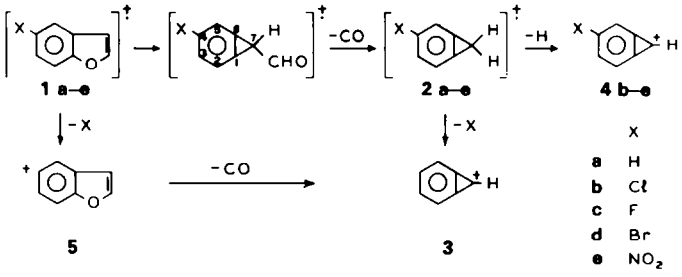
Deuterated benzofurans

The mass spectrum of benzofuran-2-d was examined in the hope that it could distinguish formyl vs. carbon monoxide loss. Its mass spectrum (Table 2) showed two major fragment peaks, one at *m/e* 91 (42%) and the other at *m/e* 90 (34%) consistent with monodeuterated ions **2a** and **3**,[6,13] respectively. These can both conceivably arise through the intermediate benzocyclopropenecarboxaldehyde radical ion. Such intermediates have been observed in the photochemical decarbonylation of furans.[14] If carbon monoxide were lost from the carboxaldehyde, or an equivalent ion, the deuterium would end up on position 7 in **2a**. But if formyl radical were lost the

TABLE 2. MASS SPECTRA OF DEUTERATED BENZOFURANS

m/e	120	119	118	92	91	90	89	65	64	63	62	40	39
Benzofuran	—	9	100	–	3	38	38	—	8	25	12	2	13
Benzofuran-2-d	20	100	2	7	42	35	10	6	18	21	11	6	13
Benzofuran-5-d	13	100	16	4	41	41	12	7	19	21	11	10	12

major fragment would probably be ion **3**, since deuterium would likely accompany the formyl radical because of its favored position in the parent ion and in the carboxaldehyde ion. The peak *m/e* 89 resulting from deuterium loss is only 10% of the base peak. Neither simple formyl radical loss or consecutive CO and hydrogen radical loss from the carboxaldehyde ion agree with this relatively small amount of deuterium loss.



The mass spectrum of benzofuran-5-d is very similar to that of the 2-d isomer. A small difference exists in the peak ratio *m/e* 89/*m/e* 90. This ratio is for 2-d, 0·28 and for 5-d, 0·30. Apparently hydrogen scrambling occurs, a phenomenon observed in other aromatic systems.[15] Scrambling occurs sometime after formation of **1a** and before a hydrogen atom is lost from **2a**. It could occur in **1a**, in the carboxaldehyde radical ion or in **2a**. The *m/e* 89 and 90 peak intensity ratio shows one deuterium atom is lost for every 4·5 hydrogen–deuterium atoms present although deuterium isotopes are distributed one out of every six in the reactant and in **2a**. Incomplete scrambling or an isotope effect leading to this particular deuterium distribution could occur to make the two deuterium labelled compounds equivalent. These data do not exclude the possibility of formyl radical loss.

Chloro- and fluorobenzofurans

Our data show halogenated benzofurans lose carbon monoxide and not a formyl radical. For some where hydrogen is not broken off in the fragmentation process the loss of formyl radical is excluded.

The base peak in the spectrum of chlorobenzofurans (Fig. 1) is the molecular ion. The carbon chlorine bond does not fragment to any extent since the abundance of ion *m/e* 117 is about the same as in the spectrum of benzofuran where a carbon hydrogen scission is necessary. Both 5- and 7-chlorobenzofuran molecular ions (**1b**) lose initially CO to give **2b**. Then a chlorine atom is lost to give *m/e* 89 (**3**). Ion **2b** is only 10% of the base peak, but the metastable peak *m/e* 101–103 agrees with the transition **1b** → **2b**. Another metastable peak *m/e* 63–64 agrees with the fragmentation of **2b** to give **3**. The alternative route loses a chlorine atom [**1b** → **5** (*m** 90·1)] which in turn loses CO [**5** → **3** (*m** 67·7)] is not supported by metastable peaks. The absence of a greater concentration of ion **5**, which from data below seems reasonably stable, opposes initial chlorine loss. A small metastable ion *m/e* 52 may correspond to simultaneous loss of carbon monoxide and chlorine or COCl radical.[16]

5,7-Dichlorobenzofuran also fragments by this scheme. The molecular ion **6**, which is the base peak, first loses carbon monoxide to give **7**. Then a chlorine atom is lost to give **4b**. Very little hydrogen is lost by **7** to give **8**.

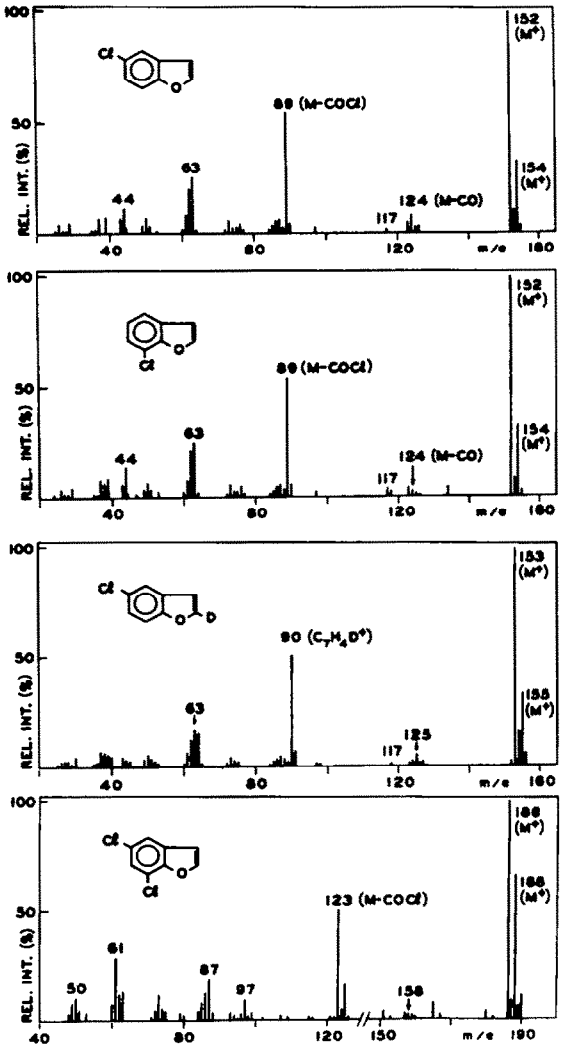
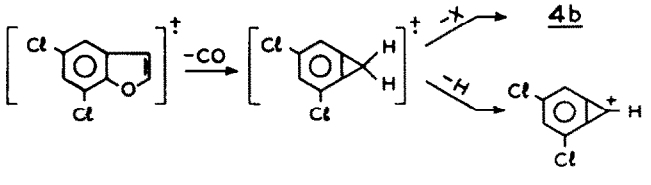


FIG. 1.

We can exclude for two reasons any scheme in which hydrogen could be lost in an early step, as in a formyl radical, and recovered in a later step. First, deuterium remains with the molecule throughout the process since 5-chlorobenzofuran-2-d fragments to *m/e* 90 without any significant *m/e* 89. Secondly, it is generally agreed



6 7 8

that intermolecular reactions are not considered in mass spectrometric mechanisms at such pressures.

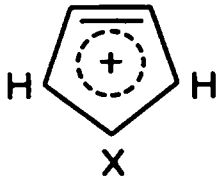
Benzofurans with very stable halogen carbon bonds, as in fluorobenzofurans fragment essentially as benzofuran itself (Table 3). Their molecular ions **1c** (4,5,6 and 7-fluorobenzofurans) lose carbon monoxide to give **2c** in the first step and then lose

TABLE 3. MASS SPECTRA OF FLUOROBENZOFURANS

m/e	Ion composition	Fluorine position			
		4	5	6	7
136	M^+	100·0	100·0	100·0	100·0
118	$(M—F)^+$	—	1·4	—	3·0
108	$(M—CO)^+$	41·4	44·8	48·4	29·5
107	$(M—HCO)^+$	45·8	44·8	51·9	46·4
89	$(M—COF)^+$	3·2	3·5	3·5	4·4
81	$C_5H_2F^+$	11·9	12·2	11·5	10·7
63	$C_5H_3^+$	8·7	9·0	10·7	10·0
62		10·4	9·4	10·7	10·5
61		6·3	6·0	6·5	5·8
57	$C_3H_2F^+$	12·2	11·2	14·0	11·5
31		8·9	10·0	9·4	9·6

a hydrogen atom in the second step to give **4c**. Negligible **3** is formed which is consistent with the absence of any COF loss.

In the spectrum of benzofuran a large peak *m/e* 63 arising from decomposition of **1a** was proposed to be **9a**.[6,7] The same peak appears prominently in the monochloro-



9 a-c

and monobromobenzofuran spectra. Dichlorobenzofuran gives this ion and a *m/e* 97–99 doublet corresponding to $C_5H_2Cl^+$ ion **9b**. In contrast the near absence of **9b** in the spectra of monochlorobenzofurans illustrates how chlorine remains in the benzocyclopropenium ion **4b** from the dichlorobenzofuran ion, but not here. Ion *m/e* 81 ($C_5H_2F^+$) in the spectrum of fluorobenzofurans is analogous to ion **9c**. These peaks are nearly equal for the different isomers which suggests the ions from which these fragments arise must be the same. If this is true, the fluorobenzocyclopropenium ion or its equivalent dehydrotropylium ion must equilibrate. The deuterated benzofurans analogously show the ion *m/e* 64 in addition to the ion *m/e* 63. This

same type of pattern is observed in the spectra of benzothiophene-3-d[7] where deuterium is retained partially in the smaller fragment ions.

Bromobenzofuran

The molecular ion from 5-bromobenzofuran (**1d**) loses bromine from the ring to give **5** which then loses CO to give **3** (Fig. 2). A broad metastable peak *m/e* 67–70 supports both transitions **1d** → **5** (*m** 69·1–69·8) and **5** → **3** (*m** 67·7). Another metastable peak *m/e* 144 supports the alternative loss of CO from **1d** to give **2d**,

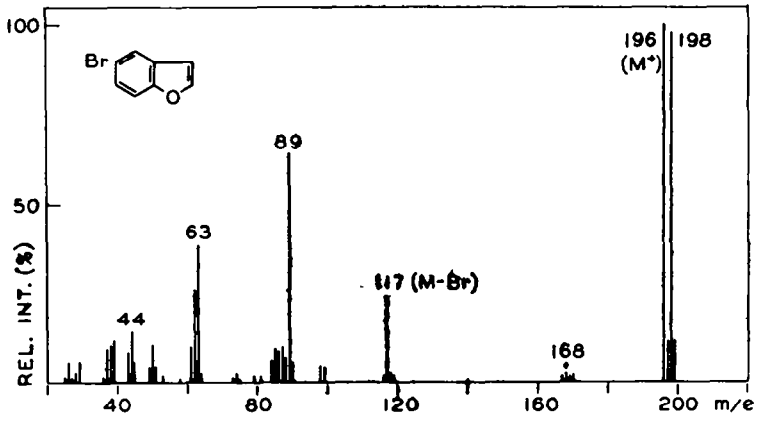


FIG. 2. Mass spectra of 5-bromobenzofuran.

although a metastable peak *m** 46·6–47·2 is not present to support loss of bromine from **2d** to give **3**. The latter process, as predicted from the spectra of the chlorobenzofurans, would likely involve a very small peak for ion **2d** coupled with an intense ion **3**. On the other hand, the relative amount of ion **3** that arises from **5** is unknown. Such a transition found in the mass spectrum of nitrobenzofuran gives us some idea of the relative amount of ion **3** that can be expected to form from ion **5** in the mass spectrum of bromobenzofuran.

Nitro- and methoxybenzofurans

As already mentioned, the molecular ion **1e** from 5-nitrobenzofuran* (Fig. 3) fragments in part like bromobenzofuran by loss of the ring substituent, NO_2 in this case, to give **5**. A competitive process involving rearrangement of the nitro group and loss of NO to give the benzofuranoxonium ion (**10**) also occurs. However, the alternative loss of CO from **1e** to give a nitrobenzocyclopropene ion *m/e* 135 (**2e**) seems

* Pyrolysis was observed in the 7·5 V spectrum at an inlet temperature of 350°C. The relative intensities of *m/e* 133 and 163 are shown:

	200°	350°
163	100	100
133	4·7	51

The spectrum reported here differs considerably from that reported previously.[5]

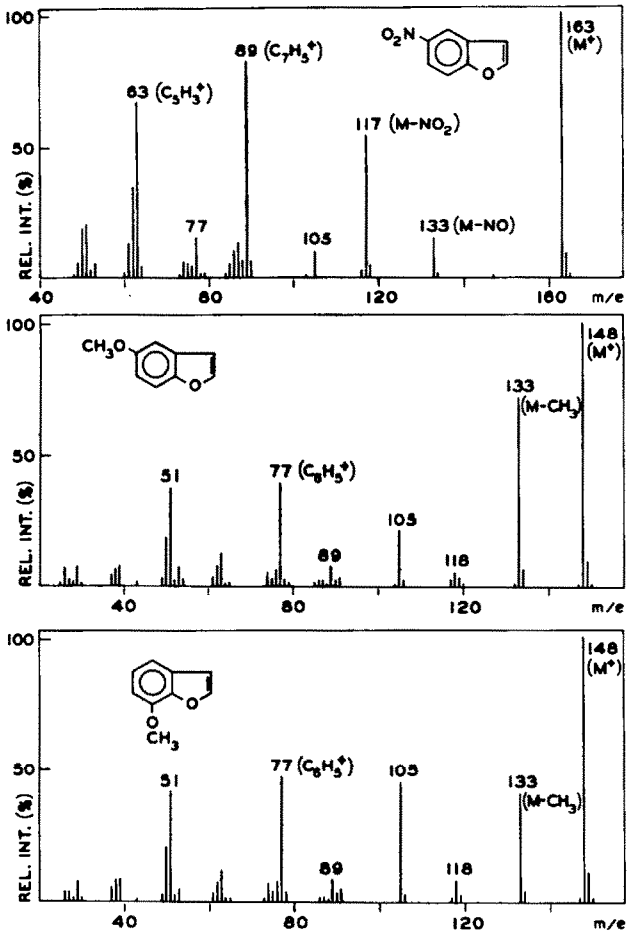
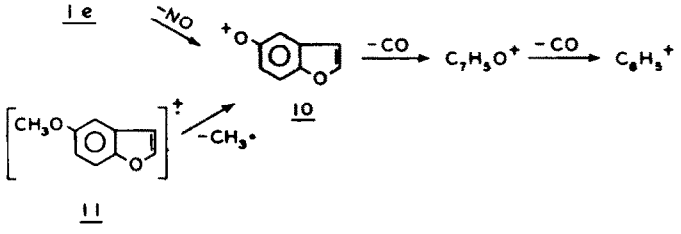


FIG. 3.

unimportant for three reasons. First, the peak intensity of ion M—CO (**2e**) is only 0·24% of the base peak which is much smaller than observed for the halogen substituted benzofurans. Secondly, Reed and Reid report no evidence for such a transition in their study.[5] Thirdly, in compounds with a nitro group attached to an aromatic ring fragmentation of the molecular ion almost always involves the nitro group, ref. 4, p. 515. Therefore, **1e** loses NO or NO_2 initially without any significant CO loss. Delineating the process involving NO loss allows us then to determine the relationship of ions **5** and **3**.



The fragmentation pattern of ion **10** is present in the mass spectra of 5- and 7-methoxybenzofurans (Fig. 3). The ion fragments from **10** are consistent with a scheme in which **10** loses one molecule of CO to give ion *m/e* 133 ($C_7H_5O_2+$) which also loses CO to give *m/e* ($C_6H_5^+$). The peaks *m/e* 117, 89 and 63 which are relatively small show minor methoxyl radical loss consistent with other methoxyl substituted oxygen heterocycles.[8,12,17] Therefore, in the mass spectrum ions *m/e* 117 and 89 are associated almost entirely with the fragmentation process **1e** → **5** → **3**. We might expect similar intensities for ions **5** and **3**.

In the mass spectrum of 5-bromobenzofuran peak **3** arises largely from **5**. Any excess **3** would be a consequence of the alternative sequence **1d** → **2d** → **3**. Obviously an excess estimate is impossible based on our data even though this process most likely occurs.

CONCLUSIONS

Halogenated benzofurans fragment by two processes. One is consistent with an initial loss of carbon monoxide involving ring collapse. Then follows halogen or hydrogen loss from the M—CO ion as for chloro- and fluorobenzofurans. The second scheme involves initial loss of halogen followed by loss of carbon monoxide as for bromobenzofuran, although some of the first type apparently occurs here also. Our data show no evidence which suggests any simultaneous loss of formyl radical.

EXPERIMENTAL

The preparations of many of these compounds were reported previously.[18] Several not reported previously are included here. The mass spectra presented here were obtained with a CEC Model 21–103 mass spectrometer with an ionizing potential of 70 eV. The inlet temperature was 100°, except in a few cases where it was 250°C. Only ion abundances greater than 1% of the base peak are reported. Melting points were obtained on a Fisher–Johns melting point block. The IR spectra were determined as neat liquid films or as KBr pellets on a Perkin–Elmer Model 337 infrared spectrophotometer.

Benzofuran-2-d

Prepared from benzofuranyl lithium and D_2O.[19] A solution of 10 g (85 m moles) of benzofuran in 300 ml of previously dried ethyl ether was placed in an ice bath under nitrogen. When cool, 81 ml (0·13 moles) of a 15% solution of butyl lithium in hexane was added slowly. After complete addition the solution was refluxed for 2 hr and cooled. The 6 ml of D_2O was added slowly. After stirring overnight the reaction mixture was poured into water and the ether layer separated and dried over magneisum sulfate. The solvent was evaporated and the product distilled (b.p. 56° at 2 mm). The IR showed strong bands at 1230, 815–820 (doublet) and 670 cm^{-1}, which were not in benzofuran, in addition to several (some were shifted slightly from benzofuran) at 1255, 1170, 1025 and 745 cm^{-1}. The 4000–1300 cm^{-1} regions were virtually identical.

5-Chlorobenzofuran-2-d was prepared by the same technique (b.p. 65° at 2 mm). The IR showed strong bands at 1260, 1170, 1070, 1030, 870, 805 and 690 cm^{-1}.

The following substituted benzofurans were prepared by the cyclization of the appropriately substituted 2-formylphenoxyacetic acid:[20] 5-nitrobenzofuran (m.p. 108–109°, lit.[21] 114–115°); 5-bromobenzofuran[22] (b.p. 96–97 at 8 mm); 7-methoxybenzofuran[23] (b.p. 98–99 at 8 mm); 5-methoxybenzofuran (m.p. 32–33°, lit.[24] 32–33°). 4-Bromo-2-formylphenoxyacetic acid prepared by reacting equal molar equivalents of bromine and 2-formylphenoxyacetic acid (m.p. 163–166°, lit.[25] 163–164°) was, in fact, a mixture of product and reactant. Recrystallization from ethyl acetate produced pure 4-bromo-2-formylphenoxyacetic acid (m.p. 174–175°). (Calc. for $C_9H_7BrO_4$: C, 41·72; H, 2·73. Found: C, 42·05; H, 2·80%).

4- and 6-Fluorobenzofurans were prepared by the cyclization of 3-fluorophenoxyacetaldehyde diethyl acetal (b.p. 96° at 0·2 mm). (Calc. for $C_{12}H_{17}FO_3$: C, 63·14; H, 7·51. Found: C, 62·99; H, 7·38.) The acetal was cyclized with zinc chloride in acetic acid.[26] The product which contained two components were separated by preparative GLPC on a 16 ft, ¼ in. o.d. column packed with 5% Bentone 34 and 5% diisodecyl phthalate on Diatoport W. The mass spectra, IR and NMR were consistent with the expected structures.

REFERENCES

[1] P. Brown and C. Djerassi, *Angew. Chem. Int. Ed.* **6**, 477 (1967); G. Spiteller in *Advances in Heterocyclic Chemistry*, Vol. 7, p. 301. (Edited by A. R. Katritzky and A. J. Boulton) Academic Press, New York (1966).

[2] J. L. Occolowitz and G. L. White, *Aust. J. Chem.* **21**, 997 (1968).

[3] P. Bommer and K. Biemann, *Ann. Rev. Phys. Chem.* **16**, 481 (1965).

[4] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, p. 622. Holden-Day, London (1967).

[5] R. I. Reed and W. K. Reid, *J. Chem. Soc.* 5938 (1963).

[6] B. Willhalm, A. F. Thomas and F. Gautschi, *Tetrahedron* **20**, 1185 (1964).

[7] Q. N. Porter, *Aust. J. Chem.* **20**, 103 (1967).

[8] C. S. Barnes and J. L. Occolowitz, *Ibid.* **17**, 975 (1964).

[9] W. T. Pike and F. W. McLafferty, *J. Am. Chem. Soc.* **89**, 5954 (1967).

[10] K. Biemann, *Mass Spectrometry*, p. 154. McGraw Hill, New York (1962).

[11] MCA Research Project Nos. 86, 89, 90, 101, 102.

[12] N. S. Vulfson, V. I. Zaretskii, and V. G. Zaikin, *Bull. Acad. Sci. USSR, Chem. Div.* 2046 (1963).

[13] J. Baldas, Q. N. Porter, I. R. C. Bick and M. J. Vernengo, *Tetrahedron Letters*, 2059 (1966).

[14] R. Srinivasan, *J. Am. Chem. Soc.* **89**, 4812 (1967), H. Hiraoka and R. Srinivasan, *Ibid.* **90** 2720 (1968).

[15] D. H. Williams, S. W. Tam and R. G. Cooks, *Ibid.* **90**, 2150 (1968).

[16] J. Seibl, *Helv. Chim. Acta* **50**, 263 (1967).

[17] R. H. Shapiro and G. Djerassi, *J. Org. Chem.* **30**, 955 (1965).

[18] E. N. Givens and P. B. Venuto, In preparation.

[19] H. Gilman and J. W. Morton, Jr., *Organic Reactions*, Vol. VIII, p. 287. John Wiley, New York (1954).

[20] A. W. Burgstahler and L. R. Worden, *Org. Synthesis* **46**, 28 (1966).

[21] H. Erlenmeyer, W. Grubenmann and H. Bloch, *Helv. Chim. Acta*, **31**, 75 (1948).

[22] R. Kurdukar and N. V. S. Rao, *Proc. Indian Acad. Sci. Sect. A*, **58**, 336 (1963); *Chem. Abstr.* **60**, 11972 g (1964).

[23] W. B. Whalley, *J. Chem. Soc.* 3482 (1953).

[24] S. Tanako, *J. Am. Chem. Soc.* **73**, 872 (1951).

[25] R. Stoermer, *Liebigs Ann.* **312**, (1900); A. Rossing, *Chem. Ber.* **17**, 2992 (1884).

[26] R. Stoermer, *Chem. Ber.* **30**, 1700 (1897); R. C. Elderfield and V. B. Meyer in *Heterocyclic Compounds*, Vol. 2, p. 15 (Edited by R. C. Elderfield). John Wiley, New York (1951).