Tetrahedron. Vol 24, pp 1875 to 1888 Pergamon Press 1968. Printed in Great Britain

ELECTRON IMPACT STUDIES—XXII[1]

MASS SPECTRA OF SUBSTITUTED BENZIMIDAZOLES

S.-O. LAWESSON and G. SCHROLL

J. H. BOWIE

and

R. G. COOKS

Department of Organic Chemistry, University of Aarhus, Aarhus C., Denmark

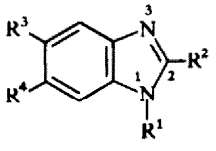
Department of Organic Chemistry, University of Adelaide, Adelaide, South Australia

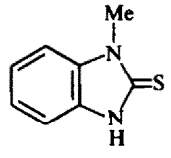
University Chemical Laboratory, Lensfield Road, Cambridge, England

(*Received in the UK* 18 *July* 1967; *accepted for publication* 21 *August* 1967)

Abstract—The mass spectra of 22 benzimidazoles are reported and discussed. The basic fragmentation patterns have been substantiated by deuterium labelling, exact mass measurements and appropriate metastable ions. Skeletal rearrangement ions produced by the process M–CO are more prominent in the spectra of 2-benzoyl than 2-acetylbenzimidazoles.

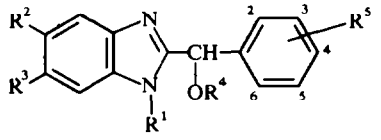
ALTHOUGH the mass spectra of imidazoles[2,3] and benzimidazolium barbiturates[4] have been discussed, no survey of the mass spectra of simple benzimidazoles has been reported. This paper is concerned with the mass spectra of the benzimidazoles (I–XXII), which are recorded in Figs 1–9 or Table 1. The compositions of ions determined by exact mass measurements are listed in Table 2. The presence of an





XXII

	R^1	R^2	R^3	R^4
I	H	H	H	H
II	D	H	H	H
III	H	Me	H	H
IV	D	Me	H	H
V	H	H	Me	Me
VI	Allyl	H	H	H
VII	H	SMe	H	H
VIII	D	SMe	H	H
IX	H	n-Pr	H	H
X	H	C_6H_5	H	H
XI	H	COMe	H	H
XII	H	COPh	H	H
XIII	H	CH(OH)Me	H	H



	R^1	R^2	R^3	R^4	R^5
XIV	H	H	H	H	H
XV	D	H	H	D	H
XVI	H	H	H	H	4-Br
XVII	D	H	H	D	4-Br
XVIII	Me	H	H	H	4-Br
XIX	H	Me	Me	H	4-Br
XX	Me	H	H	H	3-NO_2
XXI	H	Me	Me	H	3-NO_2

TABLE 1. MASS SPECTRA OF BENZIMIDAZOLES

II[a,b]	*m/e*	90	91	92	117	118	119(M)	120											
	I(%)	3	15	20	3	5	100	20											
IV[a,b,c]	*m/e*	90	93	94	104	131	132	133	134										
	I(%)	5	3	3	4	37	90	100	20										
V[a]	*m/e*	50	63	64	65	72	73	77	89	90	91	92	116	117	118	119	131	132	
	I(%)	3	6	5	7	3	3	4	4	5	22	3	5	5	10	6	66	8	
		145	146(M)	147															
		76	100	11															
VI[a]	*m/e*	41	51	52	63	65	77	90	103	104	118	129	130	131	132	156	157		
	I(%)	16	5	3	4	4	11	5	4	7	6	3	13	27	5	7	81		
		158(M)	159																
		100	12																
VIII[a,c]	*m/e*	27	39	43	44	45	63	64	77	78	90	91	92	118	119	120	122	131	132
	I(%)	4	3	3	7	3	8	5	3	3	8	7	5	16	20	6	23	57	32
		149	150	164	165	166	167												
		8	6	100	77	12	4												
XIII[d]	*m/e*	39	43	45	51	52	63	64	65	73	90	91	92	118	119	143	144	145	147
	I(%)	6	12	8	100	6	7	8	10	6	6	16	14	36	71	17	30	20	54
		162(M)	163																
		72	8																
XIV[d]	*m/e*	51	65	77	79	90	91	92	93	103	105	118	119	147	194	195	205	206	
	I(%)	6	8	23	7	6	13	9	7	8	15	33	46	22	10	18	35	80	
		207	223	224(M)	225														
		21	24	100	16														
XV[c,d]	*m/e*	39	44	51	63	64	65	77	78	79	90	91	92	103	105	106	118	119	120
	I(%)	6	7	10	7	6	8	29	9	7	8	13	11	6	20	6	23	45	28
		121	147	148	149	194	195	196	205	206	207	208	209	223	224				
		12	14	10	5	9	13	8	30	100	38	22	11	18	79				
		225	226																
		71	29																

TABLE 1—*continued*

XVII[b,c,d]	*m/e*	104	105	118	119	120	121	147	148	155	156	157	158	183	184	185
	I(%)	8	9	31	61	48	18	15	17	40	6	40	6	67	20	78
		186	187	188	189	193	194	195	200	201	202	203	205	206	207	208
		41	15	10	12	12	14	6	11	12	12	12	100	37	17	7
		272	273	274	275	284	285	286	287	288	289	300	301	302	303	304
		32	36	39	33	9	9	21	19	17	13	18	26	54	65	57
		305	306													
		45	23													
XVIII[d]	*m/e*	51	76	77	78	104	131	132	133	147	161	183	185	205	220	287	299
	I(%)	6	6	20	9	8	32	31	31	53	43	9	9	7	12	7	6
		301	315	316(M)		317	318(M)		319								
		8	27	100		43	97		16								
XIX[d]	*m/e*	77	78	91	104	131	145	146	147	155	157	175	183	185	218	219	232
	I(%)	15	6	8	6	12	12	13	36	6	6	13	10	10	8	6	10
		233	234	235	285	287	299	300	301	302	303	312	313	314	315	316	
		100	28	6	6	6	11	28	17	26	9	16	14	39	16	24	
		328	329	330(M)		331	332(M)		333								
		6	9	75		21	69		12								
XXI[d]	*m/e*	76	77	91	104	131	145	146	147	150	175	221	222	232	233	234	237
	I(%)	8	9	9	11	13	15	11	28	8	19	12	10	18	31	12	7
		249	250	251	262	265	267	281	295	296	297(M)	298					
		7	13	6	11	8	21	10	20	11	100	19					

[a] All peaks greater than 2% of the base peak (100%) are recorded.
[b] Only peaks above *m/e* 90 are recorded.
[c] Because of the M-1 and M-2 ions, the isotopic purity cannot be determined.
[d] All peaks greater than 5% of the base peak are recorded.

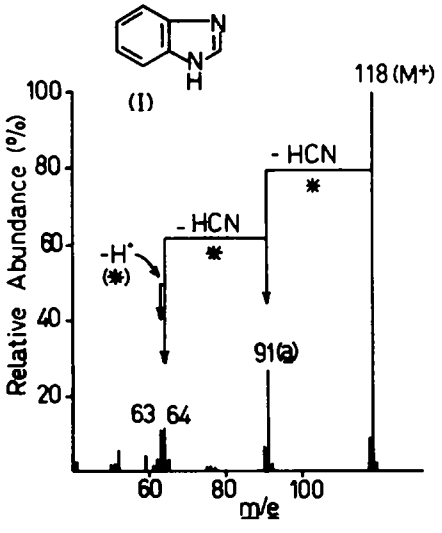


FIG. 1.

TABLE 2. COMPOSITIONS OF SOME IONS IN THE SPECTRA OF I–XX

Compound	*m/e*	Composition	Compound	*m/e*	Composition
I	63	C_5H_3	XIV	194	$C_{13}H_{10}N_2$
	64	C_5H_4		195	$C_{13}H_{11}N_2$
	91	C_6H_5N			
			XVI	205	$C_{14}H_9N_2$
V	91	C_7H_7		272/274	$C_{13}H_9N_2Br$
	118	C_8H_8N			
			XVIII	147	$C_8H_7N_2O$
VI	104	C_7H_6N		161	$C_9H_9N_2O$
	118	$C_7H_6N_2$		205	$C_{14}H_9N_2$
	131	$C_8H_7N_2$		220	$C_{15}H_{12}N_2$
				300/302	$C_{15}H_{13}N_2Br$
VII	118	$C_7H_6N_2$			
	122	C_6H_4NS	XIX	233	$C_{16}H_{13}N_2$
	131	$C_8H_7N_2$			
			XX	118	$C_7H_6N_2$
XI	117	$C_7H_5N_2$		119	$C_7H_7N_2$
	118	$C_7H_6N_2$		147	$C_8H_7N_2O$
	131	$C_8H_8N_2$		220	$C_{14}H_8N_2O$
XII	193	$C_{13}H_9N_2$	XXI	233	$C_{16}H_{13}N_2$
	194	$C_{13}H_{10}N_2$		267	$C_{15}H_{13}N_3O_2$
XIII	91	C_6H_5N	XXII	118	$C_7H_6N_2$
	92	C_6H_6N		119	$C_7H_7N_2$
	118	$C_7H_6N_2$		122	C_6H_4NS
	119	$C_7H_7N_2$			
	120	$C_7H_8N_2$			
	143	$C_9H_7N_2$			
	144	$C_9H_8N_2$			
	145	$C_9H_9N_2$			
	147	$C_8H_7N_2O$			

asterisk (*) in the text or a figure indicates that a metastable peak has been observed for the fragmentation in question.

The mass spectra (Figs 1 and 2) of benzimidazole (I) and 2-methylbenzimidazole (III) should be compared with those[3] of imidazole and 2-methylimidazole, respectively. The spectrum of benzimidazole (I) exhibits the molecular ion as the base peak, and the fragmentation process M—HCN—HCN—H· (to form $C_5H_3^+$, *m/e* 63). The initial loss of HCN probably produces *a* (*m/e* 91), and the spectrum (Table 1) of N-d_1-benzimidazole (II) shows loss of both HCN and DCN from the molecular ion, which indicates that the initial loss of HCN (Fig. 1) is non specific. This is also true of the M—HCN process in the spectrum of imidazole.[3]

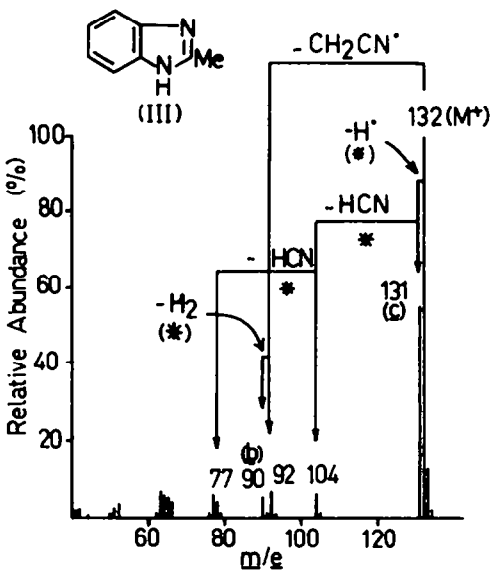
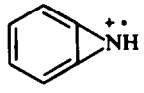
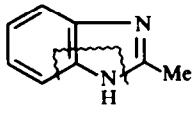


FIG. 2.

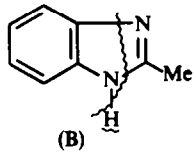
The mass spectrum (Fig. 2) of 2-methylbenzimidazole (III) exactly parallels that of 2-methylimidazole.[3] Comparison of the mass spectra of III and IV show that the M—HCN ion originates as in A (i.e. the *m/e* 104 ion in the spectrum of III remains



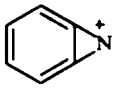
a, *m/e* 91



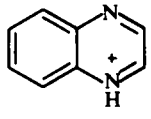
(A)



(B)



b, *m/e* 90



c, *m/e* 131

unchanged in that of IV). The M—CH_2CN· process involves the 2 and 3 positions (i.e. *m/e* 93 in III moves to 93/94 in IV), while the overall process M—CH_2CN·—H_2 (to *b*, *m/e* 90) may be explianed by the loss indicated in B (i.e. *m/e* 90 in III remains unchanged in IV). It is also probable that the M—H· ion (*m/e* 131) is formed by loss of a hydrogen atom from the Me group, with concomitant ring expansion to form the stable cation *c* (cf. Ref. 3).

The spectrum (Fig. 3) of 2-n-propylbenzimidazole (IX) shows pronounced loss of ethylene with accompanying H rearrangement to give *m/e* 132, the base peak of the spectrum. The structure of this fragment corresponds to the 2-methylbenzimidazole

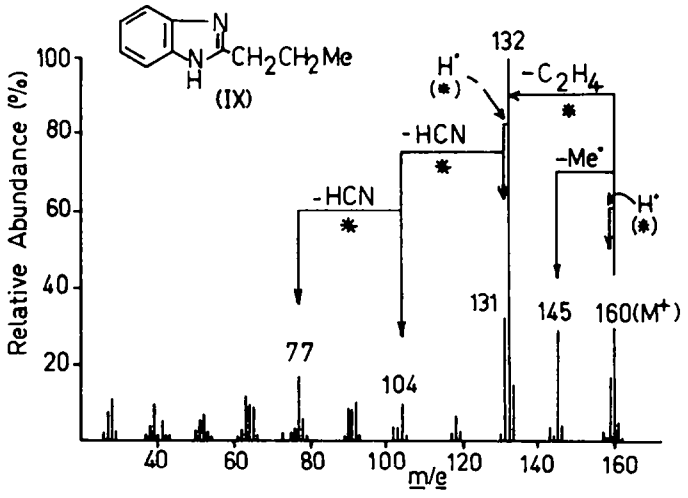
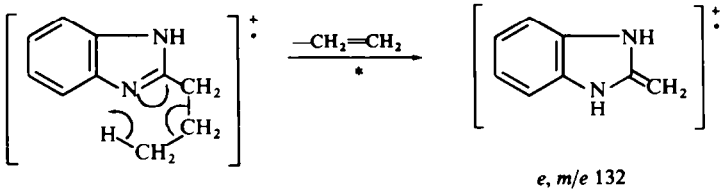


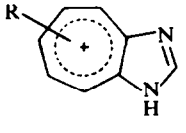
FIG. 3.

molecular ion, as the spectrum below *m/e* 132 is very similar to that (Fig. 2) of 2-methylbenzimidazole. The formation of *m/e* 132 probably proceeds by the process *d* → *e*, with *e* then rearranging to the 2-methylbenzimidazole radical ion. A similar 6-membered transition state has been invoked to explain the loss of ethylene from 3-propylpyridines.[5] 2-Alkyloxazoles (where the alkyl group is greater than ethyl) also exhibit β-cleavage with hydrogen rearrangement to produce the 2-methyloxazole radical ion.[6]

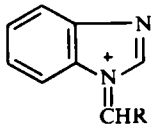


d, *m/e* 160

e, *m/e* 132



f, *m/e* 145 (R = Me)
g, *m/e* 131 (R = H)



h, *m/e* 157 (R = —CH=CH$_2$)
i, *m/e* 131 (R = H)

The spectra of V, VI and X are unexceptional. 5,6-Dimethylbenzimidazole (V), on electron impact, behaves like *o*-xylene,[7] producing prominent M—H· and M—Me· ions, which may be represented as the tropylium species *f* and *g*, respectively. The mass spectrum (Table 1) of N-allylbenzimidazole (VI) exhibits loss of both a hydrogen radical and a C_2H_3 radical from the molecular ion to form the stable cations *h* and *i*, while the molecular ion of 2-phenylbenzimidazole (X) may decompose either by loss of benzonitrile to form *a* (*m/e* 91) or by successive losses of two molecules of HCN to form *m/e* 140 ($C_{11}H_8^{+\cdot}$).

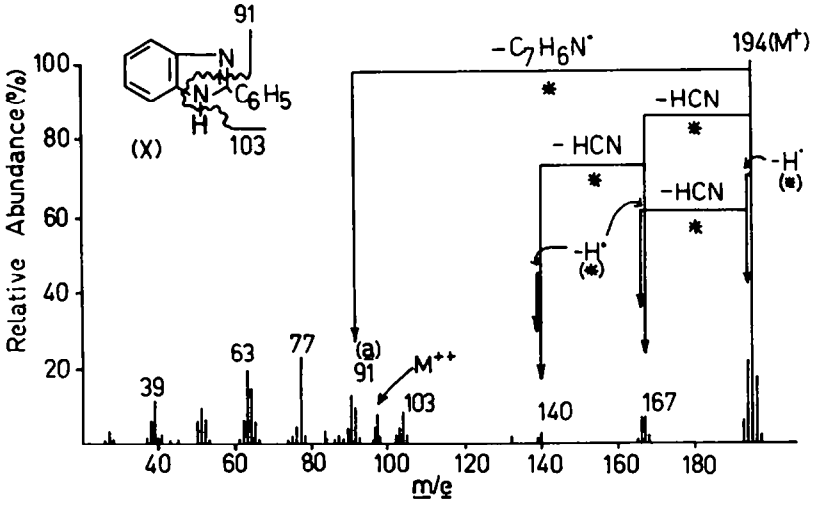
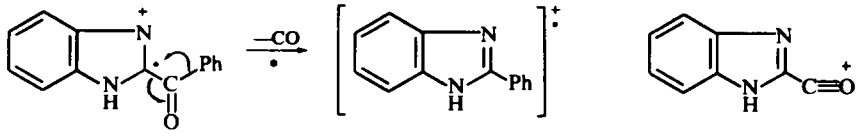


FIG. 4.

By far the most interesting features observed in the spectra (Figs 5 and 6) of the acylbenzimidazoles (XI and XII) are the pronounced skeletal rearrangement fragments which are produced by loss of carbon monoxide from the various molecular ions. Such processes are currently exciting much interest,[8] and of particular relevance are the M—CO fragments which are present in the spectra of acylthiophenes.[9] Similar processes are generally not observed in the spectra of acylbenzenes (benzophenone is an exception[10]). The M—CO fragment in the spectrum (Fig. 5) of 2-benzoylbenzimidazole is extremely pronounced (93% of the base peak), and its structure is probably that of the 2-phenylbenzimidazole radical ion (see $j \rightarrow k$), as the spectrum below *m/e* 194 is very similar to that (Fig. 4) of 2-phenylbenzimidazole, except for the presence of peaks due to the benzoyl cation (*m/e* 105) and its decomposition ions *m/e* 77 (base peak) and *m/e* 51. It is of interest to note that the expected α cleavage to carbonyl to produce the acylium cation *l* occurs only to the extent of 2% of the base peak, and that the two major processes are the formation of the skeletal rearrangement ion and the production of the benzoyl cation.



j, *m/e* 222 *k*, *m/e* 194 *l*, *m/e* 135

The skeletal rearrangement peak in the spectrum (Fig. 6) of 2-acetylbenzimidazole (XI) is not as pronounced as it is in that of XII (viz. 26% for XI, 93% for XII). The major process in this spectrum is M—CH_2CO, which forms the benzimidazole radical ion (*m/e* 118, base peak), which fragments as described above.

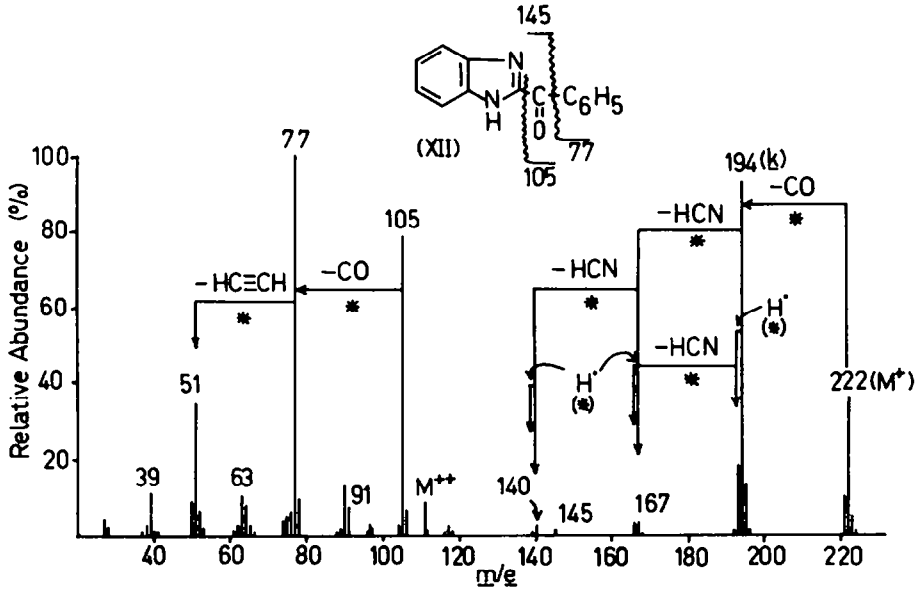


FIG. 5.

When the secondary alcohols (XIII–XXI) are introduced into the mass spectrometer through the heated inlet system, hydrogen is lost thermally, and the mass spectra obtained are those of the corresponding ketones. All these spectra contain M—CO fragments. The abundances of these ions relative to the base peaks in the spectra of the derived ketones are XIV, 100; XVI, 100; XVIII, 95; XIX, 62; XX, 43; and XXI, 92%.

The direct insertion technique was used to obtain the spectra (Figs 7 and 8 or Table 1) of the secondary alcohols XIII–XXI. Three processes are observed which are common to all spectra: (a) M—H_2—CO. The loss of hydrogen is probably thermal since no metastable ions are observed for the process M—H_2. (b) The formation of the protonated benzimidazole or N-methylbenzimidazole cation (e.g. *m* for XIV and XVI), which is formed by cleavage of the bond between C-2 and the

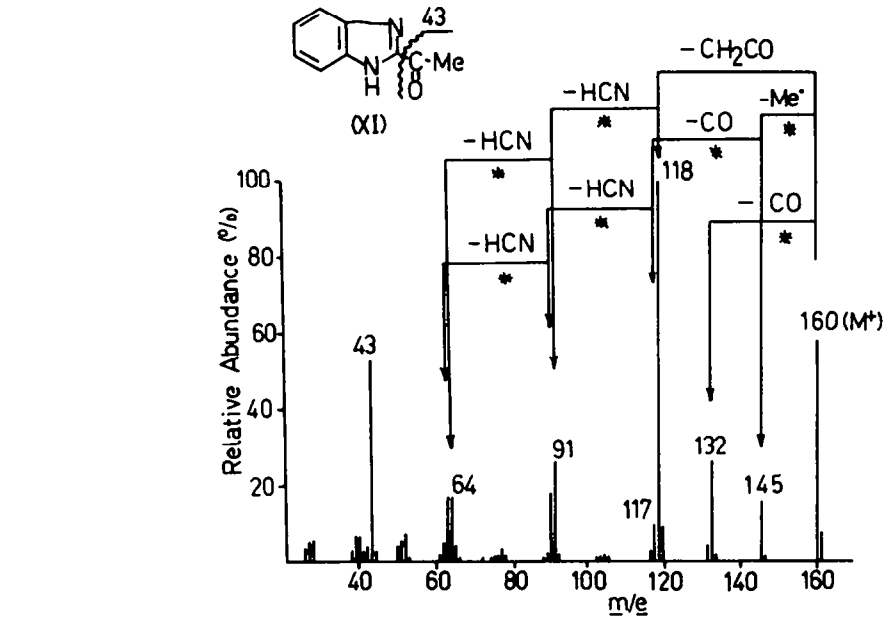

43
C-Me
O
(XI)
-HCN
-HCN
-HCN
-HCN
-CH2CO
-CO
-Me·
-CO
118
160(M+)
43
64
91
117
132
145
Relative Abundance (%)
m/e

FIG. 6.

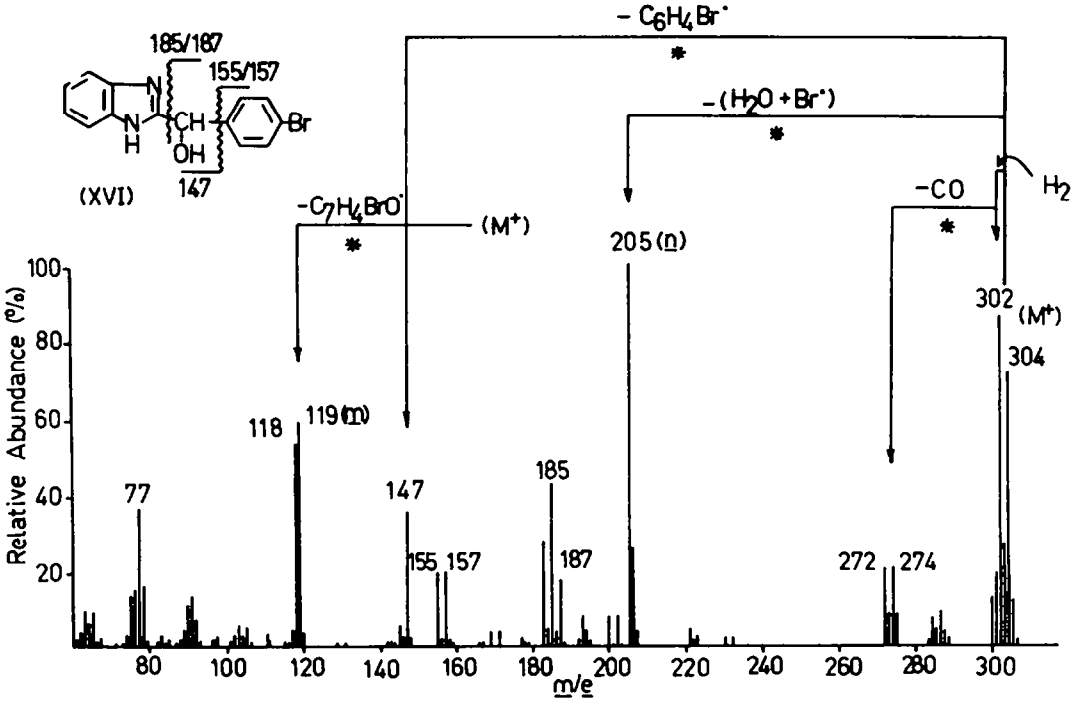

185/187
155/157
Br
OH
147
(XVI)
-C6H4Br·
-(H2O + Br·)
-C7H4BrO·
(M+)
-CO
H2
205(m)
302 (M+)
304
118
119(m)
77
147
185
155 157
187
272 274
Relative Abundance (%)
m/e

FIG. 7.

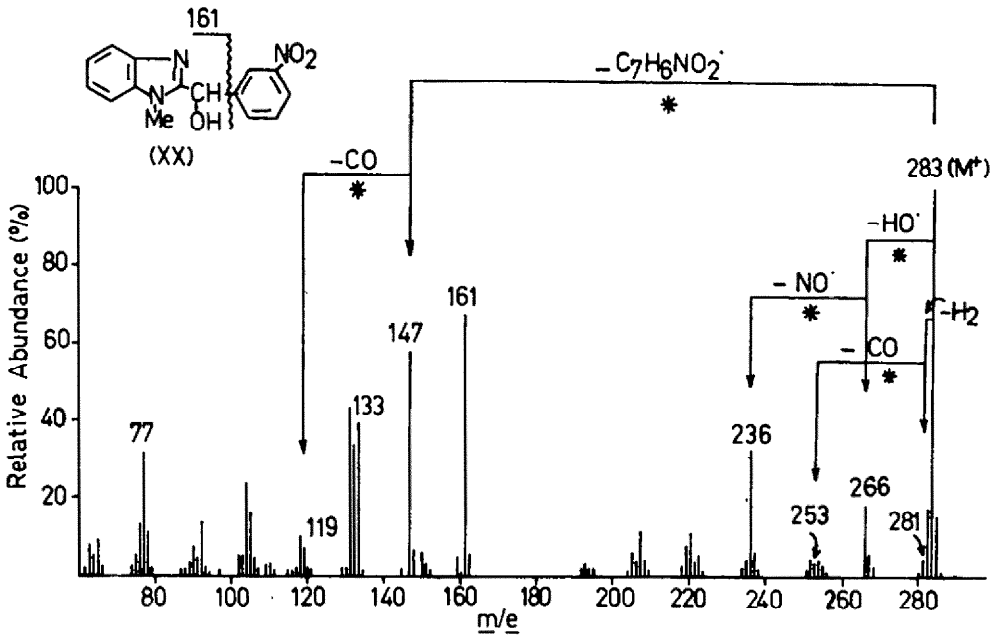
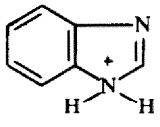
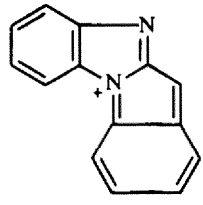


FIG. 8.

carbon bearing oxygen, with concomitant double hydrogen rearrangement. One of the migrating hydrogens is that attached to oxygen, as evidenced by the spectra (Table 1) of XV and XVII. (c) The process M—$C_6H_4R\cdot$ (R = Br or NO_2) produces an ion whose composition corresponds to the appropriate protonated formylbenzimidazole cation.



m, *m/e* 119



n, *m/e* 205

There are three further features of the spectra of the secondary alcohols (XIV–XXI) which provide information concerning the nature of the substituent on nitrogen. The spectra (Figs 7 and 8 or Table 1) of the 1-Me and 1-H benzimidazoles (XIV–XXI) show marked differences. When hydrogen is bound to nitrogen (XIV, XVI, XIX and XXI) a prominent ion (the base peak in the spectra of XVI and XIX) is produced in a one step process from the molecular ion, by combined loss of R (R = H, Br of NO_2) and water (see Fig. 7). The two hydrogens involved are those bound to nitrogen and oxygen (from the spectra of XV and XVII in Table 1). A plausible structure for this ion is *n* (*m/e* 205 in the spectrum of XV), and its presence may be used to detect

TABLE 3. MAJOR FRAGMENT IONS IN THE MASS SPECTRA OF XIV–XXI

Compound	$M-H_2-CO$		Protonated benzimidazole cation		$M-C_6H_4R$		$M-(R + H_2O)$		Skeletal rearrangement ion	
	m/e	(%)	*m/e*	(%)	*m/e*	(%)	*m/e*	(%)	*m/e*	(%)
XIV	196	10	119	46	147	22	205	35	—	—
XVI	272/274	20	119	60	147	34	205	100	—	—
XVIII	284/286	2	133	31	161	43	—	—	147	53
XIX	300/302	28	147	36	175	13	233	100	—	—
XX	253	3	133	38	161	65	—	—	147	57
XXI	267	21	147	28	175	19	233	31	—	—

the presence of the 1-H substituent. No corresponding ions are observed in the spectra (Fig. 8 or Table 1) of the secondary alcohols having 1-methylsubstituents (XVIII and XX).

Second, the spectra of the 1-H benzimidazoles (XIV, XVI, XIX and XXI) exhibit M—H_2O ions. This is particularly noticeable in the spectrum (Table 1) of XIV where the M—H_2O ion constitutes 80% of the base peak. The two hydrogens involved in the M—H_2O process are again those bound to nitrogen and oxygen (see the spectrum of XV, Table 1). This process is not observed in the spectra of XVIII or XX.

Third, the spectra (Fig. 8 or Table 1) of XVIII and XX exhibit an ion which is not present in those of the 1-H derivatives. This ion (produced in a one step process from the molecular ion) must be produced by a skeletal rearrangement process, as it is formally derived by α cleavage to C-2 with accompanying rearrangement of the alcoholic oxygen to the benzimidazole system. Although the structure of this ion (*m/e* 147, $C_8H_7N_2O$) is unknown, its presence allows the detection of the N-methyl substitutent.

The main features of the spectra of XIV–XXI are summarized in Table 3 and Figs 7 and 8. The spectrum (Table 1) of the substituted ethyl alcohol (XIII) is unexceptional; the major process being loss of an acetyl radical from the molecular ion to form the protonated benzimidazole cation *m*.

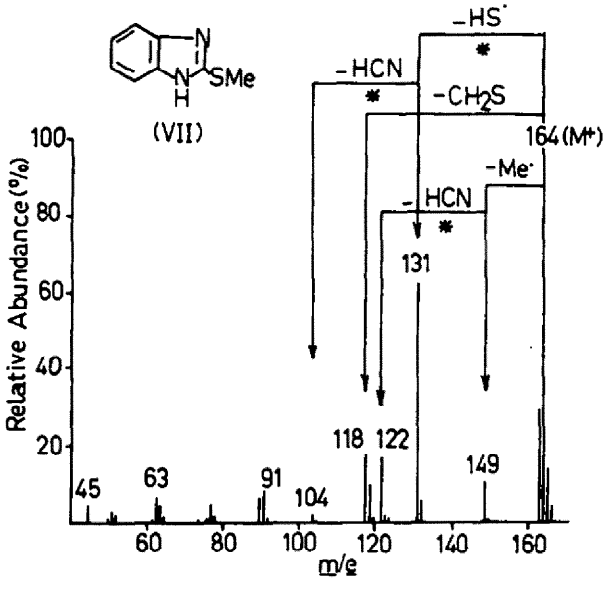
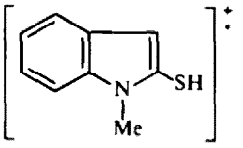


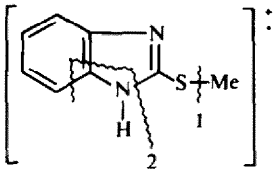
FIG. 9.

Skeletal rearrangement fragments are also observed in the spectrum (Fig. 9) of 2-thiomethylbenzimidazole (VII), where the M—SH ion (*m/e* 131) constitutes 63% of the base peak. It has been shown[11] that the M—SH process in the spectrum of thioanisole occurs from a common, rearranged molecular ion,[12] and that rearrangement processes which involve hydrogen transfers between the methyl group and the aromatic nucleus do not occur.[11] The spectra (Fig. 9, Table 1) of VII and XXII are

very similar (small differences are noted in the relative intensities of certain ions), which may indicate that they have a common molecular ion; viz. either one rearranging to the other, or with both rearranging to a common intermediate ion. The spectrum (Table 1) of 1-d_1-2-thiomethylbenzimidazole (VIII) shows that the hydrogen involved in the M—SH process is bound to carbon. The hydrogen presumably comes from the methyl group, and the rearranged molecular ion clearly cannot correspond to *o*. It is probable that the rearrangement is analogous to that observed in thioanisole.



o, *m/e* 164



p, *m/e* 164

Other processes observed in the spectrum of VII are (1) M—Me —HCN and (2) M—CH_2S. A comparison of the spectra of VII and VIII shows that process 1 occurs in a specific manner as indicated in *p* (*m/e* 122 is not shifted to *m/e* 123), while process 2 is a random one, involving loss of hydrogen attached to both carbon and nitrogen.

EXPERIMENTAL

Mass spectra were measured by the direct insertion technique with either an Hitachi Perkin–Elmer RMU 6D mass spectrometer (I–VI; IX–XII) or an A.E.I. MS9 mass spectrometer (VII, VIII and XIII–XXII) with a source temperature ca. 100°. Exact mass measurements were made with the MS9, using a resolution of 14,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses. All measurements were correct to within 15 ppm.

Compounds I, III and V were purified commercial samples. The following compounds were prepared by standard procedures: VI,[13] VII,[14] IX,[15] X,[16], XI,[17] XII,[17] XIII,[18] XIV,[18] XVI,[19] XVIII,[20] XIX,[19] XX[20] and XXI.[20]

The spectra of II, IV, VIII, XV and XVII were obtained by introducing the unlabelled compounds directly into the source with D_2O.[21]

Acknowledgements—A grant (to S.-O. L.) from Statens Almindelige Videnskabsfond, and an Elsie Ballot Fellowship (to R.G.C.) are gratefully acknowledged.

The Hitachi Perkin–Elmer RMU 6D mass spectrometer was purchased with the aid of a grant from the Australian Research Grants Commission.

Professor S. Siddappa generously provided samples (XIV, XVI, XVIII–XXI).

REFERENCES

[1] Part XXI. E. Dynesen, S.-O. Lawesson, G. Schroll, J. H. Bowie and R. G. Cooks, *J. Chem. Soc.* (B), in press.

[2] J. H. Bowie, R. G. Cooks, S.-O. Lawesson, P. Jakobsen and G. Schroll, *Chem. Commun.* 539 (1966).

[3] J. H. Bowie, R. G. Cooks, S.-O. Lawesson and G. Schroll, *Austral. J. Chem.* **20**, 1613 (1967).

[4] J. W. Clark-Lewis, J. A. Edgar, J. S. Shannon and M. J. Thompson, *Ibid.* **17**, 877 (1964).

[5] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds* p. 255. Holden-Day, San Francisco (1964).

[6] J. H. Bowie, R. G. Cooks, P. F. Donaghue, H. J. Rodda and D. H. Williams, *Organic Mass Spectrometry*, submitted for publication.

[7] H. M. Grubb and S. Meyerson, *Mass Spectrometry of Organic Ions* (Edited by F. W. McLafferty) Chap. 10. Academic Press, New York (1963).

[8] For a review see P. Brown and C. Djerassi, *Angew. Chem.* **79**, 481 (1967).
[9] J. H. Bowie, R. G. Cooks, S.-O. Lawesson and C. Nolde, *J. Chem. Soc.* (B), 616 (1967).
[10] P. Natalis and J. L. Franklin, *J. Phys. Chem.* **69**, 2943 (1965).
[11] J. H. Bowie, S.-O. Lawesson, J. Ø. Madsen, G. Schroll and D. H. Williams, *J. Chem. Soc.* (B), 951 (1966).
[12] J. H. Beynon, B. E. Job and A. E. Williams, *Z. Naturforsch.* **20a**, 883 (1965).
[13] J. G. Buchanan, A. W. Johnson, J. A. Mills and A. R. Todd, *J. Chem. Soc.* 2845 (1950).
[14] R. G. Cooks and P. Sykes, unpublished observations.
[15] W. O. Pool, H. J. Harwood and A. W. Ralston, *J. Am. Chem. Soc.* **59**, 178 (1937).
[16] D. Jerchel, H. Fischer and M. Kracht, *Liebigs Ann.* **575**, 162 (1952).
[17] G. W. H. Cheesman, *J. Chem. Soc.* 4645 (1964).
[18] M. A. Phillips, *Ibid.* 2893 (1928).
[19] K. H. Sinnur, G. R. Revankar and S. Siddappa, *Monatsh.* **97**, 417 (1966).
[20] U. V. Savant, G. R. Revankar and S. Siddappa, *J. Ind. Chem. Soc.* **43**, 194 (1966).
[21] J. S. Shannon, *Austral. J. Chem.* **15**, 265 (1962).