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THE MASS SPECTRA OF SOME ALKYL AND ARYL OXAZOLES[1]

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Abstract—The mass spectra of a variety of alkyl and aryl oxazoles have been determined and the spectra analyzed with the aid of deuterium labelling and high resolution mass spectrometry. In contrast to the corresponding benzenoid compounds, the mass spectra of isomeric alkyl oxazoles are distinctive and in this respect are akin to those of the corresponding pyridines. Further analogy to the pyridines is suggested by the unfavorable nature of a carbonium ion adjacent to the 2-position and this effect may be used to locate alkyl substituents attached to the oxazole nucleus. The loss of carbon monoxide from the molecular ions of 2,5-disubstituted oxazoles probably occurs with ring opening and migration of the C-5 substituent (e.g. Br) to the C-4 position.

ALTHOUGH the behaviour of many aromatic five-membered heterocyclic ring systems upon electron impact is now fairly well documented,[2] a detailed study of the mass spectra of oxazoles has not been reported.[3] This paper deals with the mass spectra of representative alkyl-, phenyl- and alkylphenyl-oxazoles. Details of the spectra are summarized in Table 1 and Figs. 1–12.

The mass spectrum (Table 1) of oxazole (I) itself is typical of that of an unsubstituted aromatic compound insomuch as the molecular ion (*m/e* 69) constitutes the base peak. The most abundant fragment ions in the high mass region occur at M-1 (8%), M-27 (M—HCN, 13%), M-28 (M—H_2CN and/or M—CO, 21%) and M-29 (M—CHO, 37%).

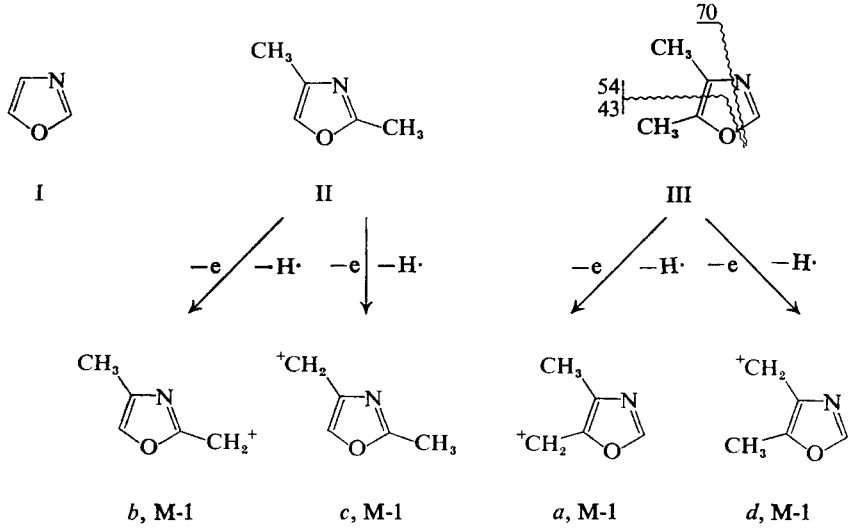
The spectra of the isomeric compounds 2,4-dimethyloxazole (II, Table 1) and 4,5-dimethyloxazole (III, Fig. 1) show characteristic differences. This behaviour is in contrast to that of the isomeric xylenes[4] and ethylmethylbenzenes,[5a] which give virtually identical spectra, but akin to that of three isomeric ethylmethylpyridines,[5a] which give distinctive spectra. Apparently, the presence of heteroatoms in the ring system prevents, or greatly retards, those processes by which the molecular ions from the isomeric xylenes, or ethylmethylbenzenes, become equivalent. The M-1 peak from III is considerably more abundant (12%) than that (2%) from II. These data parallel those for 3-ethylpyridine versus 2-ethylpyridine, the former exhibiting a much more abundant M-15 ion;[5b] the greater stability of carbonium ion *a* relative to carbonium ion *b* rationalizes the data, just as in the pyridines. Hence the M-1 peak from 2,4-dimethyloxazole (II) is probably formed largely by loss of a hydrogen atom from the 4-methyl group (see *c*) (the bond fixation within the oxazole nucleus accounts for the greater stability of *c* relative to *b*), while the M-1 peak from III will probably correspond to the formation of both *a* and *d*.

TABLE 1. MASS SPECTRA OF OXAZOLES

Compound															
I	*m/e*	38	39	40	41	42	68	69(M)	70						
	Rel. Ab.	2	4	37	21	13	8	100	4						
II	*m/e*	29	31	38	39	40	41	42	43	52	53				
	Rel. Ab.	6	27	2	4	4	9	40	4	2	2				
	m/e	54	55	56	66	68	69	96	97(M)		98				
	Rel. Ab.	5	20	8	3	34	22	2	100		6				
IV	*m/e*	26	27	28	38	39	40	41	42	43	44	53			
	Rel. Ab.	6	24	30	3	8	5	18	59	91	3	3			
	m/e	54	55	56	66	67	68	69	70	82	96	110	111(M)	11	
	Rel. Ab.	4	64	2	3	3	40	14	29	7	7	15	100		
IX	*m/e*	39	50	51	52	62	63	64	73	76	77	89	90		
	Rel. Ab.	5	4	8	2	4	8	2	3	3	6	20	38		
	m/e	103	166	117	118	145(M)		146							
	Rel. Ab.	3	9	35	3	100		11							
Xa	*m/e*	39	50	51	61	62	63	64	77	89	90	117	118		
	Rel. Ab.	8	5	6	3	9	28	8	5	60	78	5	56		
	m/e	119	145	146(M)	147										
	Rel. Ab.	4	8	100	11										
XI	*m/e*	37	38	39	41	50	51	61	62	63	64	77	88	89	116
	Rel. Ab.	6	7	23	8	12	11	8	21	42	4	8	10	100	36
	m/e	117	168	170	195	196	197	198	223(M)	224	225(M)	226			
	Rel. Ab.	6	10	9	53	6	52	5	19	2	19	2			
XIIa	*m/e*	38	39	40	41	42	43	50	51	52	53	61	62	63	
	Rel. Ab.	5	22	9	4	2	7	11	21	8	2	3	11	29	
	m/e	64	65	66	74	75	76	77	78	80	87	88	89	90	
	Rel. Ab.	19	9	8	3	4	8	16	4	4	3	3	24	54	
	m/e	91	92	103	104	105	130	131	132	133	158	159			
	Rel. Ab.	86	8	30	15	4	8	34	45	8	5	15			
	m/e	160(M)	161												
	Rel. Ab.	100	20												
XIIb	*m/e*	39	50	51	62	63	64	75	76	77	78	89	90		
	Rel. Ab.	14	9	18	12	37	12	3	6	17	4	80	98		
	m/e	103	104	105	130	131	132	133	158	159	160(M)	161			
	Rel. Ab.	36	16	10	10	27	36	4	4	16	100	15			
XIIIa	*m/e*	39	43	50	51	63	76	77	78	89	90	91	102	103	
	Rel. Ab.	5	3	9	20	8	5	42	15	7	13	50	3	19	
	m/e	104	105	119	130	131	132	133	159	160(M)	161				
	Rel. Ab.	13	20	6	11	55	17	2	11	100	12				
XIVa	*m/e*	39	43	50	51	52	61	62	63	64	75	76	77	78	
	Rel. Ab.	10	13	8	13	4	3	9	24	4	4	5	22	34	
	m/e	88	89	90	102	103	104	105	117	118	130	131			
	Rel. Ab.	3	27	7	5	35	57	12	6	7	4	15			
	m/e	132	145	159	160(M)	161									
	Rel. Ab.	2	8	7	100	12									
XV	*m/e*	39	50	51	62	63	75	76	77	78	88	89	90	91	102
	Rel. Ab.	7	3	8	3	15	2	3	21	5	2	23	10	9	2
	m/e	103	104	105	115	116	117	118	128	129	130	131	144	158	
	Rel. Ab.	48	15	7	13	6	27	7	6	2	11	6	11	100	
	m/e	159	172	173(M)	174										
	Rel. Ab.	12	7	95	15										
XVI	*m/e*	39	42	43	50	51	52	62	63	64	75	76	77	78	
	Rel. Ab.	9	6	18	6	13	3	4	11	2	2	4	21	18	
	m/e	89	90	102	103	104	105	130	131	158	172	173(M)	174		
	Rel. Ab.	10	3	3	21	62	16	7	4	6	2	100	12		

TABLE 1 (*contd.*)

Compound														
XIX	*m/e*	39	41	50	51	62	63	76	77	89	103	104	105	115
	Rel. Ab.	18	6	4	20	4	14	5	58	12	32	16	15	7
	m/e	116	117	118	128	131	139	144	163	164	165	166	167	
	Rel. Ab.	3	33	15	4	3	6	5	6	9	100	40	5	
	m/e	192	193	195	206	207	220	221	234	248	249(M)		250	
	Rel. Ab.	4	11	3	43	7	4	2	3	6	85		16	
XXI	*m/e*	39	41	43	51	55	62	63	76	77	83	89	91	103	104
	Rel. Ab.	11	21	5	13	15	2	10	5	58	8	11	5	77	41
	m/e	105	115	116	117	128	129	130	131	139	163	164	165	166	
	Rel. Ab.	29	7	3	8	5	6	12	4	4	5	6	73	15	
	m/e	167	193	206	207	234	235	236	248	249	250	262	263		
	Rel. Ab.	4	4	6	2	5	100	18	69	29	5	20	6		
	m/e	290	291(M)		292										
	Rel. Ab.	2	43		13										
XXII	*m/e*	39	50	51	76	77	88	89	90	105	115	139	163	164	
	Rel. Ab.	6	2	7	2	16	2	21	2	8	3	5	5	7	
	m/e	165	166	167	268	269	270	296	297(M)		298	299			
	Rel. Ab.	80	47	6	2	23	4	5	100		25	3			



Other distinctive features of the spectra of II and III include (i) the loss of a methyl radical from M^+ when the methyl groups are adjacent in III (Fig. 1), although this process is insignificant in the spectrum of II, (ii) no loss of HCN from the molecular ion of II, but loss of HCN from III to give *m/e* 70 [$C_4H_6O^+$; high resolution (h.r.)*] and (iii) an abundant *m/e* 43 ion ($CH_3C{\equiv}O^+$, h.r.) from III (Fig. 1), even though the *m/e* 43 ion from II is of very low abundance (4%). The complement to *m/e* 43 in Fig. 1 is *m/e* 54, formed exclusively by loss of C_2H_3O (h.r.) in a one-step process (metastable peak at *m/e* 30·1). In contrast, *m/e* 55 (Fig. 1) is due solely to $C_3H_3O^+$ [M—CH_4CN (h.r.) and no loss of CH_2CO].

There are differences between the spectra of 4,5-dimethyloxazole (III, Fig. 1) and 2,4,5-trimethyloxazole (IV, Table 1) which can be related to the ground state structures

* The latters 'h.r.' will be used subsequently in the paper to indicate the compositions of ions established by high resolution measurements.

FIG. 1

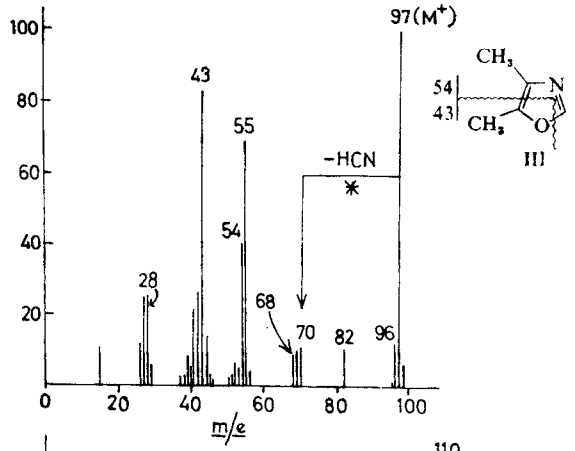


FIG. 2

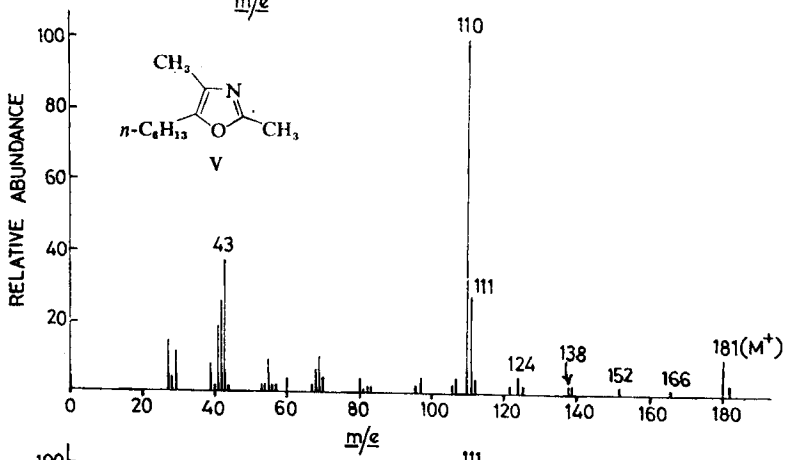
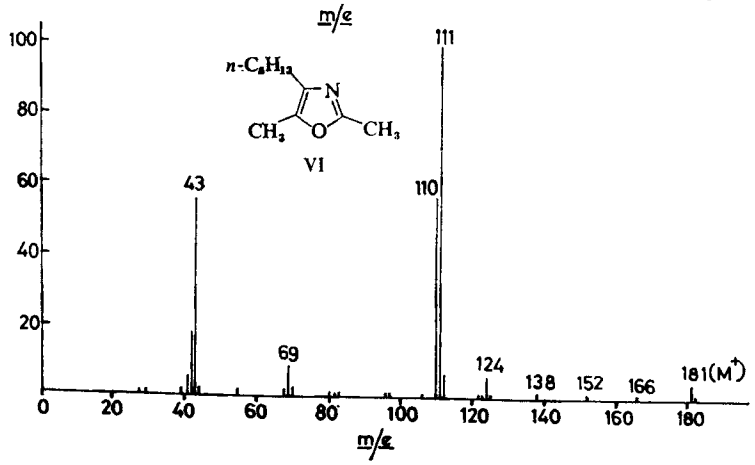


FIG. 3



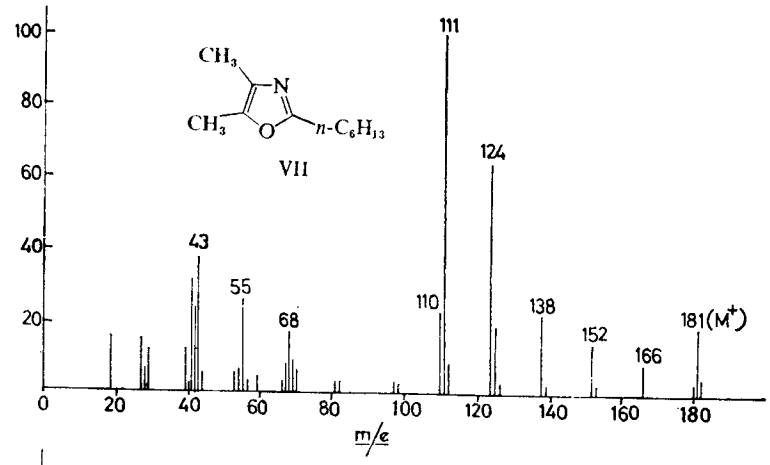


FIG. 4

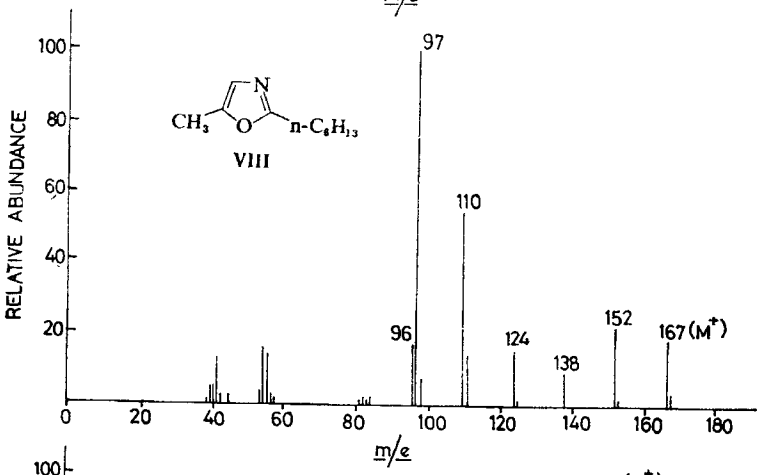


FIG. 5

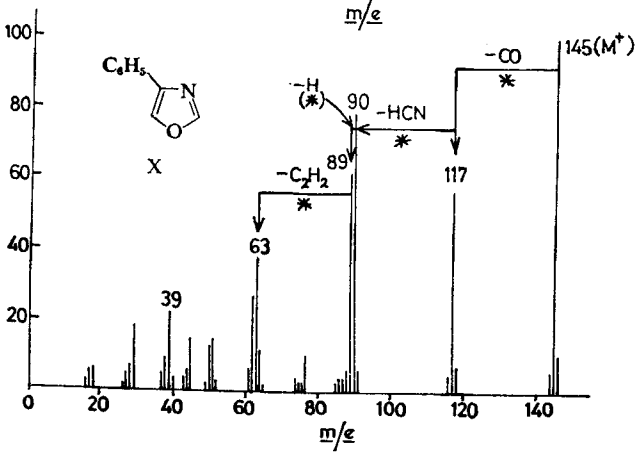


FIG. 6

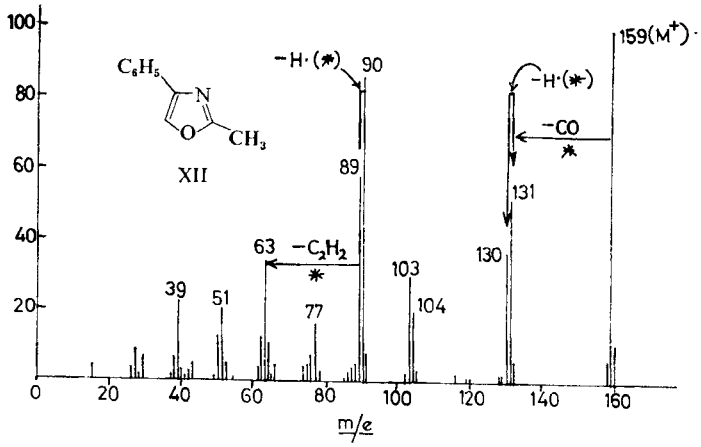


FIG. 7

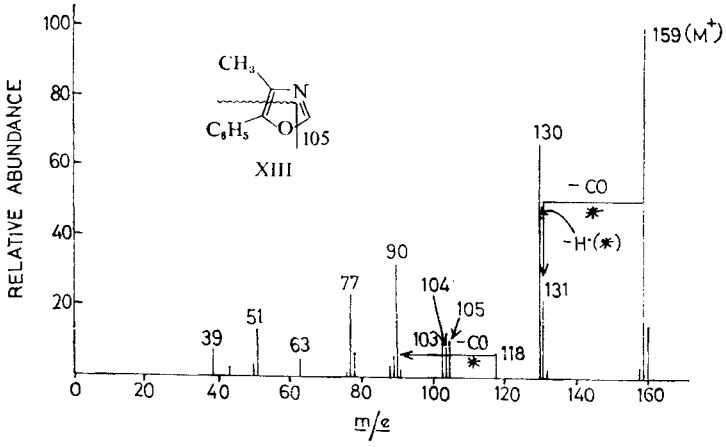


FIG. 8

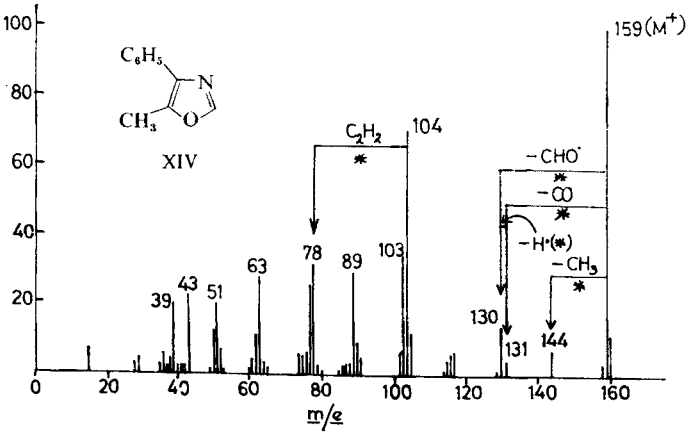
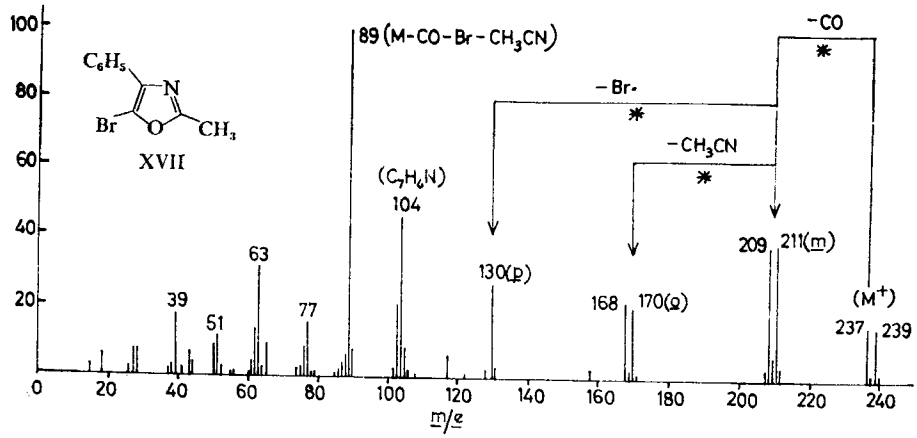
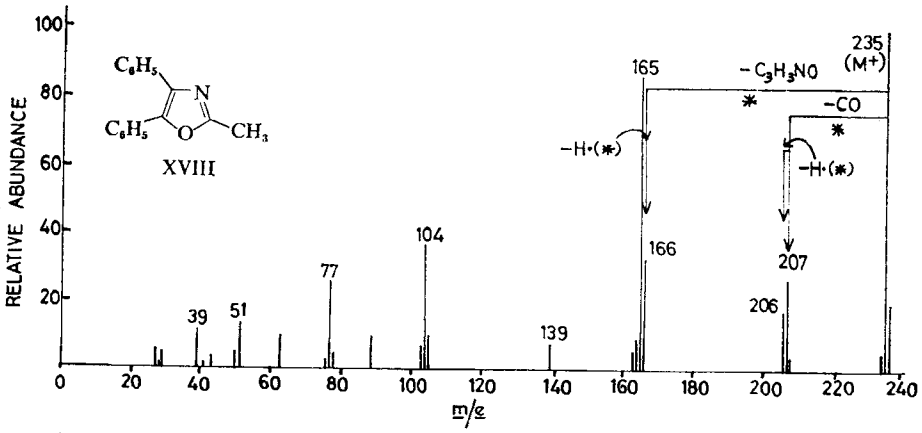


FIG. 9



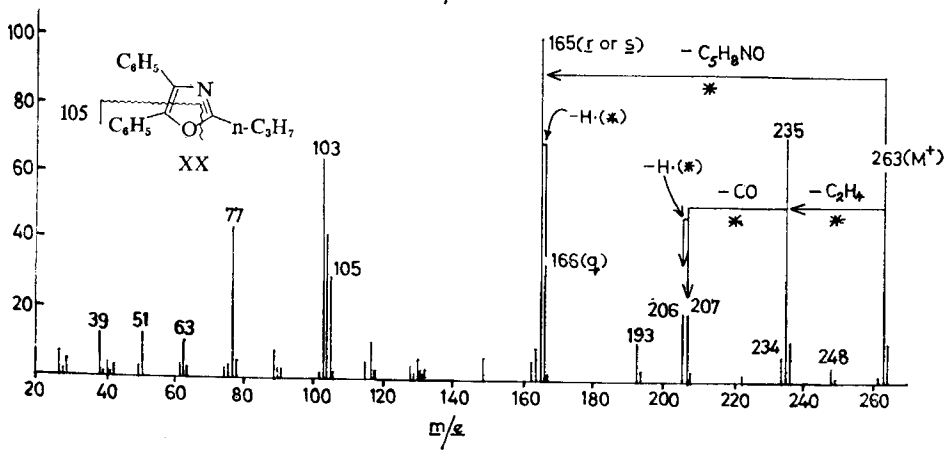
XVII

FIG. 10



XVIII

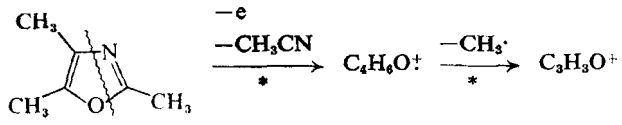
FIG. 11



XX

FIG. 12

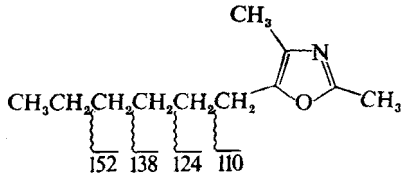
of the compounds. Thus, the M—HCN peak (*m/e* 70) of Fig. 1 is totally replaced by an M—CH_3CN peak from IV and this *m/e* 70 ion (*e*) then decomposes further by loss of a methyl radical to *m/e* 55. The one-step loss of CHO, however, from the molecular ion of IV to give *m/e* 82 ($C_5H_8N^+$, h.r.) demands a skeletal rearrangement in that form of the molecular ion undergoing this reaction, or a skeletal rearrangement



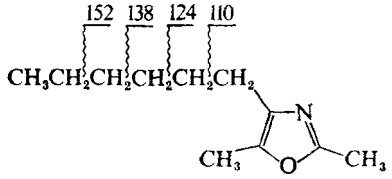
IV *e*, *m/e* 70 *m/e* 55

during the reaction leading to *m/e* 82.

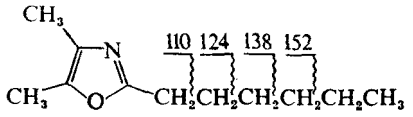
Since the only noteworthy feature of the spectra of simple methyl oxazoles is that the isomeric dimethyloxazoles II and III give different spectra, these have been dealt with rather summarily. However, since the fragmentation pattern of an aliphatic chain attached to a nitrogen heterocycle is known to vary with the site of attachment relative to the heterocyclic nitrogen atom,[5,6] the isomeric dimethyl-*n*-hexyl oxazoles V, VI and VII have been synthesized and their spectra (Figs. 2, 3 and 4) compared. 5-Methyl-2-n-hexyloxazole (VIII) was also available and its spectrum is reproduced in Fig. 5. In the spectra of the two compounds containing the *n*-hexyl chain in the 2-position (Figs. 4 and 5), the fragmentation of the side chain is very similar, and in particular the peaks due to β-cleavage (*m/e* 110 in Fig. 4 and *m/e* 96 in Fig. 5) are



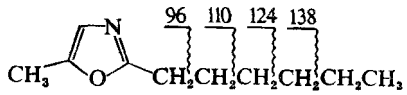
V



VI



VII



VIII

much smaller than those arising due to β-cleavage with hydrogen rearrangement (*m/e* 111 in Fig. 4 and *m/e* 97 in Fig. 5). The situation is superficially analogous (i.e. β-cleavage with hydrogen rearrangement more pronounced than simple β-cleavage) in the spectrum (Fig. 3) of 2,5-dimethyl-4-*n*-hexyloxazole (VI), but a sharp contrast is observed for the 5-*n*-hexyl isomer (Fig. 2) where β-cleavage is much more pronounced than the same process accompanied by hydrogen rearrangement [*m/e* 110 (100%, M—C_5H_{11}), *m/e* 111 (20%, M—C_5H_{10})].

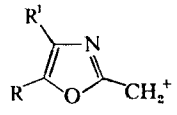
If the reasonable assumptions are made that (i) the products of the β-cleavage reactions arise predominantly from the molecular ions in one-step processes and (ii) the further decomposition reactions (if any) of these products occur at similar rates, then the ratios $[M-C_5H_{11}]/[M]$ and $[M-C_5H_{10}]/[M]$ (in terms of relative peak heights) will give the approximate relative rates of the β-cleavage processes in V–VIII.[7] The relevant data have been summarized in Table 2, which also gives data for the simple α-cleavage reaction (i.e. $[M-C_4H_9]/[M]$).

TABLE 2. APPROXIMATE RELATIVE RATES OF β-CLEAVAGE, β-CLEAVAGE WITH HYDROGEN REARRANGEMENT, AND γ-CLEAVAGE REACTIONS IN THE SPECTRA OF V–VIII*

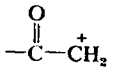
Substitution pattern	$[M-C_5H_{11}]/[M]$	$[M-C_5H_{10}]/[M]$	$[M-C_4H_9]/[M]$
2,4-Dimethyl-5-*n*-hexyl (V)	10·0	2·1	0·4
2,5-Dimethyl-4-*n*-hexyl (VI)	14·3	23·5	1·5
4,5-Dimethyl-2-*n*-hexyl (VII)	1·3	5·5	3·5
5-Methyl-2-*n*-hexyl (VIII)	1·0	5·5	3·1

* Relative peak heights are corrected for ^{13}C isotope contributions.

From the data in Table 2, it is evident that the rate of simple β-scission is much less in the 2-*n*-hexyl oxazoles VII and VIII than in the 4-*n*-hexyl-(VI) or 5-*n*-hexyl-(V) isomers. These observations again recall the relatively low abundance of the M-15 ion from 2-ethylpyridine[5b] and are compatible with the destabilization of a carbonium ion separated from a heterocyclic nitrogen atom by a double bond (*f*). This system (*f*) bears analogy to a carbonium ion adjacent to a keto group (*f'*), which is also a relatively unstable system.[5c] In contrast, when the rate of simple β-cleavage is slow, the process of γ-fission is enhanced (Table 2). Enhanced γ-cleavage reactions are also observed in the mass spectra of alkyl imines,[8] oximes,[9] semicarbazones,[10] and 2-alkylquinolines,[6] all of which contain the $-N=C-CH_2CH_2R$ system. Allylic

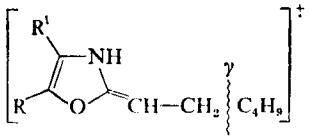


f

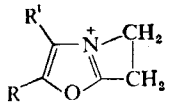


f'

cleavage in the tautomeric form *g* of the molecular ion, or formation of a cyclic ion *h* are plausible rationalizations which can account for the enhanced γ-cleavage.[11]



g

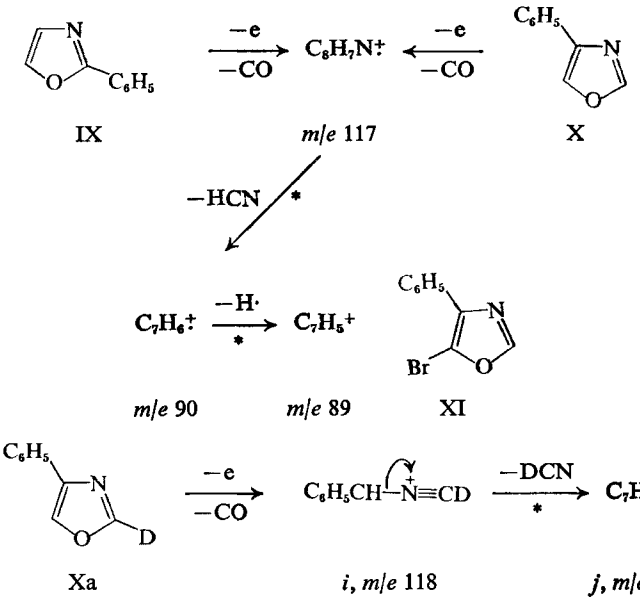


h

The reaction corresponding to β-cleavage with hydrogen rearrangement proceeds at a similar rate in the 5-hexyl compound V to the analogous reaction in *n*-butylbenzene[12] or 2-*n*-pentylfuran.[13] A significant rate enhancement is observed when

the *n*-hexyl chain is in the 2-position, and the reaction becomes very favourable when the *n*-hexyl chain is in the 4-position (Table 2 and *m/e* 111 in Fig. 3). The process of *β*-cleavage with hydrogen rearrangement is also favoured in alkylpyrazines[5d] and 2-alkylquinolines.[6]

The fragmentation reactions occurring in the isomeric phenyloxazoles, 2-phenyloxazole (IX, Table 1) and 4-phenyloxazole (X, Fig. 6) are very similar, both molecular ions sequentially eliminating CO (h.r., broad metastable peaks at *m/e* 94·5) and HCN (metastable peaks at *m/e* 69·3) to give *m/e* 90. The *m/e* 90 ion then loses a hydrogen atom to give *m/e* 89. However, the two hydrogens of the oxazole ring are predominantly not randomized in the M—CO ion from 4-phenyloxazole (X), since the M—CO ion from 2-d_1-4-phenyloxazole (Xa, Table 1) decomposes almost completely (94%)



by loss of DCN rather than by loss of HCN (4%). The M—CO ion from Xa is therefore represented as *i* (*m/e* 118), which can lose DCN to give *j* (*m/e* 90).

The introduction of a bromine atom at C-5 into 4-phenyloxazole (X) does not greatly change the fragmentation pattern, 4-phenyl-5-bromo-oxazole (XI) sequentially eliminating CO, HCN and Br (i.e. *m/e* 223/225 → 195/197 (h.r.) → 168/170 (h.r.) → 89, see Table 1). The only competing decomposition involves overall loss of COBr to give *m/e* 116.

The spectrum (Fig. 7) of 2-methyl-4-phenyloxazole (XII) has been analysed with the aid of high resolution data (Table 3) and the spectra (Table 1) of 5-d_1-2-methyl-4-phenyloxazole (XIIa) and 2-d_1-methyl-4-phenyloxazole (XIIb).

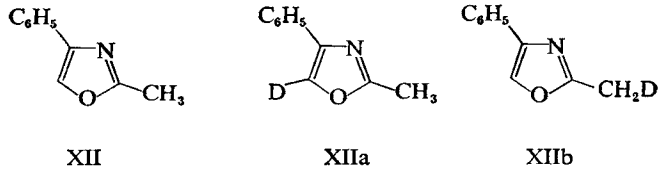
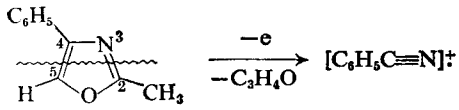


TABLE 3. COMPOSITIONS OF ABUNDANT FRAGMENT IONS IN THE SPECTRUM (Fig. 7) OF 2-METHYL-4-PHENYLOXAZOLE (XII)

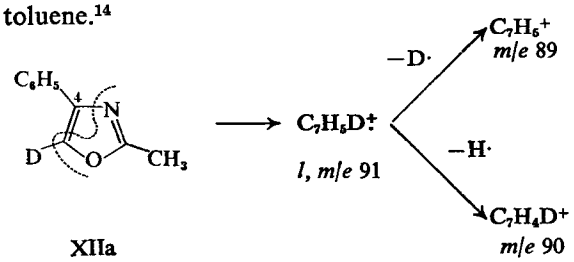
Ion (*m/e*)	Composition	Derivation
131	C_9H_9N	M—CO
130	C_9H_8N	M—CHO
104	C_7H_6N (60%)	M—C_3H_3O
	C_8H_8 (40%)	M—CO—HCN
103	C_7H_5N (95%)	M—C_3H_4O
	C_8H_7 (5%)	M—CHO—HCN
90	C_7H_6	M—CO—CH_3CN
89	C_7H_5	M—CO—CH_3CN—H

The *m/e* 131 ion of Fig. 7 is formed by loss of carbon monoxide from the molecular ion and the further loss of a hydrogen radical to *m/e* 130 involves loss of the C-5 hydrogen to the extent of less than 10% [as evidenced by the almost complete shift of *m/e* 130 to *m/e* 131 in the spectrum of XIIa (Table 1), after correction for a small amount of d_0-contaminant]. A rough calculation applied to the spectrum (Table 1) of the 2-d_1-methyl derivative (XIIb) implicates the methyl hydrogens in this reaction to the extent of approximately 60%. Although 40% of the *m/e* 104 ion formally corresponds to a fragment ion produced by sequential loss of CO and HCN, there is no metastable peak to establish the *m/e* 131 → 104 transition. The *m/e* 103 peak (Fig. 7) is formed almost exclusively by loss of C_3H_4O from the molecular ion and is not shifted in the spectra of either XIIa or XIIb. Hence the *m/e* 103 peak corresponds to ionized benzonitrile (*k*) formed by cleavage of the 2,3- and 4,5-bonds.



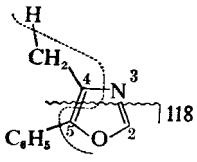
XII *k*, *m/e* 103

The large peak at *m/e* 90 (Fig. 7) is almost quantitatively shifted to *m/e* 91 in the spectrum of XIIa but very largely remains at *m/e* 90 in the spectrum of XIIb. Since *m/e* 90 arises by formal loss of CO and CH_3CN (Table 3), the C-5 deuterium of XIIa most probably migrates to C-4, or less likely, to the phenyl ring, in this reaction (XIIa → I). The ion I then decomposes by loss of a deuterium atom or a hydrogen atom, as evidenced by the only partial shift of *m/e* 89 (Fig. 7) to *m/e* 90 in the spectrum (Table 1) of XIIa. These observations again emphasize that the hydrogens of the aromatic oxazole ring are not randomized with the hydrogens of a methyl substituent for the reactions under consideration, in contrast to the almost complete randomization observed for toluene.[14]

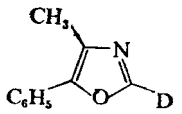


XIIa

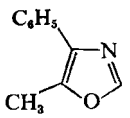
The spectra (Figs. 8 and 9) of 4-methyl-5-phenyloxazole (XIII) and 4-phenyl-5-methyloxazole (XIV) are quite different from each other (and from that of XII) and hence fragmentation does not proceed after the production of a common molecular ion. For example, *m/e* 103 from XIII is solely due to $C_8H_7^+$ (h.r., M—C_2H_2NO) [the spectrum (Table 1) of the 2-d_1-derivative XIIIa establishes the loss of the C-2 hydrogen atom in its formation, perhaps with phenyl migration as indicated by the dotted lines in XIII], while *m/e* 103 from XIV is solely due to $C_7H_5N^+$ [ionized benzonitrile]. This fragmentation also gives rise to a peak at *m/e* 103 in the spectrum of the 2-d_1-derivative XIVb (Table 1). In addition, *m/e* 104 from XIII is solely due to $C_8H_8^+$ (M—CO—HCN, h.r.), whereas the *m/e* 104 peak from XIV is solely due to $C_7H_4O^+$. The spectra of the labelled derivatives establish that the C-2 hydrogen is lost in the formation of these ions, but their origins are not simple.



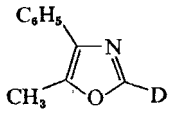
XIII



XIIIa



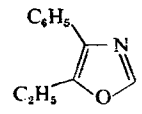
XIV



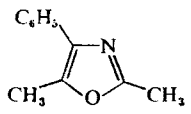
XIVa

Fragmentation of XIII also occurs via rupture of 2,3- and 4,5-bonds, but with charge retention by the oxygen-containing fragment ($C_8H_6O^+$, h.r., M—CH_3CN, *m/e* 118); the *m/e* 118 ion then decomposes by loss of carbon monoxide to *m/e* 90 (Fig. 8). As expected, the *m/e* 118 and *m/e* 90 ions of Fig. 8 are quantitatively shifted to *m/e* 119 and *m/e* 91 in the spectrum (Table 1) of XIIIa. In both spectra (Figs. 8 and 9), loss of CO from the molecular ion affords ions of mass *m/e* 131 which then undergo the pronounced loss of a hydrogen atom to *m/e* 130 (cf. also Fig. 7), although the *m/e* 130 ion is also formed in a one-step process from XIV. Surprisingly, a metastable peak at *m/e* 107·3 in the spectrum of XIVa establishes that XIVa loses CHO in the one-step process rather than CDO, this implying rearrangement in the molecular ion prior to this fragmentation. The *m/e* 105 ion from XIII (Fig. 8) is associated with the benzoyl ion ($C_6H_5C{\equiv}O^+$, h.r.).

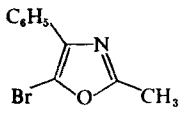
One of the most intriguing features of the spectra so far discussed is the marked tendency for many of the oxazoles (see Figs. 6–9) to eliminate carbon monoxide from the molecular ion. In the compounds hitherto described, this process has necessitated only the migration of a hydrogen atom, but it was considered of interest to study this reaction in compounds in which both positions 2 and 5 carried substituent groupings. A variety of additional oxazoles (XV–XXII) were therefore synthesized, the majority of which (XVI–XXII) carried alkyl, aryl or bromine substituents in both the 2- and 5-positions.



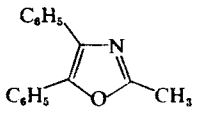
XV



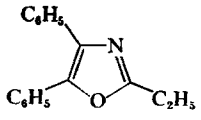
XVI



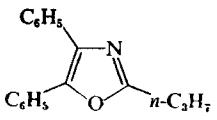
XVII



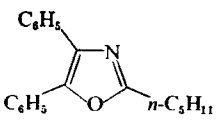
XVIII



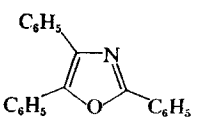
XIX



XX



XXI



XXII

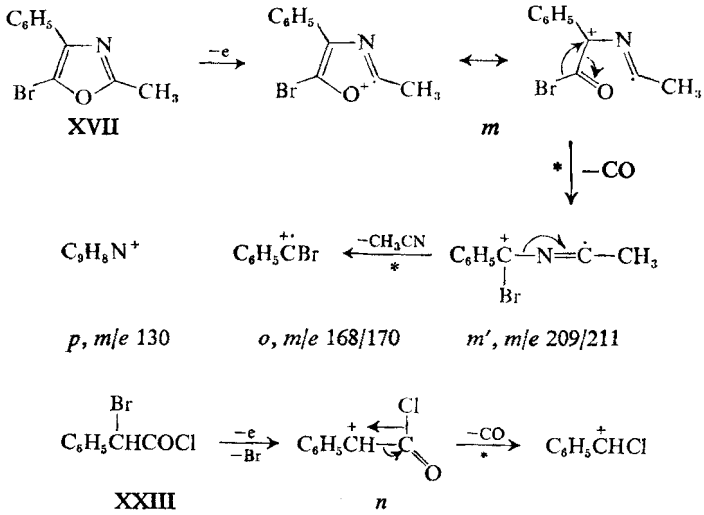
The abundances of the M-28 ions, and their compositions as established by high resolution measurements, are summarized in Table 4.

The data in Table 4 show that (i) the loss of carbon monoxide from the molecular ions of compounds containing ethyl or larger saturated alkyl substituents at C-2 or C-5 does not occur (XV, XX, XXI) or is a very minor process (XIX), (ii) when the substituents in both the 2- and 5-positions are methyl groups (XVI), no loss of CO

TABLE 4. ABUNDANCES AND COMPOSITIONS OF M-28 IONS FROM THE OXAZOLES XV–XXII

Compound	Rel. Ab. [M-28](%)	Composition
XV	1	M—C_2H_4
XVI	0	—
XVII	78	M—CO
XVIII	27	M—CO
XIX	2	M—CO
XX	72	M—C_2H_4
XXI	4	M—C_2H_4
XXII	23	M—CO

occurs but a metastable peak establishes the loss of ketene in a one-step process from the molecular ion to give *m/e* 131 (Table 1), (iii) if the C-5 substituent is bromine (XVII) or phenyl (XVIII, XXII) and any alkyl substituents present are not larger than methyl (XVII, XVIII), the loss of CO from the molecular ion is a prevalent process. The last point may be illustrated by reference to the spectra (Figs. 10 and 11) of 2-methyl-4-phenyl-5-bromo-oxazole (XVII) and 2-methyl-4,5-diphenyloxazole (XVIII). In the former spectrum (Fig. 10) all the peaks in the high mass region stem from the M—CO ion (*m/e* 209/211). Since the presence of methyl groups in both the 2- and 5-positions does not permit loss of CO from XVI, it must be concluded that bromine migrates prior to loss of CO from XVII and that phenyl groups migrate prior to the loss of CO from XVIII and XXII. Thus, if ionization of XVII occurs to some extent with ring opening to give *m*, then bromine migration to the carbonium ion centre with concerted loss of CO will afford *m'* (*m/e* 209/211). Such 1,2-shifts to carbonium ion centres generated upon electron impact are well established[15] (e.g. chlorine migration in the M—Br ion *n* from α-bromo-α-phenylacetyl chloride XXIII[15]). The decomposition of *m'* by loss of CH_3CN and Br, established by metastable peaks (Fig. 10), can then proceed to *o* and *p*.



XVII

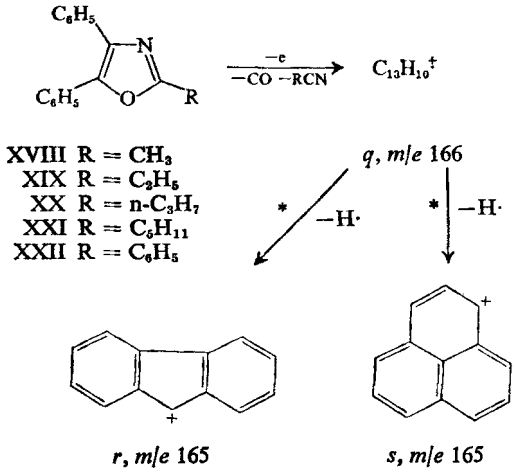
m

p, *m/e* 130 *o*, *m/e* 168/170 *m'*, *m/e* 209/211

XXIII

n

Bond forming reactions also occur during the fragmentation of 4,5-diphenyloxazoles (XVIII–XXII) as evidenced by abundant ions of mass *m/e* 165 and 166 in their spectra (see Figs. 11 and 12, and Table 1). The *m/e* 165 ion ($C_{13}H_9^+$) corresponds to the base peak, or greater than 70% of the base peak abundance in all cases. Appropriate metastable peaks and low voltage spectra establish that the *m/e* 165 species are daughter ions of *m/e* 166 (*q*, $C_{13}H_{10}^{+\cdot}$), which formally originates from the two phenyl rings and one carbon atom of the oxazole nucleus.* The facile loss of a hydrogen atom is almost certainly associated with rearrangement to the fluorenyl cation *r* (*m/e* 165) or to the phenalenium cation *s* (*m/e* 165, by more extensive rearrangement). When R is ethyl or larger (XIX–XXI) fragmentation within the alkyl group may precede the formation of *m/e* 165 and 166, but in a number of the spectra metastable peaks suggest the formation of *m/e* 166 (and even *m/e* 165, see Fig. 12) from the molecular ion in a one step process. Such metastable peaks do not however exclude the operation of a two-step process.[16]



XVIII R = CH_3
XIX R = C_2H_5
XX R = n-C_3H_7
XXI R = C_6H_{11}
XXII R = C_6H_5

q, *m/e* 166

r, *m/e* 165 *s*, *m/e* 165

* The origin of *m/e* 165 ions in related systems will be the subject of a subsequent publication.

The analytical usefulness of the generalizations outlined in this paper are emphasized in the spectrum (Fig. 12) of 2-*n*-propyl-4,5-diphenyloxazole (XX). The large peak (*m/e* 235) due to loss of ethylene from the molecular ion, but only a small peak (*m/e* 234) due to loss of an ethyl radical, suggests the presence of a *n*-propyl substituent at C-2 (cf. Table 2), whereas the occurrence of the base peak at *m/e* 165 (*r* or *s*) is indicative of the two phenyl substituents. It is noteworthy that the M—C_2H_4 ion (*m/e* 235, Fig. 12) behaves in the same manner as the molecular ion of XVIII (Fig. 11) in sequentially eliminating CO and H to give *m/e* 207 ($C_{15}H_{13}N$, h.r.) and *m/e* 206 ($C_{15}H_{12}N$; h.r.). In an analogous manner 2-*n*-pentyl-4,5-diphenyloxazole sequentially eliminates C_4H_8, CO and H to give *m/e* 206 (Table 1). In the case of 2-ethyl-4,5-diphenyloxazole (XIX) such a sequence cannot operate, but the *m/e* 206 ion is still abundant (Table 1) and is apparently formed from the molecular ion by loss of an acetyl radical in a one-step process (metastable peak at *m/e* 170·3). Such a reaction would require extensive rearrangement in the molecular ion, and while this is not excluded, the sequential loss of CO and CH_3[16] would seem more plausible.

To summarise, the present study establishes that (i) the isomeric alkyl oxazoles studied give different spectra, in contrast to the behaviour of the simple alkyl benzenes; thus common intermediates are not generated from these isomeric alkyl oxazoles upon electron impact, (ii) deuterium atoms inserted into the oxazole nucleus, or incorporated in methyl groups attached to the oxazole nucleus, are not randomized with hydrogen atoms at other nuclear positions prior to the major fragmentation pathways, again in contrast to the simple alkyl benzenes, (iii) the position (2, 4 or 5) of an alkyl substituent (*n*-propyl or larger) is indicated by its characteristic fragmentation pattern, and (iv) the elimination of CO occurs even from the molecular ion of 2,5-disubstituted compounds, probably via ring opening to an ionized ketone and subsequent (or associated) migration of the C-5 substituent to C-4.

EXPERIMENTAL

Mass spectra were measured with an Hitachi Perkin-Elmer R.M.U. 6D mass spectrometer operating at 75 eV, with an inlet and source temperature of ca. 150°. Exact mass measurements were determined with an A.E.I. MS 9 mass spectrometer using a resolution of 15,000 (10% valley definition) with heptacosafluorotributylamine providing reference masses.

All samples (with the exception of XXII, which was recrystallized) were purified by preparative vapour phase chromatography (using a 30 ft SE 30 column) and were additionally checked by nuclear magnetic resonance spectroscopy.

The following compounds were synthesized by reported procedures: III,[17] IV,[17] X,[18] XII,[17] XIII,[18] XIV,[18] XV,[18] XVI,[17] XVIII,[19] XX,[17] XXI,[20] and XXII.[19]

3-*Hydroxybutan*-2-*one heptoate*. Potassium heptoate (39 g) was added to 3-bromobutan-2-one (34·5 g) in ethanol (150 ml) containing 2 drops of concentrated sulphuric acid, and the mixture stirred and heated under reflux for eight hours. Removal of the solvent under reduced pressure gave a yellow oil, which was distilled *in vacuo* to give 3-hydroxybutan-2-one heptoate (17 g, 37%), b.p. 126–128°/12 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{20}O_3$: C, 65·95; H, 10·05. Found: C, 65·6; H, 10·0%.)

2-*n*-*Hexyl*-4,5-*dimethyloxazole* (VII). 3-Hydroxybutan-2-one heptoate (17 g) and ammonium acetate (43 g) in glacial acetic acid (120 ml) were heated under reflux for two hours. The cooled solution was poured onto ice (200 g) and extracted with ether (4 × 100 ml). The ethereal extract was washed with aqueous sodium hydrogen carbonate and water, and dried (Na_2SO_4). After removal of the ether, the residual oil was distilled *in vacuo* to give 2-*n*-hexyl-4,5-dimethyloxazole (7·55 g, 48%), b.p. 91–92°/4·5 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$. C, 72·9; H, 10·5; N, 7·7: Found: C, 72·9; H, 10·5; N, 7·6%.)

2-Hydroxynonan-3-one. To a stirred solution of n-hexyl lithium [from lithium (14 g) and n-hexylbromide (165 g)] in ether (500 ml) at −10° under nitrogen, was added a solution of lactic acid (20 g) in ether (100 ml) over a period of thirty minutes. The temperature was kept below −5° during the addition, then the mixture was stirred at 0° for three hours, allowed to rise to room temperature and stirred for an additional five hours. The solution was cooled to 0°, decomposed with water, and the ethereal layer separated. The ether layer was washed with aqueous sodium hydroxide (10%), dilute hydrochloric acid (2%), water, and then dried (Na_2SO_4). Removal of the ether under reduced pressure gave a yellow oil, which on distillation *in vacuo* gave 2-hydroxynonan-3-one (3·7 g, 12%), b.p. 85–87°/3·8 mm Hg. This compound was characterized as the acetate (prepared by treatment of the keto alcohol with acetic anhydride in pyridine), b.p. 96–97°/9 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{20}O_3$: C, 65·95; H, 10·05. Found: C, 66·35; H, 10·0%.)

4-n-Hexyl-2,5-dimethyloxazole (VI). 2-Hydroxynonan-3-one (5·3 g) acetyl chloride (7 ml) and pyridine (1·5 ml) were treated under reflux for thirty minutes. The solution was cooled, dry benzene (25 ml) added, the solvent removed under reduced pressure, and the crude ester remaining together with ammonium acetate (20 g) was dissolved in glacial acetic acid (70 ml) and heated under reflux for 1·5 hours. After cooling, the solution was poured onto ice (300 g), extracted with ether (2 × 100 ml), and the extract washed with aqueous sodium carbonate, water, and then dried (Na_2SO_4). Removal of the ether and distillation of the remaining oil *in vacuo* gave 4-*n*-hexyl-2,5-dimethyloxazole (2·8 g, 46%), b.p. 70–76°/2·6 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$: C, 72·9; H, 10·5; N, 7·7. Found: C, 72·7; H, 10·4; N, 8·2%.)

5-n-Hexyl-2,4-dimethyloxazole (V). Prepared as for VI. 3-Hydroxynonan-2-one[25] (6·0 g) gave 5-n-hexyl-2,4-dimethyloxazole (1·7 g, 23%), b.p. 79–80°/4 mm Hg. (*Anal.*: Calcd. for $C_{11}H_{19}NO$: C, 72·9; H, 10·5; N, 7·7. Found: C, 72·85; H, 10·4; N, 8·1%.)

5-Bromo-4-phenyloxazole (XI). To a stirred solution of 4-phenyloxazole[22] (14·5 g) in carbon tetrachloride (100 ml) containing dibenzoylperoxide (10 mg) was added N-bromosuccinimide (17·8 g) over a period of 2 hours at room temperature. The reaction mixture was stirred for a further two hours, filtered, the solvent removed, and the oil remaining was sublimed at 80°/0·05 mm Hg, giving 5-bromo-4-phenyloxazole (19·3 g, 86%), m.p. 44–45°. (*Anal.*: Calcd. for C_9H_6NOBr: C, 48·25; H, 2·7; N, 6·25; Br, 35·6. Found: C, 48·4; H, 3·0; N, 6·1; Br. 35·3%.) Treatment of 5-bromo-4-phenyloxazole with methyl magnesium iodide quantitatively produced 5-methyl-4-phenyloxazole (XIV) identical with an authentic specimen (V.P.C. and infrared spectrum).

5-Bromo-2-methyl-4-phenyloxazole (XVII). Prepared as for XI. 2-Methyl-4-phenyloxazole (6·4 g) gave 5-bromo-2-methyl-4-phenyloxazole (7·8 g, 83%) as a colourless solid, m.p. 54–56°, after sublimation (90°/0·1 mm Hg.). (*Anal.*: Calcd. for $C_{10}H_8NOBr$: C, 50·65; H, 3·4; N, 5·9; Br, 33·6. Found: C, 50·9; H, 3·65; N, 5·5; Br, 32·3%.) The NMR spectrum lacks the singlet at $\delta = 7{\cdot}67$ ppm indicative of the 5-H of the oxazole system.[22]

2-n-Pentyl-4,5-diphenyloxazole (XXI). A solution of benzoin hexoate (50 g) and ammonium acetate (62 g) in glacial acetic acid (150 ml) was heated under reflux for two hours. The solution was cooled, poured onto ice (300 g) and extracted with ether (4 × 100 ml). The ethereal extract was washed with aqueous sodium carbonate (10%), water, and dried (Na_2SO_4). After removal of the ether, the residual oil was distilled *in vacuo* to yield 2-*n*-pentyl-4,5-diphenyloxazole (28·6 g, 64%), b.p. 177–178°/0·6 mm Hg. (*Anal.*: Calcd. for $C_{20}H_{21}NO$: C, 82·6; H, 7·2; N, 4·8. Found: C, 82·2; H, 7·3; N, 5·0%.)

Isotopically labelled compounds

All labelled compounds were produced in high yield and purified by preparative vapour phase chromatography.

2-d_1-4-Phenyloxazole (Xa). 4-Phenyloxazole (0·29 g) was treated with *n*-butyl lithium [prepared from *n*-butyl bromide (0·68 g) and lithium (0·086 g) in ether (30 ml)] at −65° for two hours. Addition of deuterium oxide (5 ml) gave 2-d_1-4-phenyloxazole, b.p. 89-90°/4 mm.

5-d_1-2-Methyl-4-phenyloxazole (XIIa). 5-Bromo-2-methyl-4-phenyloxazole (0·48 g) was treated with *n*-butyl lithium [as for (Xa)] at −65° for ten minutes. Addition of deuterium oxide (5 ml) gave 5-d_1-2-methyl-4-phenyloxazole, m.p. 54–56°.

2-(d_1-Methyl)-4-phenyloxazole (XIIb). 2-Methyl-4-phenyloxazole (0·32 g) in ether (30 ml) was added to a stirred solution of *n*-butyl lithium [as for (Xa)] at −65°. Stirring was continued (at −65°) for 2·5 hours, then deuterium oxide (5 ml) added, yielding 2-(d_1-methyl)-4-phenyloxazole,

m.p. 54–56°. The NMR spectrum showed that all deuterium was incorporated into the methyl group.

2-d_1-4-*Methyl*-5-*phenyloxazole* (XIIIa). As for Xa. 4-Methyl-5-phenyloxazole (0·32 g) gave 2-d_1-4-methyl-5-phenyloxazole, b.p. 107–108°/3 mm Hg.

2-d_1-5-*Methyl*-4-*phenyloxazole* (XIVa). As for Xa. 5-Methyl-4-phenyloxazole (0·32 g) gave 2-d_1-5-methyl-4-phenyloxazole, b.p. 87–88°/0·05 mm Hg.

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