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THE LABILITY OF NITROGEN-OXYGEN LINKAGE OF ISOXAZOLES UPON ELECTRON IMPACT

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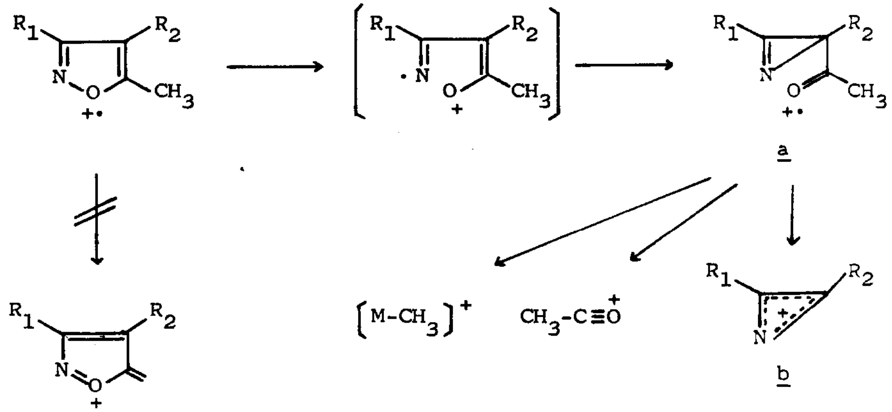
Although the mass spectra of furans,[1)] pyroles,[2)] thiophens,[3)] and thiazoles[4)] have been studied extensively, no systematic investigation of isoxazoles has been reported. The behavior of isoxazoles upon electron impact might reflect their unique character[5)] among five membered heterocyclics due to their aromaticity together with the lability of the N-O bond under chemical reactions. Furthermore recent developments to make use of isoxazoles as intermediates in the synthetic field[6)] have required the convenient identification tool for such intermediates. This paper deals with mass spectra of some simple 3,5-dimethyl-4-(3-oxoalkyl)-isoxazoles (Stork's intermediates[6)]) as well as related isoxazoles in order to characterize their fragmentation patterns.

3,5-Dimethylisoxazole (1) gives a strong molecular ion and the subsequent fragmentation is nicely formulated via an intermediate a (R_1= CH_3, R_2= H) which is similar to those of methylfurans.[1)] This fragmentation process accounts for the spectra of 3-aminoisoxazole (4) and its d_2 analog, i.e., both exhibit distinct peaks at m/e 43 but an abundant ion at m/e 55 in the former shifts to m/e 57 in the latter. These fragmentations are summarized in Scheme 1.

The striking difference between the spectrum of 1 and those of methylfurans[1,7a)] or thiophens[7b)] as to the relative abundance of M-1 peak is notewor-

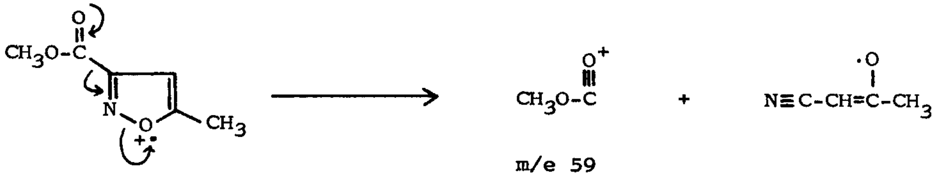


Scheme 1

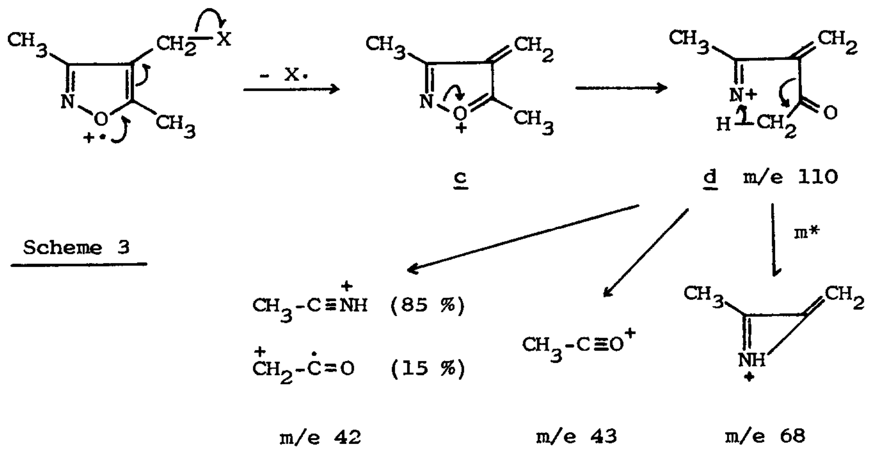
1) R_1= CH_3 , R_2= H m/e 54
2) R_1 = R_2 = CH_3 m/e 68
4) R_1= NH_2 , R_2= H m/e 55
$4d_2$) R_1= ND_2 , R_2= H m/e 57

thy, i.e., in case of the latter, the M-1 peak appears as a very abundant ion whereas in the former loss of a hydrogen radical is negligible. This is characteristic for isoxazoles and is probably due to the preferential cleavage of N-O linkage rather than a benzylic C-H bond rupture. Furthermore, in the spectrum of 3, the composition of the base peak at m/e 59 is established by accurate mass measurement as $C_2H_3O_2$, probably methoxycarbonyl ion. This suggests that concerted bond cleavages as shown in Scheme 2 may take place preferentially in this compound in accordance with the lability of N-O bond of isoxazole nucleus.

If an alkyl substituent is present at 4 position in 3,5-dimethylisoxazoles such as Stork's intermediates, strong peaks at m/e 110, 68, and 43 are common in their spectra and these peaks seem to be diagnostic of 4-alkyl-3,5-dimethylisoxazoles. The strong peak at m/e 110 in the spectra of 5 - 12 suggests the occurrence of the familiar aryl cleavage to give c, or the further N-O bond



Scheme 2



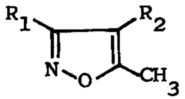
Scheme 3

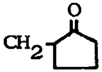
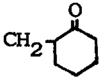
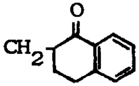
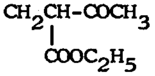
cleavage to give d, as shown in Scheme 3. The loss of 42 mass units from the m/e 110 ion afforded m/e 68 fragment, the composition of which was demonstrated as C_4H_6N by accurate mass measurement. One step formation of this fragment from m/e 110 ion was confirmed by the appearance of a meta-stable ion peak at m/e 42.0. These results suggest that a hydrogen migration is involved in this process and the step would be represented by a displacement type rearrangement[8)] (see arrows in d). The subsequent cyclization would lead to the m/e 68 ion. Therefore, d might be prefered to c for the structure of the m/e 110 ion, and the formation of d from the molecular ion may presumably take place in a concerted manner.

The mass spectra of 5 and 6 exhibit pronounced m/e 42 peaks of $C_2H_4N^+$ (85 %) plus $C_2H_2O^{+\cdot}$ (15 %). High resolution mass measurements also showed that strong m/e 43 peaks are due solely to $C_2H_3O^+$. These fragmentations are summarized in Scheme 3.

The general features of the spectra of Stork's intermediates (5 - 12) are very characteristic and show the above mentioned isoxazole peaks predominating over other fragmentations originating from carbonyl groups. The rest of the significant peaks listed in the last column of Table 1 are interpreted in terms of well-defined fragmentations of other functional groups in these compounds.

Table I : Principal Mass Spectral Peaks of Some 5-Methylisoxazoles* ** :



No.	R_1	R_2	$M^{+\cdot}$	M-15	M-43	m/e 110	m/e 68	m/e 43	m/e 42	others
1	CH_3	H	m/e 97 (60)	(77)	(83)	-	-	(100)	(14)	-
2	CH_3	CH_3	111 (100)	(86)	(85)	(16)	(85)	(85)	(71)	m/e 55 (58)
3	$COOCH_3$	H	141 (9)	-	-	-	-	(50)	(7)	59 (100) 82 (22)
4	NH_2	H	98 (100)	(5)	(55)	-	-	(38)	(8)	-
5	CH_3	CH_2OH	127 (100)	(12)	(64)	(25)	(75)	(88)	(82)	109 (36) 82 (64)
6	CH_3	CH_2Cl	145 (15)	-	-	(100)	(94)	(80)	(65)	-
7	CH_3	$CH_2CH_2COCH_3$	167 (16)	-	(8)	(33)	(44)	(100)	(16)	-
8	CH_3		193 (32)	-	(6)	(100)	(59)	(41)	(12)	-
9	CH_3		207 (23)	-	(4)	(100)	(46)	(35)	(10)	95 (17)
10	CH_3	$CH_2CH(COCH_3)_2$	209 (3)	-	(73)	(41)	(45)	(100)	(9)	124 (24)
11	CH_3		255 (45)	-	(29)	(100)	(64)	(58)	(12)	146 (46)
12	CH_3	 $CH_2CH(COOC_2H_5)\text{-}COCH_3$	239 (7)	-	(36)	(72)	(58)	(100)	(23)	166 (17) 124 (21)

* Relative abundances are shown in parentheses.

** All mass spectra were measured with a Hitachi RMU-6E double-focussing mass spectrometer, by using an all-glass inlet system heated to 200°C. The ionizing energy was maintained at 70 eV. and the ionizing total current at 80 µA.

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