MASS SPECTRA OF 3,4-DIHYDRO-4-IMINO-3-METHYLPYRIMIDINES, THEIR METHYLAMINO-ISOMERS, AND RELATED SYSTEMS

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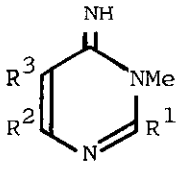
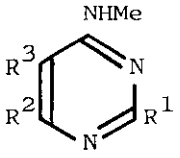
Those 3,4-dihydro-4-imino-3-methylpyrimidines and related systems, which undergo rapid Dimroth rearrangement in solution, have mass spectra indistinguishable from their methylamino-isomers. Similar imines, which do not rearrange easily, have their own fragmentation patterns. 4-Methylamino, methoxy, methylthio, and hydroxymethyl derivatives of pyrimidine and quinazoline, as well as the corresponding 6-substituted purines, have a common fragmentation pathway, hitherto unrecognized.

A rapid Dimroth-like rearrangement of 3,4-dihydro-4-imino-3-methyl-pyrimidine (1a) into 4-methylaminopyrimidine (2a) on electron bombardment has been postulated recently[1] to account for the identity in fragmentation pattern of both pyrimidines. The comparable mass spectra[2] of N^1- and N^6-methyladenosine probably stem[3] from the same type of isomerization.

This theory is supported by the data in Table 1: the 3,6-dimethylated imine (1b), which rearranges easily in aqueous alkali,[4] had a pattern



(1)



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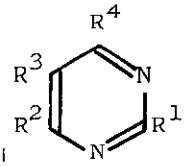


(3)

	R^1	R^2	R^3
a:	H	H	H
b:	H	Me	H
c:	Me	H	H
d:	H	H	Me
e:	Me	H	Me
f:	H	$-(CH_2)_3-$	
g:	H	$-(CH{:}CH)_2-$	
h:	Me	$-(CH{:}CH)_2-$	

R^1	R^2	R^3	R^4
H	H	H	CH_2OH
Me	Me	H	CH_2OH
H	$-(CH{:}CH)_2-$		OMe
H	-NH.CH:N-		NHMe
H	-NH.CH:N-		SMe
Me	-NH.CH:N-		SMe
H	-NH.CH:N-		SCD_3

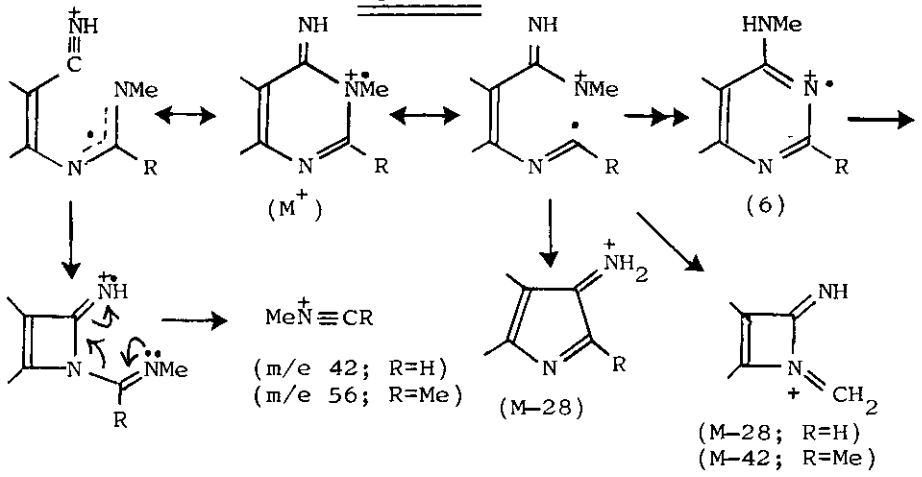
Table 1. Mass spectra of imines and isomeric methylamines

Cpd.	m/e (% abundance) [m* (derivation)]
(1a)	109(100), 80(20), 53(26), 42(28)
(2a)	109(100), 80(38) [58.8(80^2/109)], 53(49) [35.1(53^2/80)]
(1b)	123(100), 94(54) [71.7(94^2/123)], 67(41) [47.8(67^2/94)]
(2b)	123(100), 94(60) [71.7(94^2/123)], 67(52) [47.8(67^2/94)]
(1c)	123(100), 95(7), 81(13), 56(36)
(2c)	123(100), 94(67) [71.8(94^2/123)], 53(25), 42(44)
(1d)	123(100), 108(12), 95(32) [73.5(95^2/123)], 81(22) [60.7(81^2/108)], 42(55)
(2d)	123(100), 94(45) [71.8(94^2/123)], 67(40) [47.8(67^2/94)]
(1e)	137(100), 122(9), 109(8), 95(44), 81(10), 56(37)
(2e)	137(100), 108(53) [85.1(108^2/137)], 67(52) [41.6(67^2/108)], 42(25)
(1f)	149(100), 148(80), 134(3), 121(14), 107(22) [77.4(107^2/148)], 93(5), 42(34)
(2f)	149(100), 148(68), 120(43), 93(25), 65(16)
(1g)	159(100), 131(47), 118(75), 104(27), 91(15), 76(7), 63(6), 42(21)
(2g)	159(100), 130(49), 103(46) [81.6(103^3/130)], 76(9)
(1h)	173(100), 145(27), 131(33), 118(15), 104(45), 90(12), 76(21), 56(60)
(2h)	173(100), 144(75), 103(64) [73.7(103^2/144)], 76(30)

identical with that of its methylamino-isomer (2b); on the other hand, the 2- and/or 5-alkylated imines (1c-f), all of which undergo very slow rearrange-ment in solution,[4] exhibited fragmentation patterns quite different from those of their respective isomers (2c-f). Likewise the patterns for the 4-iminoquinazolines (1g,h), which rearrange very slowly,[5] differed from those for the 4-methylaminoquinazolines (2g,h).

Thus the imines (1c-f), which do not rearrange easily, fragment as in Scheme 1. In contrast, the imines (1a,b) undergo initial rearrangement to (6), as on the top line of Scheme 1, and then fragment as do the corresponding 4-methylaminopyrimidines[4] (Scheme 2). The latter pattern is seen as a general mechanism for the fragmentation of 4-NHMe, 4-SMe, 4-OMe, and even 4-CH_2OH derivatives of pyrimidine and quinazoline as well as similar 6-substituted purines. Indeed, it explains, for the first time in a satisfactory way, the data[6-9] summarised in Table 2. Although the α-bridged imines (4, n>5) do undergo rearrangement to β-bridged isomers (5, n>5) in solution, both systems have abnormal mass spectra[1,3] fitting neither of the

SCHEME 1



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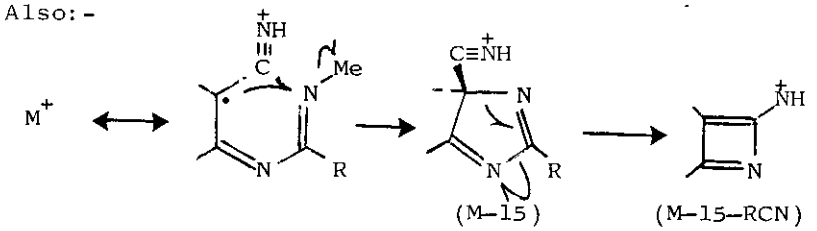


SCHEME 2

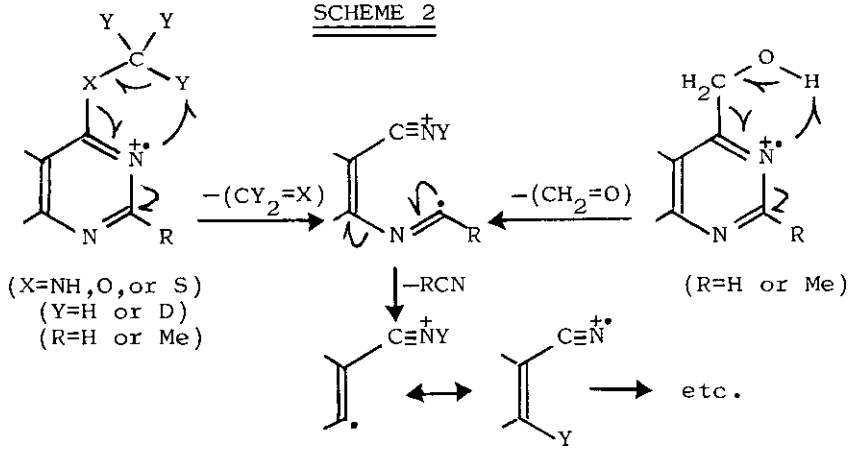
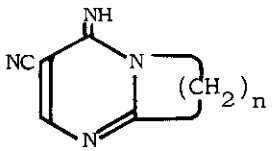


Table 2. Examples of the fragmentation of 4-methylaminopyrimidines and related compounds according to Scheme 2

Cpd	M^+	$-(CH_2=X)$	$-(RCN)$	$-(HCN)$	Cpd	M^+	$-(CY_2=X)$	$-(RCN)$	$-(HCN)$
(2a)	109 *→	80 *→	53 →	-	(3c)[b]	160 →	130 →	103 →	76
(2c)	123 *→	94 →	53 →	-	(3d)[c]	149 *→	120 *→	93 →	66
(2g)	159 →	130 *→	103 →	76	(3e)[d]	166 →	120 →	93 →	66
(3a)[a]	110 →	80 →	53 →	26	(3f)[d]	180 →	134 →	93 →	66
(3b)[a]	138 →	108 →	67 →	40	(3g)[d]	169 →	121 →	94 →	67,68

*Metastable peak visible. [a]Ref.6. [b]Ref.7. [c]Ref.8. [d]Ref.9.



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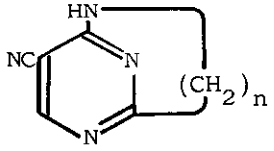

(5)

above patterns: each undergoes complete degradation of the polymethylene bridge by several routes prior to any fragmentation of the pyrimidine ring.

Imines were obtained as free bases for mass spectral measurement by briefly shaking their hydriodides with cold M-sodium hydroxide and chloroform, followed by evaporation of the lower layer. ^1H N.m.r. spectra indicated that no rearrangement had taken place. Mass spectra were kindly measured by Dr J.K. MacLeod on an MS9 instrument.

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