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The Mass Spectra of Pyrido[2,3-*d*]pyrimidines

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Mass spectra of 4-substituted pyrido[2,3-*d*]pyrimidines were examined.

Fragmentations of pyrido[2,3-*d*]pyrimidine (I), 4(3H)-pyrido[2,3-*d*]pyrimidinone (VIII), 4-chloropyrido[2,3-*d*]pyrimidine (IX) and 4-methoxypyrido[2,3-*d*]pyrimidine (X) were analogous to those of corresponding quinazoline derivatives, respectively. Fragmentation of 4-methylpyrido[2,3-*d*]pyrimidine (II) afforded $(M-\cdot H)^+$ intermediate written as diazatropylium ion **3′** in pathway leading to $[M-(\cdot H+CH{\equiv}CH)]^+$ ion **4**. 4-Ethylpyrido[2,3-*d*]pyrimidine (III), 4-phenylpyrido[2,3-*d*]pyrimidine (V) and 4-phenyl-3,4-dihydropyrido[2,3-*d*]pyrimidine (VI) gave intermediate written as cyclic fragment ion (**8**, **12**, **16**) as same as shown in fragmentation of 2-ethylquinoline and 1-ethylisoquinoline. In any way the predominant fragmentation of 4-substituted pyrido[2,3-*d*]pyrimidines was proceeded by consecutive loss of cyano radical and hydrogen cyanide accompanied with breakdown or migration of the substituent.

No systematic mass spectral investigation of pyrido[2,3-*d*]pyrimidines has been reported, although the mass spectral studies were performed on various simple quinazolines, and in several instances the techniques of deutrium labelling and low voltage mass spectrometry were utilized.[2]

Now we present the mass spectra of pyrido[2,3-*d*]pyridimine (I) and certain of its derivatives[3] prepared by T. Higashino and his co-worker and discuss their fragmentation under electron impact.

The compounds studied in this paper are as follows; pyrido[2,3-*d*]pyrimidine (I), 4-methylpyrido[2,3-*d*]pyrimidine (II), 4-ethylpyrido[2,3-*d*]pyrimidine (III), 4-pyrido[2,3-*d*]-pyrimidinecarbonitrile (IV), 4-phenylpyrido[2,3-*d*]pyrimidine (V), 4-phenyl-3,4-dihydropyrido[2,3-*d*]pyrimidine (VI), 2-(3,4-dihydro-4-pyrido[2,3-*d*]pyrimidinyl)acetophenone (VII), 4(3H)-pyrido[2,3-*d*]pyrimidinone (VIII), 4-chloropyrido[2,3-*d*]pyrimidine (IX) and 4-methoxypyrido[2,3-*d*]pyrimidine (X).[3] The mass spectra of these compounds are shown in Chart 1 to 10 and Table I in which all peaks have an abundance of 2 percent or greater relative to the base peak (100%). The observed metastable peaks are in Table II. The asterisk under the arrow in Chart denotes an appropriate metastable peak has been observed in its mass spectrum.

Table I. Mass Spectra of 4-Substituted Pyrido[2,3-*d*]pyrimidines

Compounds																	
I	*m/e*	132	131	130	105	104	103	78	77	76	75						
	I (%)	13	100	4	4	42	9	6	60	20	7						
II	*m/e*	146	145	144	131	130	119	118	117	105	104	103	92	91	90	78	77
	I (%)	11	100	10	2	9	2	13	3	4	27	17	2	8	3	11	28
	m/e	76	75														
	I (%)	12	4														
III	*m/e*	159	158	157	132	131	130	129	105	104	103	90	79	78	77	76	75
	I (%)	93	100	6	10	30	2	2	5	35	18	2	2	6	18	16	4

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[1] Location: *2-2-1 Oshika, Shizuoka-Shi.*

[2] J.S. Fitzgerald, S.R. John, J.A. Lamberton and A.H. Redcliffe, *Austral. J. Chem.*, **19**, 151 (1966); T.J. Batterham, A.C.K. Triffett and J.A. Wunderlich, *J. Chem. Soc.* (B), **1967**, 892.

[3] T. Higashino and E. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **18**, 1457 (1970).

Compounds																	
IV	*m/e*	157	156	132	131	130	129	105	104	103	102	101	78	77	76	75	
	I (%)	13	100	3	22	5	15	5	45	10	17	4	7	44	19	11	
V	*m/e*	208	207	206	205	181	180	179	178	154	153	152	151	128	127	126	125
	I (%)	21	100	73	3	4	20	36	3	3	8	10	2	2	5	5	3
	m/e	104	103	102	101	100	99	88	87	78	77	76	75	74			
	I (%)	7	12	3	2	2	2	2	2	5	23	15	6	3			
VI	*m/e*	210	209	208	207	206	181	180	179	178	165	154	153	152	133	132	131
	I (%)	12	37	69	11	10	2	8	3	4	3	3	3	2	12	100	11
	m/e	128	127	126	105	104	103	102	90	89	79	78	77	76	75	74	
	I (%)	2	7	3	8	15	3	2	3	3	6	13	11	4	3	2	
VII	*m/e*	252	251	147	146	145	133	132	131	129	120	119	118	106	105	104	103
	I (%)	3	9	14	100	2	6	50	8	3	6	3	2	2	20	6	3
	m/e	102	91	79	78	77	76	75									
	I (%)	2	3	2	14	25	4	3									
VIII	*m/e*	149	148	147	146	121	120	119	118	93	92	91	78	77	76	75	67
	I (%)	4	9	100	2	2	8	20	4	10	24	6	2	3	4	2	2
	m/e	66	65	64	63												
	I (%)	2	7	8	3												
IX	*m/e*	168	167	166	165	131	130	105	104	78	77	76					
	I (%)	4	26	9	78	8	63	11	100	8	38	13					
X	*m/e*	162	161	160	134	133	132	131	130	105	104	103	93	92	91	79	78
	I (%)	12	100	30	2	5	19	23	2	13	63	15	2	3	10	2	2
	m/e	77	76	75													
	I (%)	18	16	4													

TABLE II. Metastable Peaks and Associated Transitions[a]

Compounds						
I	131—104 (82.6) 83.0	104— 77 (57.0) 57.5				
II	145—144 (143.0) 142.5	144—118 (96.7) 96.3	118— 91 (70.2) 70.0	145—130 (116.5) 116.5	130—104 (83.2) 82.7	104— 77 (57.0) 57.7
III	159—158 (157.0) 157.0	158—130 (107.0) 107.5[b]	159—131 (107.9) 107.5[b]	130—104 (83.2) 83.0	104— 77 (57.0) 57.7	
IV	156—104 (69.3) 69.0	104— 77 (57.0) 57.0[c]	156—129 (106.7) 107.0	129—103 (82.2) 81.7	103— 77 (57.6) 57.0[c]	
V	207—206 (205.0) 205.0	206—180 (157.3) 157.2	103— 77 (57.6) 57.5	179—153 (130.7) 129.5		
VI	209—132 (83.4) 83.0[d]	207—180 (156.5) 156.0	207—131 (82.9) 83.0[d]			
VII	251→146 (84.9) 84.5	131→104 (82.6) 82.5	104→ 77 (57.0) 57.5[e]	146→129 (114.0) 114.0	105→ 77 (56.5) 57.5[e]	
VIII	147→119 (96.3) 96.5	119→ 92 (71.1) 71.3[f]	147→120 (98.0) 98.0	120→ 92 (70.5) 71.3[f]		
IX	167→130 (101.2) 102.0[g]	165→130 (102.4) 102.0[g]	130→104 (83.2) 83.0	104→ 77 (57.0) 57.0		
X	161→131 (106.6) 107.0	131→104 (82.6) 82.5	104→ 77 (57.0) 57.5			

a): Values in parentheses are theoretical maxima for the metastable peaks. *b*, *c*, *d*, *e*, *f*, and *g*: These metastable peaks appear in overlapping.

Pyrido[2,3-*d*]pyrimidine (I)

The mass spectrum of I is rather simple, exhibiting two successive elimination of hydrogen cyanide from molecular ion (I). It is seemed that the predominant fragment path of the formation of radical ion **2** may be *via* an intermediate such as radical ion **1** according to that of [4-$^2H_1$]-quinazoline[2] indicated that 90 percent of initially ejected hydgogen cyanide molecule encompassed C-4. Pyridyne radical ion **2**, *m/e* 77 corresponds to benzyne radical ion, *m/e* 76 in the spectrum of quinazoline.[2]

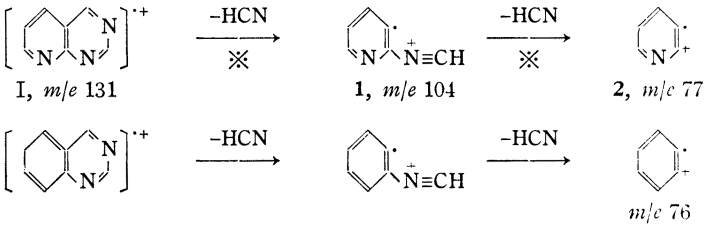

Chart 1

4-Methylpyrido[2,3-*d*]pyrimidine (II)

The fragmentation of II under electron impact is proceeded by two dissociation path.

One is a loss of hydrogen radical from molecular ion II. Acetylene is then expelled from this (M—·H)$^+$ species to give [M-(·H+CH≡CH)]$^+$ fragment (**4**) which then loses hydrogen cyanide to form fragment ion **5**, *m/e* 91. The (M—·H)$^+$ intermediate, in question, may be writtern as diazatropylium type ion (**3**′) according to the fragmentation of 2-methylquinoline and 1-methylisoquinoline.[4] And the rearrangement process from **3** to **3**′ may be analogous to conversion of benzyl cation to tropylium ion.[5]

The another is elimination of methyl radical to give evenelectron pyrido[2,3-*d*]pyrimidinium cation[2] (**6**), *m/e* 130 which then loses cyano radical to form radical ion **1**, *m/e* 104.

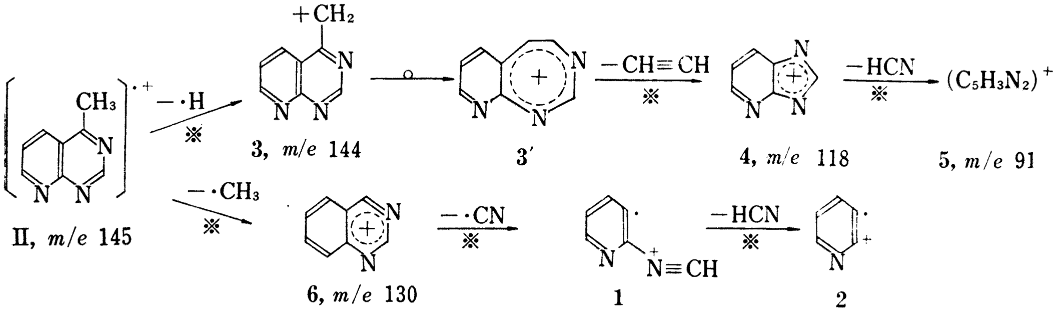

Chart 2

4-Ethylpyrido[2,3-*d*]pyrimidine (III)

The fragmentation is proceeded by two dissociation path.

One is first elimination of hydrogen radical to form (M—·H)$^+$ species (base peak) which then loses of ethylene molecule to give [M—(·H+CH_2=CH_2)]$^+$ ion **6**. The (M—·H)$^+$ intermediate may be written as the immonium ion **8** as similar as that of 2-ethylquinolnine.[4]

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4) S.D. Sample, D.A. Lightner, O. Buchardt, and C. Djerassi, *J. Org. Chem.*, **32**, 997 (1967).

5) H.M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions", Academic Press Inc., F. McLafferty, Ed., New York, N.Y., 1963, Chapter 10; H. Budzikiewicz, C. Djerassi, and D.H. Williams in "Mass Spectrometry of Organic Compounds", Holden-Day, Inc., San Francisco, California, 1967, Chapter 1.

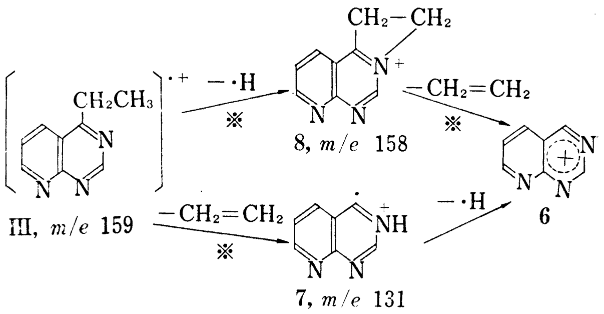

Chart 3

The another is first expulsion of ethylene molecule from molecular ion III to give fragment ion **7**, *m/e* 131 which then loses hydrogen radical to form fragment ion **6**.

4-Pyrido[2,3-*d*]pyrimidinecarbonitrile (IV)

The fragmentation of IV is proceeded by two dissociation path.

In the mass spectrum of IV at the low ionization energy (20 eV) the abundance of radical ion **1** to that of molecular ion (base peak) is greater than that at the ionization energy normally used (80 eV). This fact suggests that the preferred pathway is loss of cyanogen to form radical ion **1**.

The another is first loss of hydrogen cyanide molecule from N-1 and C-2 to give radical ion **9**, *m/e* 129 which loses two cyano radical, in successive step, to form radical ion **2** *via* intermediate fragment ion **10**, *m/e* 102 as shown in Chart 4.

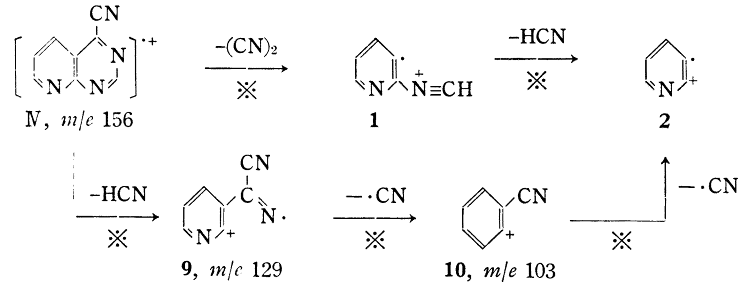

Chart 4

4-Phenylpyrido[2,3-*d*]pyrimidine (V)

The fragmentation of V differs from that of 4-alkylpyrido[2,3-*d*]pyrimidine. Molecular ion loses hydrogen radical to form ion **11**, *m/e* 206 which then does cyano and hydrogen radical, in the two step, to give fragment ion **12**, *m/e* 179 *via* **12′**, *m/e* 180. This intermediate, in question, may be written as cyclic cation represented by **12** as shown in Chart 5. Sequent fragmentation of **12** may be proceeded by two dissociation path.

One is loss of benzyne to give fragment ion **10** which then loses cyano radical to form radical ion **2**. But metastable peak appropriated from ion **12** to **10** can not be observed. The another is loss of cyano radical to give fragment ion **13**, *m/e* 153.

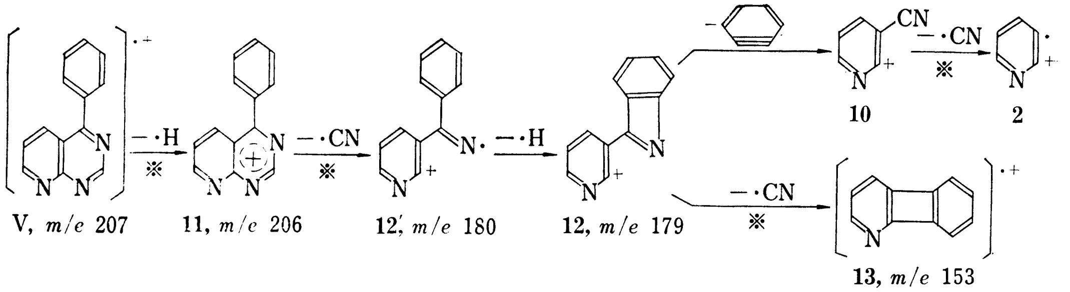

Chart 5

4-Phenyl-3,4-dihydropyrido[2,3-*d*]pyrimidine (VI)

The main dissociation path of VI involves first loss of phenyl radical to form fragment ion **14**, *m/e* 132 (base peak) which then loses of hydrogen radical to give pyrido[2,3-*d*]pyridinium cation I.

The dissociation bypath may be as follow. $(\mathrm{M}-\cdot\mathrm{H})^+$ ion loses hydrogen radical from phenyl group to form $(\mathrm{M}-2\cdot\mathrm{H})^+$ ion. This ion, in question, may be written as cyclic radical ion represented by **16** as shown in Chart 6. Sequent fragmentation of **16** may be proceeded by two dissociation path. One is loss of benzyne to form radical ion I. The another is two successive loss of hydrogen cyanide molecule to give radical ion **13** *via* radical ion **17**, *m/e* 180.

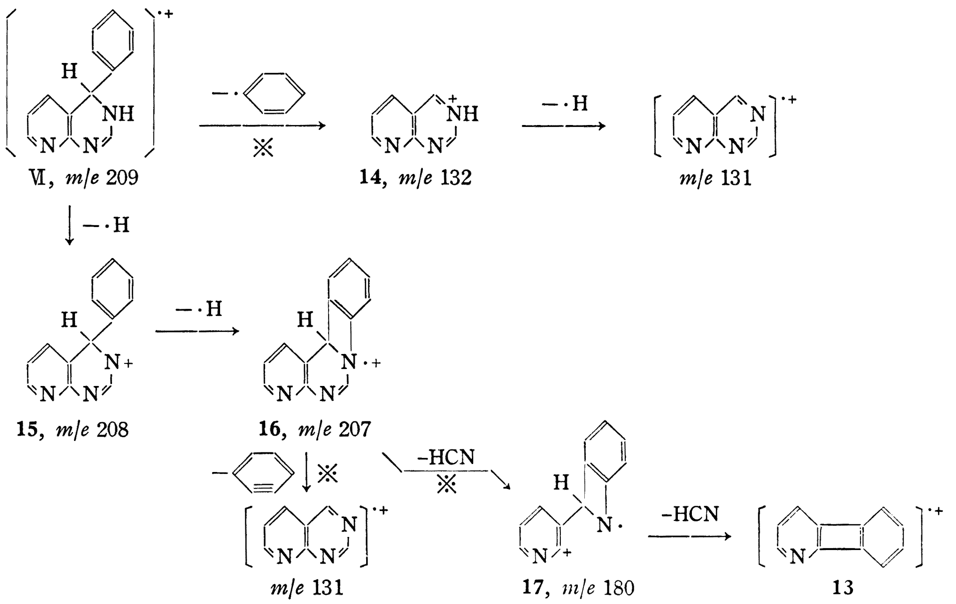

Chart 6

2-(3,4-Dihydro-4-pyrido[2,3-*d*]pyrimidinyl)acetophenone (VII)

Under electron impact VII gives base peak $(\mathrm{M}-\cdot\mathrm{CO}\text{-}\mathrm{C_6H_5})^+$ ion at *m/e* 146. Metastable peak in this spectrum shows that this fragment ion **18** is originated by loss of benzoyl radical from molecular ion VII. Fragment ion **18** loses carbene as diradical to give ion **14** which then does hydrogen radical to form radical ion I. Peak at *m/e* 105 may be benzoyl cation formed through *β* cleavage of VII.

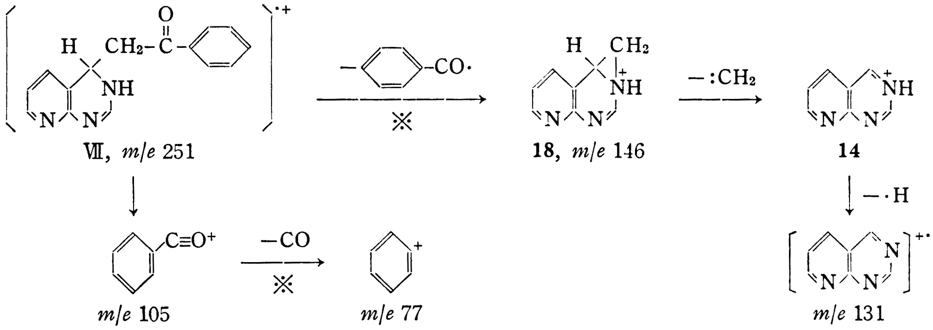

Chart 7

4(3H)-Pyrido[2,3-*d*]pyrimidinone (VIII)

The fragmentation of VIII is proceeded by two dissociation path.

One is first loss of carbon monoxide to give molecular ion of imidazolopyridine **19** which then loses two hydrogen cyanide molecule, in successive step, to form radical ion *m/e* 65 *via* radical ion *m/e* 92.

The another is first loss of hydrogen cyanide from C-2 and N-3 to form radical ion **20** which is then decomposed by consecutive loss of carbon monoxide and hydrogen cyanide.

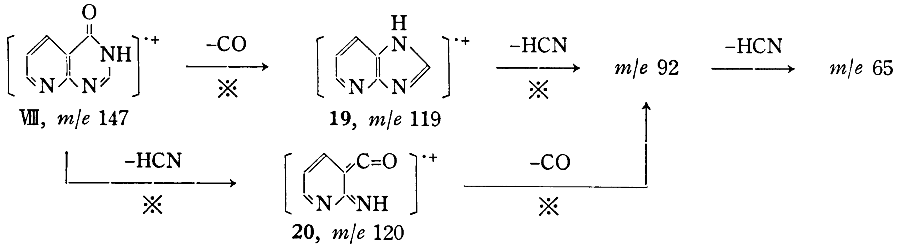

Chart 8

4-Chloropyrido[2,3-*d*]pyrimidine (IX)

Molecular ion of IX is loss of chloro radical to give fragment ion **6** which then loses of cyano radical to form radical ion **1** as shown in Chart 9.

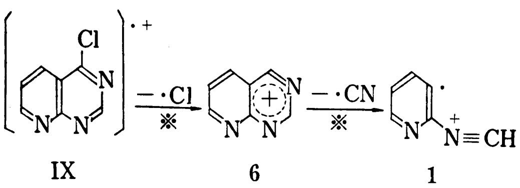

Chart 9

4-Methoxypyrido[2,3-*d*]pyrimidine (X)

The main dissociation path may be as following. Elimination of formaldehyde from molecular ion of X leads to radical ion **7** which then loses hydrogen cyanide to form radical ion **1** as shown in Chart 10. We can not clear how to solve dissociation bypath.

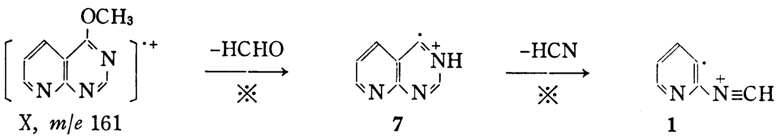

Chart 10

It may be shown the following conclusion through the foregoing mass spectral data. Fragmentations of I, VIII, IX and X are analogous to those of corresponding quinazoline derivatives, respectively.[2] Fragmentation of II affords (M-·H)$^+$ intermediate written as diazatropylium ion **3′** in pathway leading to [M-(·H+CH≡CH)]$^+$ ion. III, V and VI gives intermediate written as cyclic fragment ion (**8**, **12**, **16**) as same as shown in fragmentation of 2-ethylquinoline and 1-ethylisoquinoline.[4] In any way the predominant fragmentation of 4-substituted pyrido[2,3-*d*]pyrimidines occurs by consecutive loss of cyano radical and hydrogen cyanide molecule accompanied with breakdown or migration of the substituent.

Experimental

Mass spectra were recorded on a Hitachi RMS-4 singlefocusing mass spectrometer. The ionization energy normally used was 80 eV. In order to simplify complexed spectra all samples were also studied at lower energy (20 eV). Samples were vaporised in a glass inlet system for compounds having melting point below 150° or a direct inlet system for those above 150°.

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