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ALKYL MIGRATIONS AND NITRENE/FORMIMINE ELIMINATIONS IN ALKYLAMINO HETEROAROMATIC COMPOUNDS

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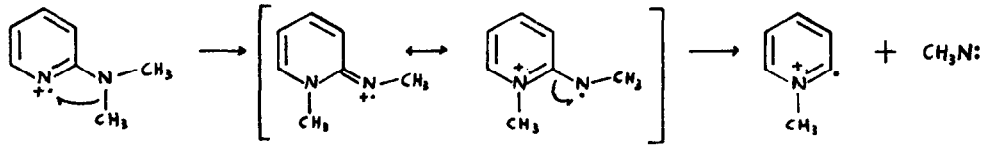
Recently Rahamim, Sharvit, Mandelbaum and Sprecher (1) reported that the mass spectra of 2-dimethylamino-5-nitropyrimidine and 6-dimethylaminopurine show intense M-29 peaks. These authors considered the M-29 peak to arise from elimination of a neutral fragment, CH_3N, from the dimethylamino substituent as formimine with a simultaneous migration of a methyl group to a ring nitrogen atom. Independent results obtained in our laboratories have indicated that this type of rearrangement is general for a variety of alkylaminoheteroaromatic systems.

Table I shows the major fragment ions observed in the mass spectra of some methylalkylamino substituted heteroaromatic compounds. In each case the observed M-29 peak was accompanied by a corresponding metastable peak. High resolution measurements in the case of 2-dimethylamino-pyridine confirm the loss of CH_3N as the neutral fragment and an intense M-30 peak in the mass spectrum of 2-dimethyl-N^{15}-aminopyridine proves that the elimination involves the exocyclic nitrogen atom. In these respects the assumptions of Rahamim *et al.* are confirmed.

However the similarity between the mass spectra of a 2-dimethylaminopyridine (Fig. 1) and 1,2-dihydro-1-methyl-2-methyliminopyridine (Fig. 2) may indicate a stepwise mechanism although not ruling out the concerted mechanism suggested by Rahamim *et al.*

For example



where the fragment CH_3N is eliminated as a nitrene or by migration of a hydrogen atom as formimine. Other mechanisms, involving migration of a methyl group to a ring carbon atom or rearrangement of the dimethylamino group to a methylaminomethyl substituent, all seem unlikely particularly as the mass spectra of 3-dimethylaminopyridine, 4-dimethylaminopyridine and 2-(methylaminomethyl)-pyridine fail to show M-29 peaks.

TABLE I

Relative Abundance of the Major Fragment Ions in the Mass Spectra of 2-Methylalkylaminopyridines and Related Compounds

Compound	M m/e	$\%\Sigma_{40}$	M-15 m/e	$\%\Sigma_{40}$	M-29 m/e	$\%\Sigma_{40}$	Base Peak	$\%\Sigma_{40}$
2-dimethylaminopyridine	122	14.3	107	11.6	93	15.2	93	
2-dimethylamino-4-methylpyridine	136	10.8	121	13.4	107	12.7	107	
2-dimethylamino-5-nitropyridine	167	6.2	152	3.0	138	7.9	44	18.5
2-dimethylamino-5-hydroxymethylpyridine	152	4.4	137	4.6	123	6.8	123	
2-benzylmethylaminopyridine	198	7.1	183	11.0	169	1.7	107	12.2
2-benzylmethylamino-5-hydroxymethyl-pyridine	228	3.8	213	7.9	199	1.9	91	15.0
6,6'-bis(dimethylamino)-3,3'-dipyridyl-methane	256	23.3	241	10.8	227	10.9	256	
6,6'-bis(benzylmethylamino)-3,3'-dipyridylmethane	408	17.6	393	9.8	379	3.1	408	
2-dimethylaminopyrimidine	123	12.9	108	11.1	94	12.6	123	
2-dimethylaminolepidine	186	14.3	171	11.7	157	13.9	186	
5,6-dimethyl-4-dimethylaminopteridine	203	25.6	188	17.8	174	20.1	203	
1,2-dihydro-1-methyl-2-methylimino-pyridine	122	14.8	107	5.5	93	15.2	93	

TABLE II

Relative Abundance of the Major Fragment Ions in the Mass Spectra of 2-Diethylaminopyridines and Related Compounds

Compound	M m/e	$\%\Sigma_{40}$	M-15 m/e	$\%\Sigma_{40}$	M-29 m/e	$\%\Sigma_{40}$	M-43 m/e	$\%\Sigma_{40}$	Base Peak
2-diethylamino-4,6-dimethyl-pyrimidine	179	8.0	164	13.0	150	16.5	136	11.2	150
4-diethylamino-2,6-dimethyl-pyrimidine	179	6.3	164	4.2	150	20.4	136	8.1	150
2-diethylaminolepidine	214	8.3	199	4.1	185	27.1	171	8.0	185
2-diethylamino-5-nitropyridine	195	6.3	180	11.9	166	10.5	152	7.2	180

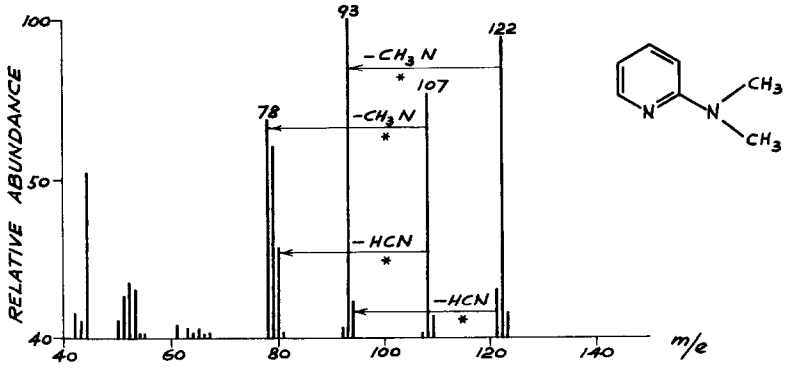


FIG. 1. Mass spectrum of 2-dimethylaminopyridine

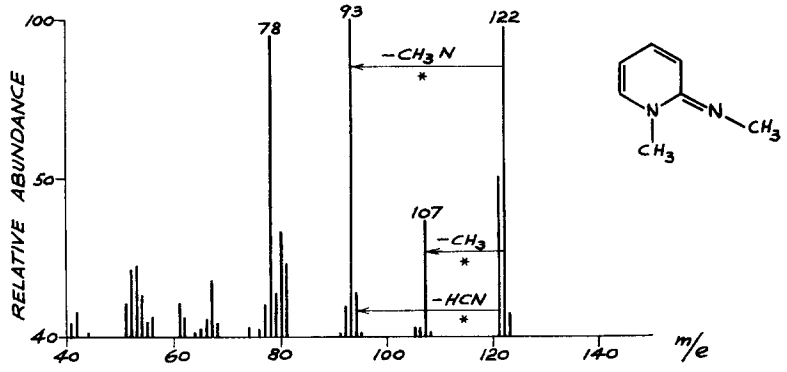
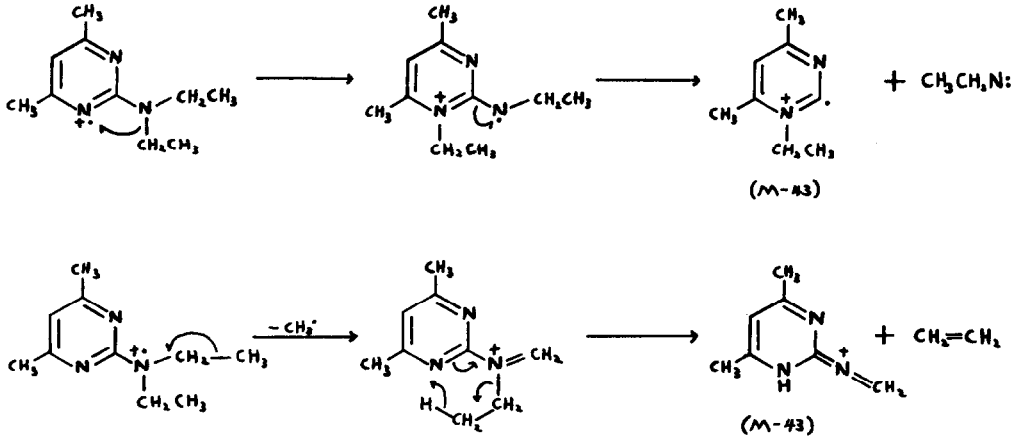


FIG. 2. Mass spectrum of 1,2-dihydro-1-methyl-2-methyliminopyridine

The rearrangement has been shown to fail in the case of 2-dimethylamino-5-phenyl-sulphonamidopyrimidine (1). In the present work 2-dimethylamino-3-nitropyridine also failed to eliminate CH_3N on electron impact, however this is readily explained on the basis of interaction between the two adjacent substituents (c.f. nitroanilines (2)). Apart from this instance no other substituent effects were observed.

An extension of this investigation to diethylamino compounds (Table II) showed that electron impact induced ethyl migrations can also occur, however high resolution studies show that a competing reaction operates. For example in the case of 2-diethylamino-4,6-dimethylpyrimidine, the peak at m/e 136 (M-43) is found to consist of two fragment ions $C_7H_{10}N_3$ and $C_8H_{12}N_2$ with a relative abundance of 5:1. The two pathways can be visualised as follows:



In recent years several authors (3,4,5) have drawn comparisons between fragmentations occurring on electron impact and those occurring on pyrolysis. In the present work pyrolysis of 2-dimethylaminopyridine at 800° with a contact time of 0.05 sec. and a pressure of 0.05 mm. gave largely unchanged starting material (76%) together with small amounts of pyridine (7.2%) and α-picoline (6.0%). The thermal rearrangement of trimethyl-2-pyridyl-ammonium salts (6) bears a closer resemblance to the present rearrangement.

Correct analyses were obtained for all new compounds which were synthesized by standard procedures. 2-Dimethyl-N^{15}-aminopyridine was synthesized from the reaction of methyl iodide and sodium hydride on 2-N^{15}-aminopyridine. The latter is obtained by a Hofmann reaction on picolin-N^{15}-amide. The overall yield from picolinic ester and N^{15} ammonia was 70%.

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