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MASS SPECTRAL STUDIES OF AZATHIOPRINE ANALOGUES

Ashish K. Tewari[a], Anil Mishra[a]* and D.S. Bhakuni[b]

[a]Department of Chemistry, Lucknow University, Lucknow - 226 007 (India)
[b]Medicinal Chemistry Division, CDRI, Lucknow - 226 001 (India)

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ABSTRACT

The mass spectral analysis of several analogues of azathioprine has been carried out. The general observation is that the nitroimidazole ring is cleaved first. The C-S-C bond is so labile that the molecular ion peak is not observed by the EI technique, however it has been observed by the FD mass technique. A consistent fragmentation pattern has been observed in all the compounds.

INTRODUCTION

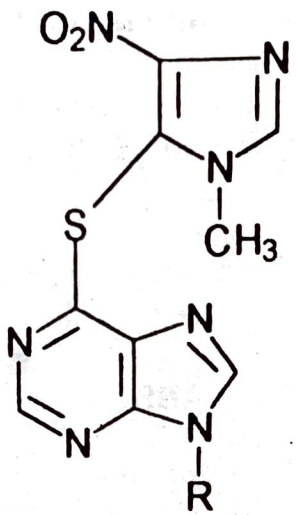
Azathioprine, a drug in the clinical use in the transplantation of organs and effective against transplantable tumors and chronic granulocytic leukemia[1], is a 6-mercaptopurine derivative. There are several reports here riboside[2,3,4], deoxyriboside and arabinoside[5] have been found more effective than the parent base. Further the cyclic and alicyclic analogues of the bases probably act as pro-drugs[5]. Prompted by these reports a series of 9-subsitituted-6-[(1-methyl-4-nitrominidazo-5-yl)thio] purines (1-5) have been synthesized[6]. The mass spectra of these compounds have been analyzed in detail using EI technique and a consistent pattern has been observed. Various peaks observed are given in Table-1. Mass spectral studies of a series of 9-substituted-6-[(1-methyl-4-nitrominidazo-5-yl)thio]purines (1-5) have shown that the 1-nitroimidazo-5-yl group suffered the cleavage of S-C bond without undergoing any type of rearrangement. Fragmentation pattern of these compounds deviates from the ordinary mode where the mass spectra of nucleosides represent three major peaks for B, B^+ & S. This characteristic fragmentation helps to elucidate the structure of unusual C-N nucleosides including substitued adenosine cytokinins and antibiotic cordycepin.

The general pattern of fragmentation represents the cleavage of sulfur-imidazole bond indicated by the peak at M^+-125. In fact the molecular ion peak is not observed in any of these compounds. However the molecular ion peak is seenin the FD mass spectra. In the next step of fragmentation the substituent at position 9 attached to nitrogen of purine underwent rearrangement, as a result sugar or non-sugar moiety has been chalked out with or without rearrangement. It has been observed that in the spectra of these compounds most abundant peak is that of the purine base.

RESULT AND DISCUSSION

Mass fragmentation pattern of 6-[(1-methyl-4-nitroimidazo-5-yl)thio]-9-α-D-arabinofuranosyl purine (1) has been described in Scheme-1. Compound (1) has shown the major peaks at m/e 284, 193, 180, 152, 134, 126 and 120. The first major peaks occuring in the spectrum is at m/e 284 (1.1) indicating the cleavage of (1-methyl-4-nitro-5-yl)thio-imidazole followed by the fragmentation in sugar moiety. Cleavage in the sugar moiety was responsible for the peak at m/e 193 (1.2). The radical ion 1.2 again fragmented to give 1.3 at m/e 180. Complete cleavage of the sugar moiety resulted in the formation of the radical ion at m/e 152 (1.4). The base peak is observed at m/e 120 (1.5), which is the purine base. Two peaks are also observed at m/e 125 (1.6) and 134 (1.7), which are for the 1-methyl-4-nitroimidazo-5-yl and the sugar moieties respectively. Apart from these prominent peaks, several peaks are also observed at m/e 93, 78, 67 and 56, which are for the fragmentation of the purine and the imidazole moieties.

A similar pattern of fragmentation has been obseved in all the compounds. As all these compounds differ only in the substituent at position 9 and therefore there is not much variation in their



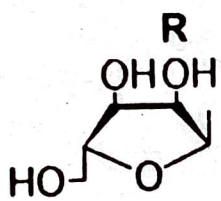
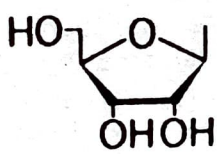
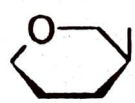
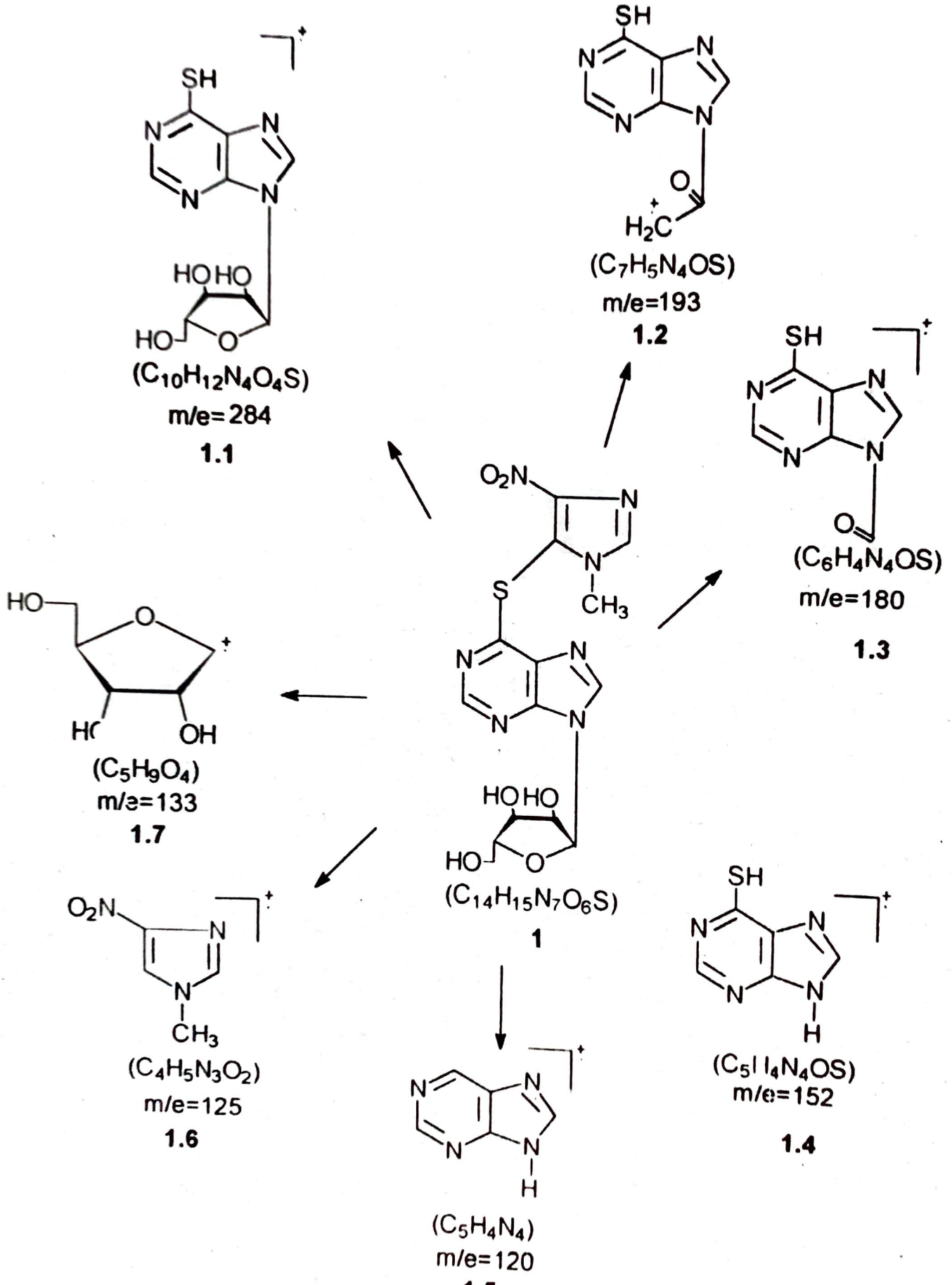
	R	m/e
1		284, 193,180, 152, 133, 125, 120, 93, 78, 67, 56
2		284, 193,180, 152, 133, 125, 120, 93, 78, 67, 56
3		226, 180, 152, 125, 120, 93, 78, 74, 67, 56
4		222, 193, 152, 125, 120, 93, 78, 71, 67, 56
5		236, 193, 152, 125, 120, 93, 85, 78, 67, 56

Table - 1



Scheme – 1 Mass fragmentation pattern of 6-[(1-methyl-4-nitroimidazo-5-yl)thio]-9-α-D-arabinofuranosyl purine

fragmentation pattern. The M-nitroimidazole peak is present in the spectra of all the compounds. The fragment for the sugar or non-sugar moiety at position 9 has also been observed. The details of the peaks are given in Table 1.

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REFERENCES

1. *Enzyme inhibitors as Drugs*, Marton Sandler (ed) Macmillian Press, London (1980)
2. Silberman, H.R. and Wyngaarden, J.B., *Biochem Biophys. Acta*, **47**, 178 (1961)
3. Bennett, L.L., Simpson, L., Golden, J., and Barber, T,L., *Cancer Res.*, **23**, 1574 (1963)
4. Solvero, J.J., *Drugs of Today*, **23**, 575 (1987)
5. Homo-Delerch, F., Bach, J.F., and Dardenne, M., *Prostagl.*, **35**, 479 (1988)
6. Mishra, A., Pratap, R., and Bhakuni, D.S., *Indian J. Chem.*, **26B**, 847 (1987)