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Mass Spectral Fragmentation Modes of Pyrimidine Derivatives

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Abstract : Mass spectral studies of some aryl amido pyrimidines established on comparison with other derivatives of pyrimidines are being presented in this paper. Aryl amido pyrimidines showed regular fragmentation pattern.
Key words: 5-(N-Aryl amino carbonyl) pyrimidines, 5-Cyano pyrimidines, Mass spectral fragmentation.

INTRODUCTION

Primidines as well as thiazoles are systems with multifarious importance. Thiazoles are pesticides[1] antimicrobial[2] anti inflammatory and analgesic[3-5] as well as anticancerous[6]. On the other hand pyrimidines have been subjected to a large number of different modifications in order to obtain derivatives having different biological properties. Several groups have studied the chemistry and pharmacological properties of pyrimidine derivatives. Pyrimidines have been found to have a broad range of biological effects including antiviral, anti tumor, antibacterial, anti-inflammatory[7], antihypertensive[8], cardiovascular[9] and calcium channel blocking[10]activity.The versatile biological properties of thiazole and pyrimidine derivatives prompted us to take up this task to synthesize and analyze some novel derivatives.

EXPERIMENTAL

5-(5'-Methyl thiazol-2'-yl)amino carbonyl -2-hydroxy/mercapto-4-ayl-6-(propan-2'-yl)-3,4-dihydro pyrimidine (**I** to **III**), 5-methyl amino carbonyl-2-hydroxy-4-phenyl-6-methyl-3,4-dihydropyrimidine (**IV**) and 6-p-methoxy phenyl-5-cyano-3-N-methyl-2-methylthio-3,4-dihydro pyrimidin-4-one (**V**) were synthesized by conventional methods[11-15]. Purity of the compounds was checked on silica gel G coated TLC plates. Structure of from internal TMS standard). Mass spectra were recorded on compounds was elucidated by the interpretation of their IR and PMR spectra run on Shimadzu-8400 IR spectrophotometer, Bruker - 300 MHZ NMR (expressed in ppm unit [δ] down field API 2000 Q TRAP mass spectrometer using ESI-Electron system- spray ionization technique (+Q1) and Figures given in parentheses represent relative intensity corresponding to the base peak.

RESULTS AND DISCUSSION

Mass spectral studies of substituted pyrimidine derivatives reveal a set pattern of fragmentation of these compounds. A number of aryl amino carbonyl pyrimidines synthesized during the course of the investigation, were characterized by their spectral studies. On the bases of these studies, it has been possible to make some generalizations regarding fragmentation modes of their molecular ions.

As expected from the M.F. $C_{18}H_{20}O_2N_4S$ the molecular ion of 5-(5'-Methyl thiazol-2'-yl) amino carbonyl -2-hydroxy-4-phenyl-6-(propan-2'-yl)-3,4-dihydropyrimidine (**I**) appeared as the base peak at m/z 356/357. Loss of hydroxyl radical from the molecular ion generated A'' (m/z 339). In addition the mass spectrum displayed prominent ions representing the characteristic modes of fragmentation of pyrimidines and thiazoles ring systems. Further, some investigating fragmentations of the molecular ions were also noted. All these pathways depicted in fig**. 1** are discussed below.

The molecular ion underwent fragmentation principally via 2 distinct ways: The presence of pyrimidine moiety triggered cleavage (path a) affording ion A (m/z 329) lost of phenyl afforded A' (m/z 251).

Another cleavage triggered by the presence of pyrimidine amide derivative involved at amide link (path b), with loss of 5-methyl-2-amino thiazolo radical ion, which generating radical ion H (m/z 243), loss of C=O from H accompanied by rearrangement afforded I (m/z 217). Ion I underwent the expected elision of NH_3 bringing the ion J (m/z 200). Fusion of molecular ion J involved cleavage at two places along with rearrangement generating molecular ion K (m/z 132). Loss of $^{+}CH{=}CH_2$ with rearrangement produced L (m/z 105) which furnished benzyl cat ion M.

With a view to provide further support to the structures assigned to 5-substituted aryl/alkyl amino carbonyl pyrimidines (**II**), (**III**), (**IV**) and 6-p-methoxy phenyl-5-cyano-3-N-methyl-2-methylthio-3,4-dihydro pyrimidin-4-one (**V**). Their mass spectra were also analyzed. The molecular ions invariably constituting the base peaks were in conformity with their molecular weights. In addition to locating the molecular ions, the spectra were also investigated to delineate the characteristic modes of fragmentation as expected from their molecular frame work.

The molecular ion of (**II**) M.F. $C_{18}H_{19}O_2N_4SF$ for instance, appeared as a base peak at m/z 374/375, which underwent fragmentation along the following pathways (Fig. 2).

The presence of pyrimidine ring triggered the expected extrusion of C=O (path a) yielding cat ion A (m/z 347) which on loss of C_6H_5F gives cat ion A' (m/z 251). The presence of thiazole moiety triggered the elimination of CH≡CH or C≡N with accompanying rearrangement to give B (m/z 321) or B' (m/z 321) respectively. Elision of C≡N from B or elimination of CH≡CH from B' afforded radical ion C (m/z 295) which produced two radical ions D (m/z 88) and E (m/z 209) with accompanying rearrangement, while on expulsion of C_6H_5F, E yielding F (m/z 117), cleavage of radical ion F yielding G (m/z 61).

Fission of the molecular ion across the amide bond which linking thiazole and pyrimidine rings (path b) resulted in the formation of radical ion (m/z 261), cleavage of thiazolo moiety presumably through path c yielding ion I (m/z 289).

The mass spectrum of compound (**III**) was also examined with a view to further establish the structure assigned to it.

On the basis of above expected value of fragments as well as comparison of mass spectra of compound (**I-III**) with compound (**IV**) and (**V**) it proposes that compounds of type (**I-III**) showed regular fragmentation pattern, the identical ion/radical ion are furnished from compound (**I-III**) e.g. Radical ion H, ion A, A', B etc. While in case of compound (**IV**) and (**V**) such ions are absent.

The fragmentation modes of (**III**),(**IV**) and (**V**) depicted in fig. **3**, **4** and **5** respectively,were further established by the appearance of the corresponding ions in the mass spectra of all these compounds. The significant ions observed in the mass spectra of these compounds, arranged in Table-**1**, display the peak to peak correspondence of various fragment ions.

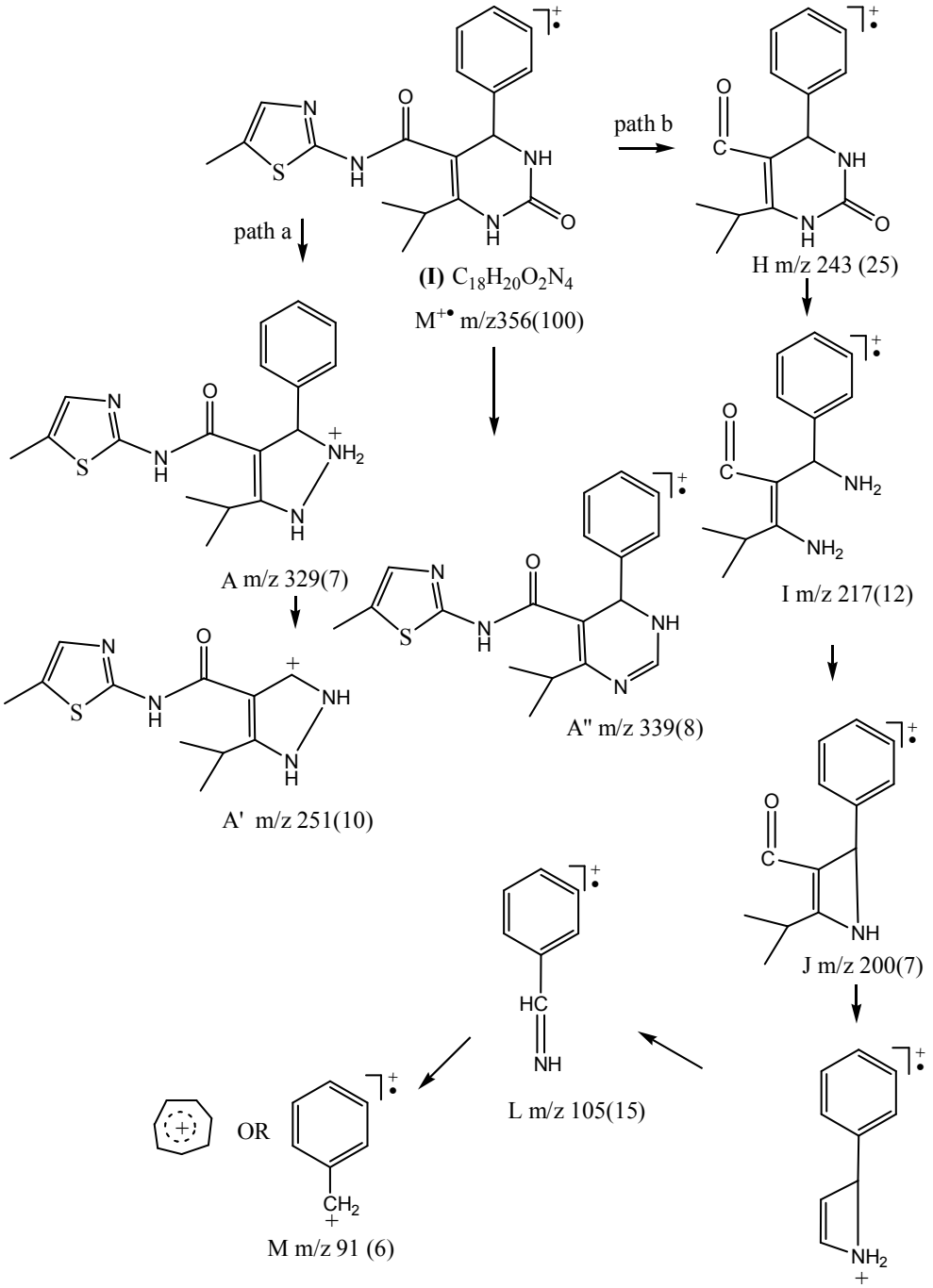

path a
path b
(I) $C_{18}H_{20}O_2N_4$
$M^{+\bullet}$ m/z356(100)
H m/z 243 (25)
I m/z 217(12)
A m/z 329(7)
A" m/z 339(8)
A' m/z 251(10)
J m/z 200(7)
L m/z 105(15)
OR
M m/z 91 (6)
K m/z 132(6)

Fig. 1

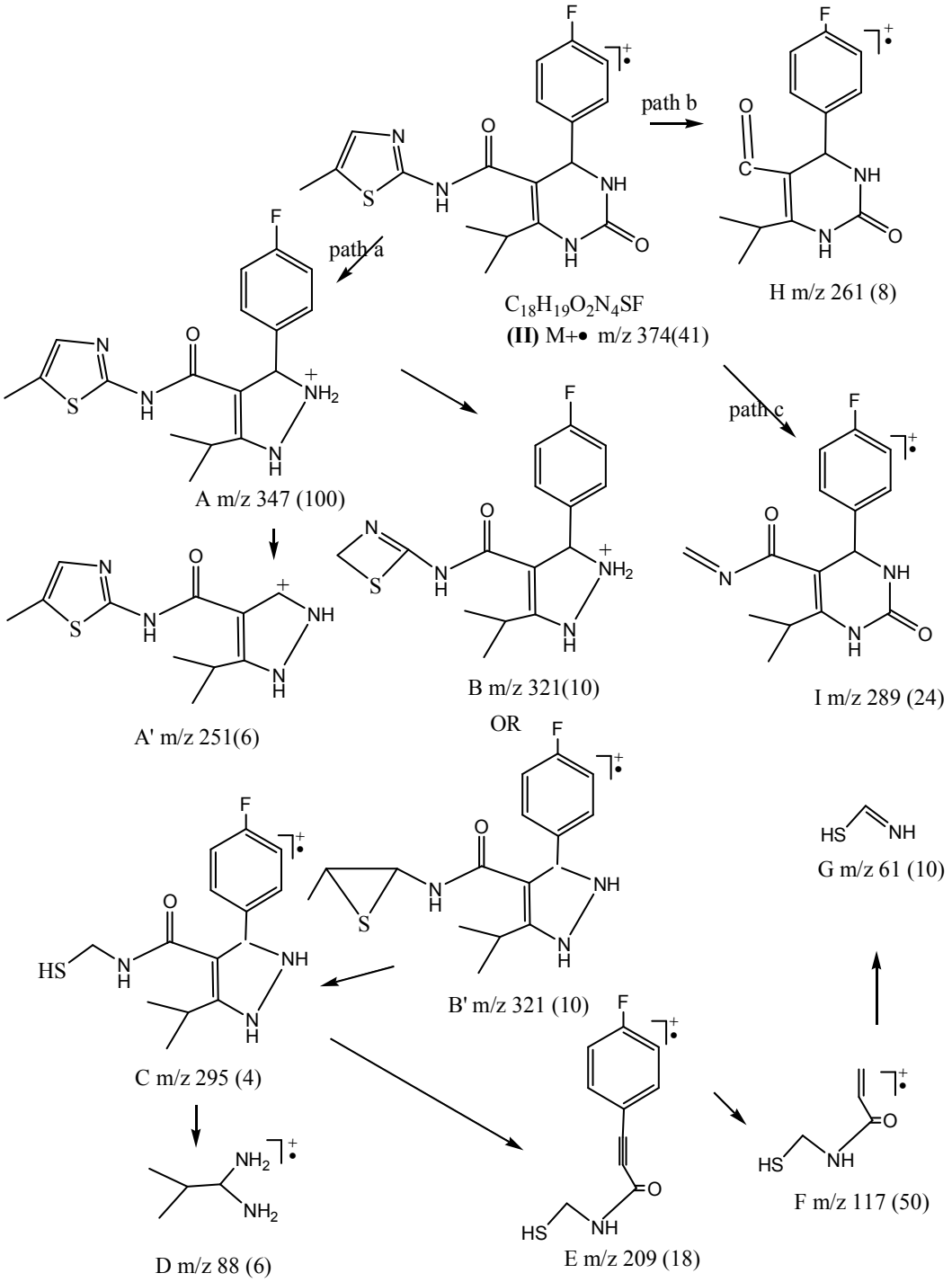

path a
path b
path c
$C_{18}H_{19}O_2N_4SF$
(II) M+• m/z 374(41)
H m/z 261 (8)
A m/z 347 (100)
A' m/z 251(6)
B m/z 321(10)
I m/z 289 (24)
OR
B' m/z 321 (10)
C m/z 295 (4)
D m/z 88 (6)
E m/z 209 (18)
F m/z 117 (50)
G m/z 61 (10)

Fig.2

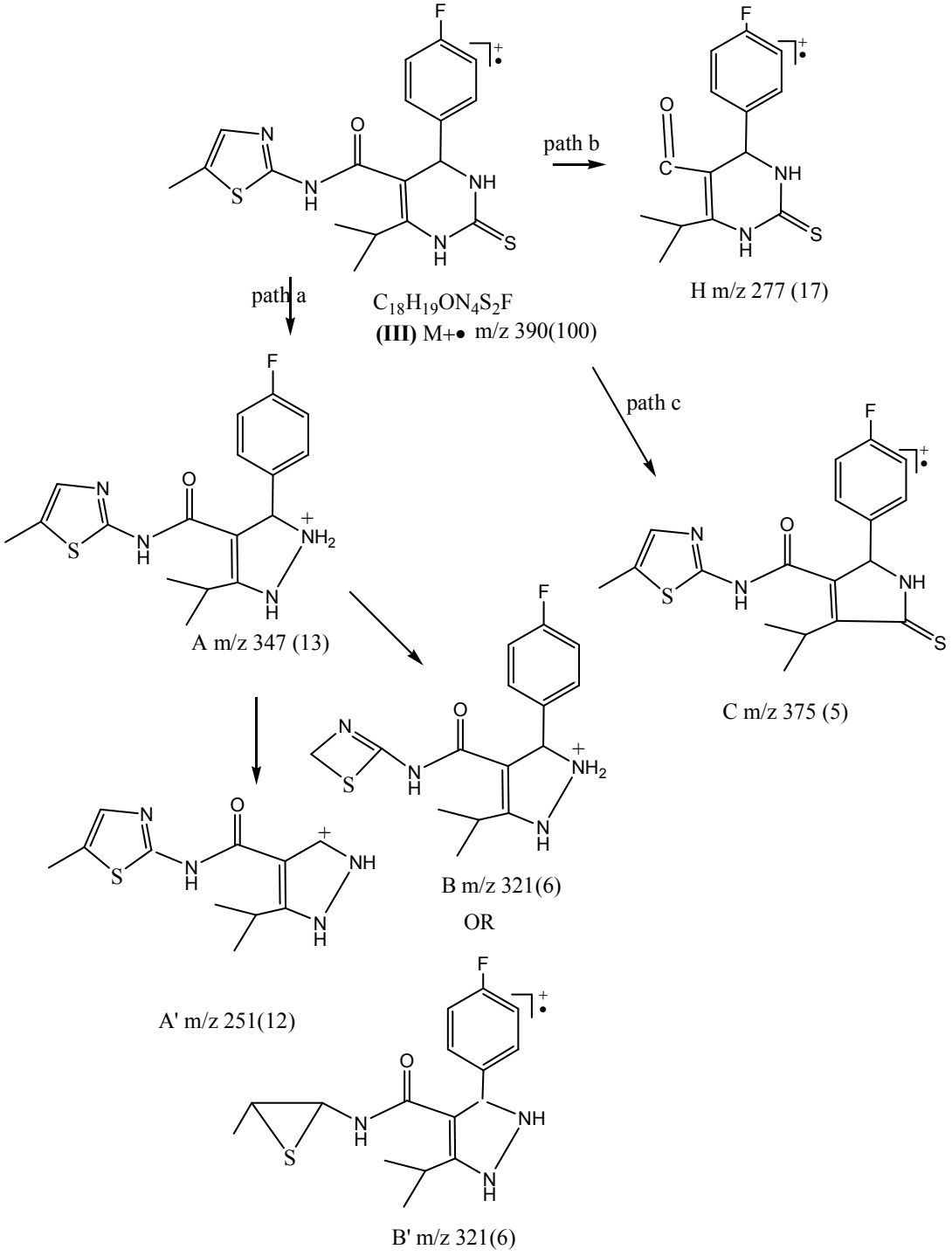

path b
path a
path c
$C_{18}H_{19}ON_4S_2F$
(III) M+• m/z 390(100)
H m/z 277 (17)
A m/z 347 (13)
C m/z 375 (5)
B m/z 321(6)
OR
A' m/z 251(12)
B' m/z 321(6)

Fig. 3

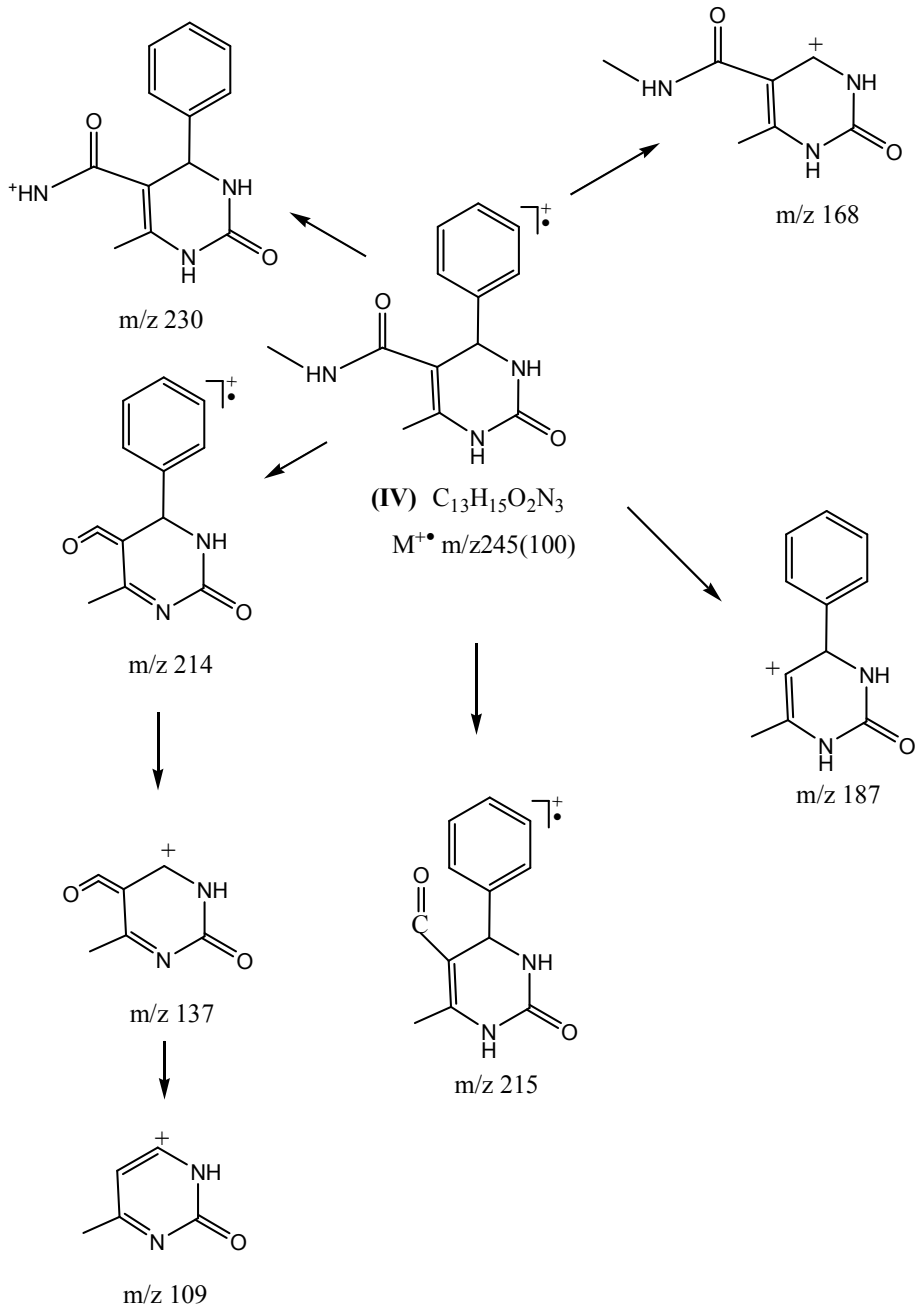

m/z 230
m/z 168
(IV) $C_{13}H_{15}O_2N_3$
$M^{+\bullet}$ m/z245(100)
m/z 214
m/z 187
m/z 137
m/z 215
m/z 109

Fig. 4

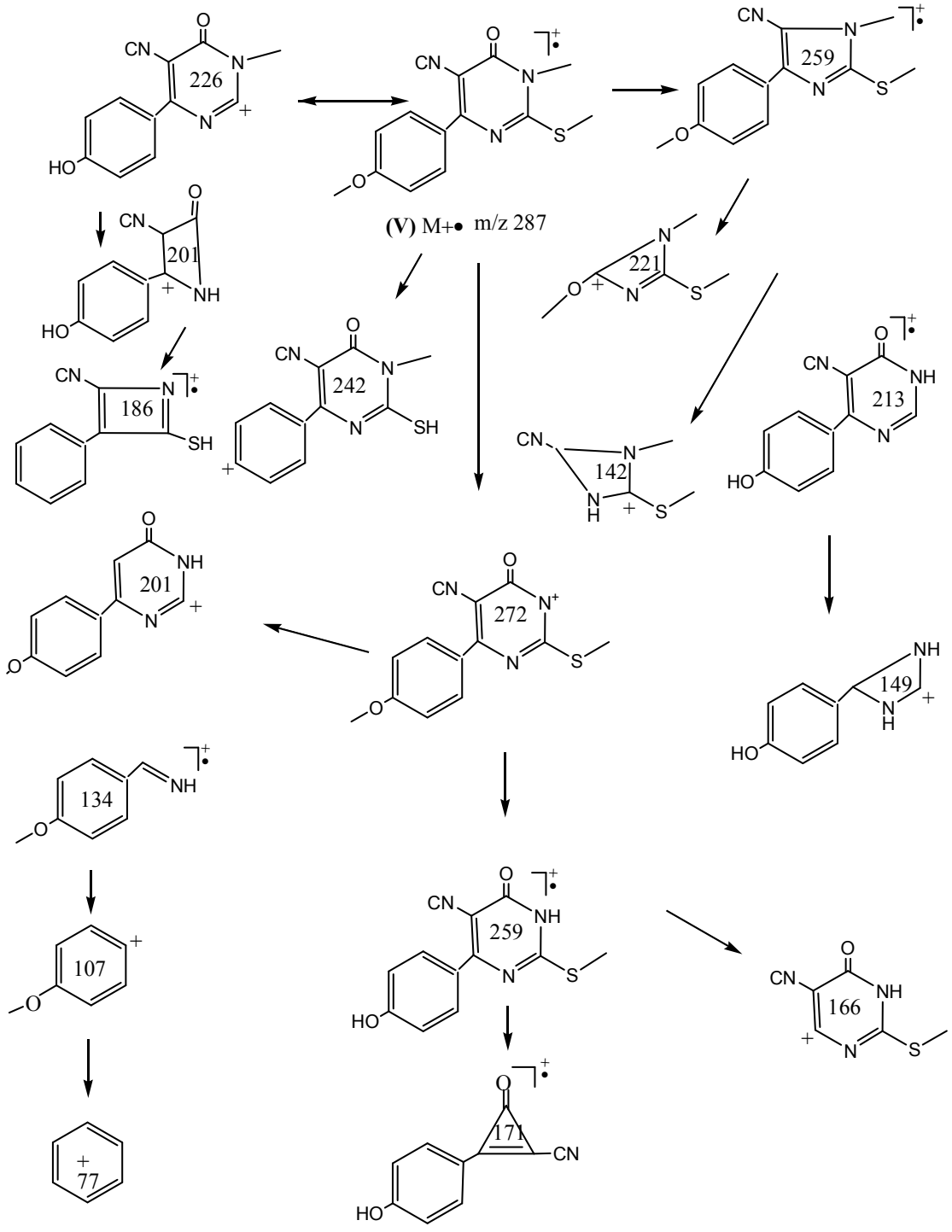
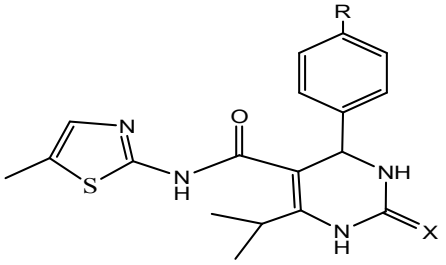

(V) M+• m/z 287
226
259
201
221
186
242
213
142
201
272
149
134
259
107
166
171
77

Fig. 5

Table 1

SIGNIFICANT MASS SPECTRAL DATA OF (I – III) ARRANGE TO DISPLAY THE PEAK TO PEAK CORRESEPONDANCE OF FRAGMENT IONS



M+°	(**I**)	(**II**)	(**III**)
Fragment ions	R = H, X = O	R = F, X = O	R = F, X = S
A	356 (100)	374(41)	390(100)
A'	329 (7)	347(100)	347(13)
B	-	321(10)	321(6)
H	243 (25)	261(8)	277(17)

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