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Mass Spectral Studies of Some 6-(2-N-Substituted aminothiazol-4-yl)chromones and Flavones

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Mass spectral studies of some 6-(2-N-substituted aminothiazol-4-yl) chromones and flavones are being presented in this paper which showed regular fragmentation patterns of chromones and thiazoles as well as other heterocyclic rings present in the molecule (*e.g.*, morpholine).

Key Words: Chromones, Flavones, Mass spectral fragmentation, Retro-Diels Alder fragmentation.

INTRODUCTION

Thiazoles as well as chromones are systems with multiferous importance. Thiazoles are pesticides[1] antimicrobial[2] antiinflammatory and analgesic[3-5] as well as anticancerous[6]. On the other hand chromones are antimicrobials[7,8], antiinflammatory[9], diuretic[10,11] in addition to have other activities. Studies of medicinal importance of the systems having these two ring systems are in current trend. Mass spectral characteristics of thiazolyl chromones have also been studied[12-14]. Adding to this chain mass spectral fragmentation modes of some 6-(2-N-substituted aminothiazol-4-yl) chromones and flavones are being reported in this paper.

EXPERIMENTAL

6-(2-N-Substituted aminothiazol-4-yl) chromones were synthesised by previous reports[9,15,16]. Purity of the compounds was checked on Silica gel-G coated TLC-plates. Structures of compounds were elucidated by the interpretation of their IR and PMR spectra run on IR-20 Beckmann spectrophotometer and Perkin-Elmer R-32 machine (expressed in ppm units [δ] downfield from internal TMS standard). Mass spectra were recorded on a VG 70-S mass spectrometer using 11-250 Jt system and Hewett Packard GC/MS 5985 operating at 70 eV. Figures given in parentheses represent relative intensities corresponding to the base peak.

RESULTS AND DISCUSSION

A number of thiazolyl chromones, synthesized during the course of the investigation, were characterized by their mass spectral studies. On the basis of

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these studies, it has been possible to make some generalizations regarding fragmentation modes of their molecular ions.

As expected from the m.f. $C_{18}H_{18}N_2O_3S$, the molecular ion of (I) appeared as the base peak at m/z 342. Loss of a hydrogen radical from the molecular ion generated A (m/z 341). In addition, the mass spectrum displayed prominent ions representing the characteristic modes of fragmentation of chromones, thiazoles and morpholine ring systems. Futher, some interesting fragmentations of the molecular ion were also noted. All these pathways, depicted in Fig. 1 are discussed below:

The molecular ion underwent fragmentation principally *via* 5 distinct pathways:

The presence of morpholine moiety triggered β-cleavage (path a) affording an isomeric radical ion A' which lost CH_2O giving rise to the ion B (m/z 312). Elision of C_2H_4 from B afforded C (m/z 284). In a competitive process, which incidentally constitutes the major pathway, B generated an abundant ion D (m/z 285) by the loss CH_2=CH accompanying rearrangement. The thierene radical ion, F (m/z 230) (frequently observed in the electron impact-induced fragmentation of thiazoles) was obtained by two sequential losses of HCN from the ion C *via* E (m/z 257). Extrusion of sulphur from F afforded G (m/z 198) which underwent the characteristic retro-Diels Alder (RDA) cleavage of chromone ring to give H (m/z 144). Sequential loses of two molecules of CO from H gave rise to ion I (m/z 116) and J (m/z 88), respectively.

Another mode of fragmentation triggered by the presence of morpholine moiety involved β-cleavage at two places (path b), alongwith rearrangement, generating ion K (m/z 299). Loss of CH_2 from K accompanied by another rearrangement afforded D.

Fission of the molecular ion along the bond linking the morpholine and thiazole moieties (path c) generated the thiazolylchromone cation L (m/z 256) alongwith the morpholinyl cation M (m/z 86). Ion M underwent the expected elision of CH_2O yielding the ion N (m/z 56).

Fission of thiazole ring (path d) produced morpholinyl cyanide ion O (m/z 112) alongwith the thierene radical ion F. The ion O underwent further cleavage through two alternate routes. Elimination of $^{\bullet}CN$ from O gave M. Alternatively, sequential losses of CH_2O and C_2H_4 produced ions P (m/z 82) and R (m/z 54), respectively. Expulsion of CH_2=CH from P yielded ion Q (m/z 55).

Cleavage of the molecular ion along the C-C bond linking thiazole and chromone rings (path e) gave ions S (m/z 169) and T (m/z 173). Further, scission of S produced the thierene cation X (m/z 57) and the ion O. The RDA fragmentation of T produced the quinonoid cation U (m/z 119) which underwent sequential losses of two molecules of CO producing V (m/z 91) and W (m/z 63), respectively.

With a view to provide further support to the structures assigned to 6-(2-N-substituted amino-5-methylthiazol-4-yl) chromones (**II**, **III**, **IV**), their mass spectra were also analyzed. The molecular ions invariably constituting tha base peaks, were in conformity with their molecular weights. In addition to locating the molecular

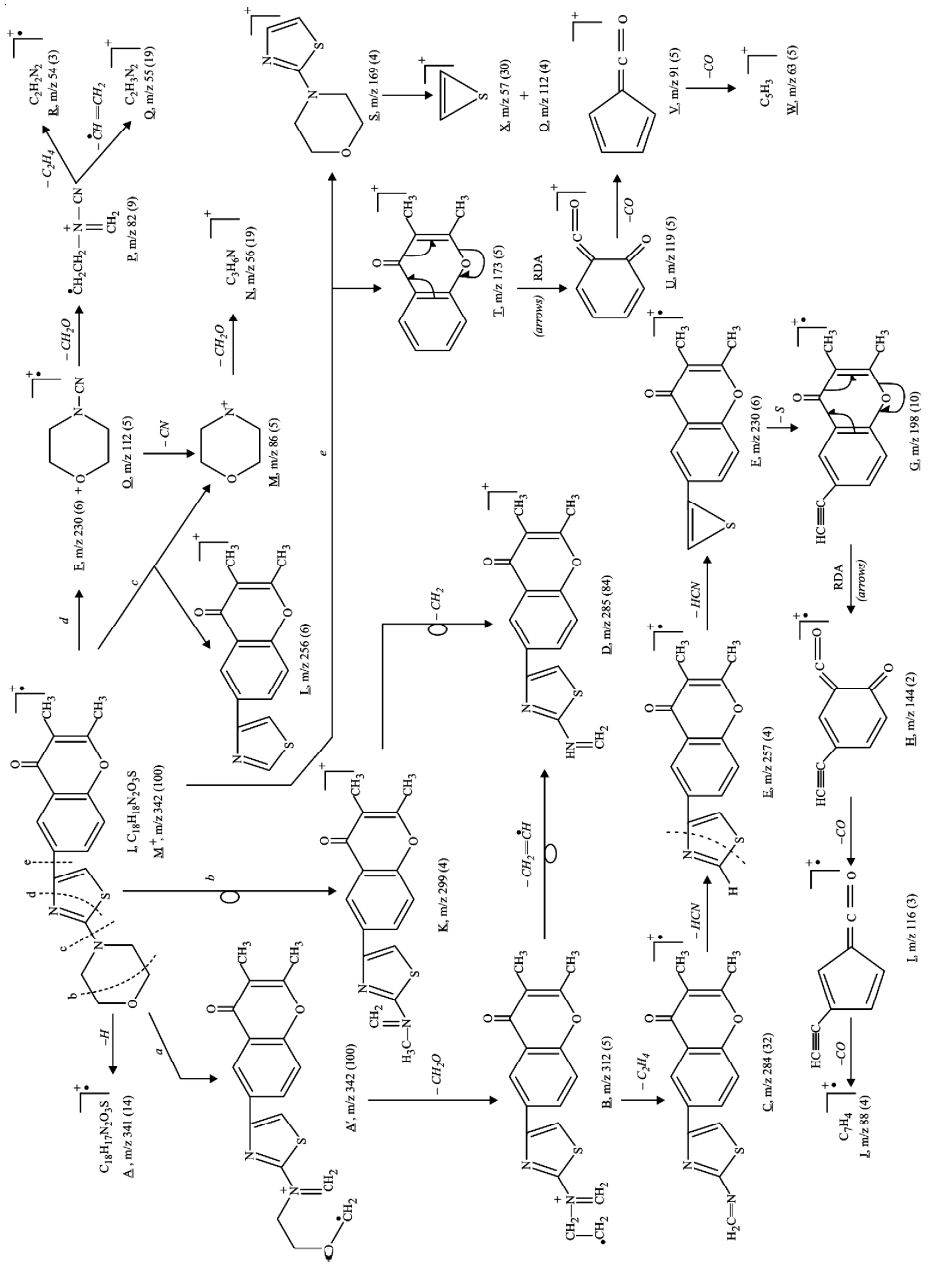


Fig. 1

ions, the spectra were also investigated to delineate the characteristic modes of fragmentation as expected from their molecular framework.

The molecular ion of **II**, for instance, appeared as a base peak at m/z 300. It underwent fragmentation along the following pathways (Fig. 2).

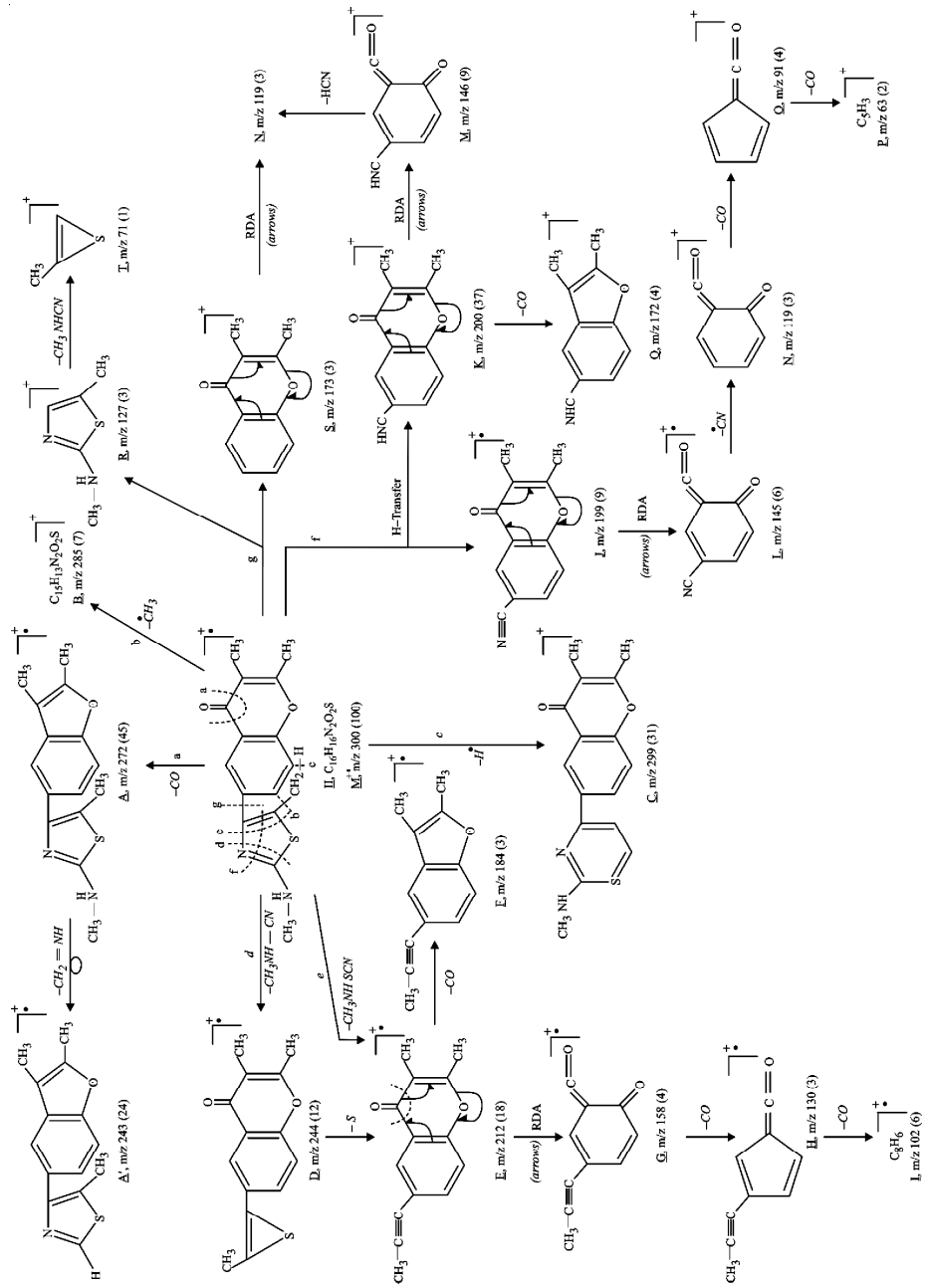


Fig. 2

- The presence of chromone ring triggered the expected extrusion of CO (path a) yielding an abundant ion A (m/z 272) which eliminated CH_2=NH with accompanying rearrangement to give A' (m/z 243).

• Elision of CH_3, from molecular ion (path b) generated a low intensity ion B (m/z 285).

• Expulsion of H' involving β-cleavage of C_5-CH_3 (path c) of thiazole moiety, formed a high intensity ion C (m/z 299).

• The presence of thiazole moiety triggered the elimination of CH_3NHCN (path d) forming the thierene radical ion D (m/z 244). Extrusion of sulphur from D gave the ion E (m/z 212). Ion E could also have arisen through a competitive process (path e) involving the expulsion of CH_3NHSCN. Further, cleavage of ion E took place by two alternate routes involving losses of CO and RDA fragmentation to give ions F (m/z 184) and G (m/z 158), respectively. Sequential losses of two molecules of CO from G afforded ions H (m/z 130) and I (m/z 102), respectively.

• Cleavage of thiazole moiety, presumably through path f, yielded the ions J (m/z 199) and K (m/z 200). The latter forming as a result of accompanying hydrogen transfer. The RDA fragmentation of both these ions afforded the corresponding ions L (m/z 145) and M (m/z 146), respectively. Elision of $^{\bullet}CN$ from L and HCN from M yielded the ion N (m/z 119) which underwent loss of two CO molecules in sequence generating the ions O (m/z 91) and P (m/z 63), respectively. In an alternate mode of fission, typical of chromones, expulsion of CO from ion K afforded ion Q (m/z 172).

• Fission of the molecular ion across the bond linking thiazole and chromone rings (path g) resulted in the formation of ions R (m/z 127) and S (m/z 173). The ion R gave rise to the thierene radical ion T (m/z 71) by the expulsion of CH_3NHCN, while the ion S afforded the corresponding quinonoid ion N by RDA fragmentation.

The fragmentation modes of **II**, depicted in Fig. 2, were further established by the appearance of the corresponding ions in the mass spectra of **III** and **IV**. 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.

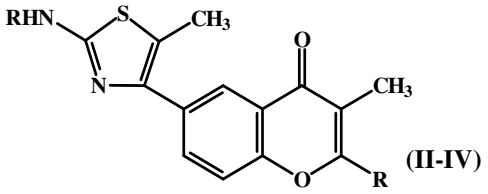
Electron impact-induced fragmentation of **V** was also investigated. Like other thiazolylchromones, the molecular ion appearing as a base peak at m/z 319 was in conformity with its molecular weight. It underwent fragmentation by two alternate pathways, one involving rupture of thiazole ring with and without hydrogen transfer and the other involving cleavage of chromone ring with or without hydrogen transfer. These modes, discussed below, are depicted in Fig. 3.

• The presence of chromone ring triggered RDA fragmentation yielding an intense ion B (m/z 217) alongwith the expected phenylacetylene radical ion C (m/z 102). The ion A (m/z 218) has been formed by the RDA cleavage of molecular ion with hydrogen transfer. Sequential losses of two molecules of CO from B afforded D (m/z 189) and E (m/z 161). Fission of thiazole ring in D gave low intensity ion F (m/z 117) alongwith a high intensity thierene radical ion G (m/z 72). Elision of $H^{\bullet}$ from G gave another abundant ion H (m/z 71). In a competitive process, D yielded I (m/z 118) by the fission of thiazole ring involving hydrogen transfer. These processes are quite characteristic of the mass spectral cleavage of thiazoles.

Elimination of CO followed by •CN or *vice-versa* from F afforded ion L (m/z 63) *via* the intermediate ion J (m/z 89) and K (m/z 91), respectively.

Fragmentation of ion C involved expulsion of •C≡CH and CH≡CH giving rise to two low intensity ions M (m/z 77) and N (m/z 76), respectively.

TABLE-1
SIGNIFICANT MASS SPECTRAL DATA OF **II**, **III** AND **IV** (ARRANGED TO DISPLAY THE PEAK-TO-PEAK CORRESPONDENCE OF FRAGMENT IONS)



(II-IV)

	II R = CH_3, R' = CH_3	**III** R = CH_3, R' = C_6H_4Cl	**IV** R = C_6H_5 R' = C_6H_5
M^+	300 (100)	396/398 (100)	424
Fragment ions			
A	272 (50)	–	–
A•	243 (24)	243 (9)	305 (8)
B	285 (7)	381/383 (19)	409 (5)
C	299 (31)	295/297 (24)	423 (26)
D	244 (12)	244 (9)	–
E	212 (18)	212 (9)	–
F	184 (3)	184 (11)	–
G	158 (4)	158 (2)	158 (4)
H	130 (3)	130 (1)	130 (2)
I	102 (5)	102 (4)	102 (3)
J	199 (9)	199 (10)	261 (5)
K	200 (37)	200 (18)	262 (5)
L	145 (6)	145 (3)	145 (3)
M	146 (9)	146 (5)	146 (4)
N	119 (3)	119 (1)	119 (4)
O	91 (4)	91 (2)	91 (7)
P	63 (2)	63 (1)	63 (4)
Q	172 (4)	172 (3)	234 (2)
R	127 (3)	–	189 (2)
S	173 (3)	173 (2)	235 (3)
T	71 (1)	71 (1)	71 (12)

• The expected cleavage of thiazole ring with or without hydrogen transfer generated thierene radical ion G alongwith a moderate intensity ion O (m/z 248) and a weak ion P (m/z 247), respectively. The RDA cleavage of O and P yielded ions Q (m/z 146) and R (m/z145), respectively, alongwith phenylacetylene radical ion C.

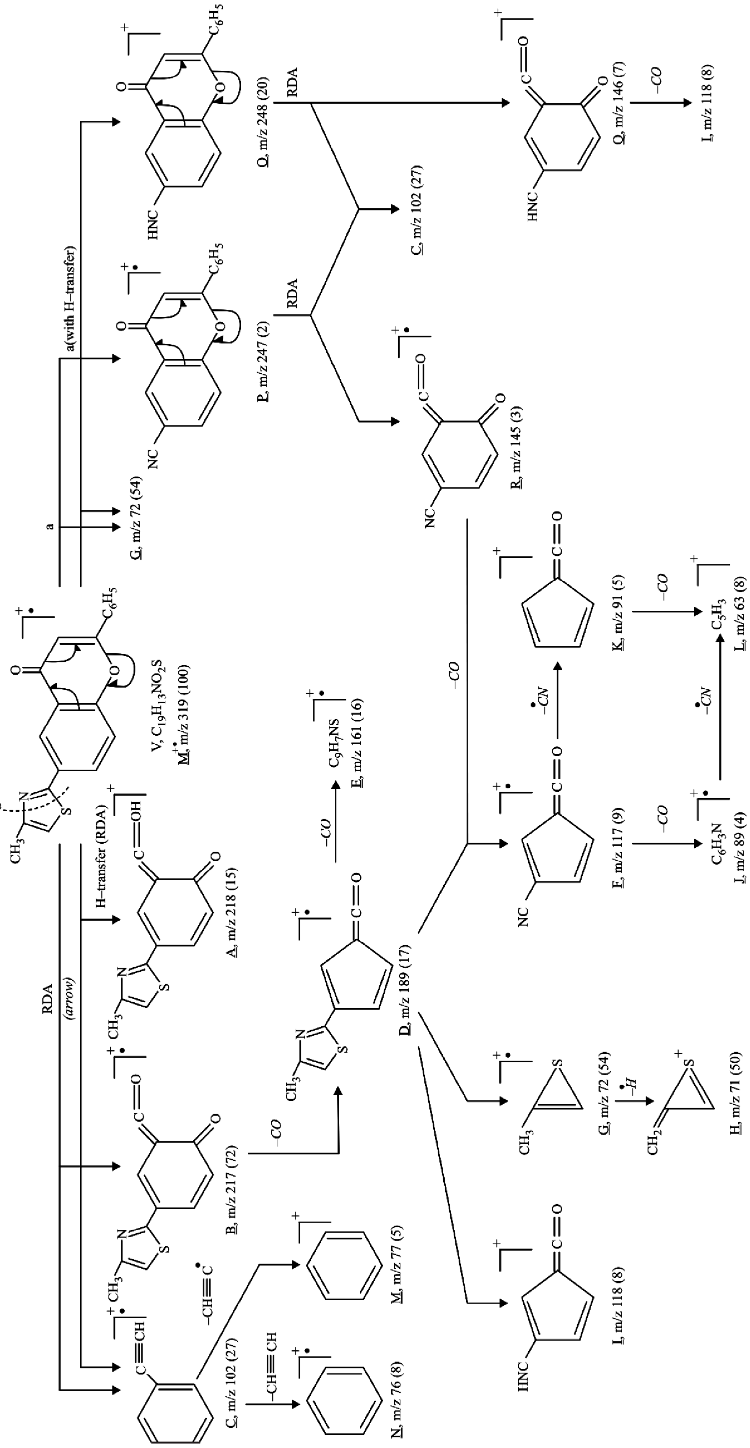

V, $C_{19}H_{13}NO_2S$
M, m/z 319 (100)
RDA
(arrow)
H–transfer (RDA)
a
a(with H–transfer)
RDA
RDA
G, m/z 72 (54)
P, m/z 247 (2)
O, m/z 248 (20)
C, m/z 102 (27)
R, m/z 145 (3)
Q, m/z 146 (7)
–CO
I, m/z 118 (8)
A, m/z 218 (15)
B, m/z 217 (72)
–CO
C_9H_7NS
E, m/z 161 (16)
D, m/z 189 (17)
–CO
F, m/z 117 (9)
–CN
K, m/z 91 (5)
–CO
–CO
C_6H_3N
J, m/z 89 (4)
–CN
C_5H_3
L, m/z 63 (8)
G, m/z 72 (54)
–H
H, m/z 71 (50)
I, m/z 118 (8)
C, m/z 102 (27)
–CH≡C
M, m/z 77 (5)
–CH≡CH
N, m/z 76 (8)

Fig. 3

The mass spectral studies of thiazolylchromones have established that the fission of thiazole moiety is energetically more feasible than that of chromone ring. This fact is borne out by the observation that the commonly seen retro Diels-Alder fragmentation of chromones does not take place directly from the molecular ion. It occurs only after the thiazole ring has undergone fission. The only exception is the compound **V** in which the chromone ring is attached to 2-position of the thiazole nucleus.

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