2-Aminothiazole Derivatives. I. Mass Spectra of 2-Acetylacetamidothiazoles and *N*-(2-Thiazolyl)-β-(2′-thiazolylamino)crotonamides

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2-Acetylacetamidothiazoles (**2**) and *N*-(2-thiazolyl)-β-(2′-thiazolylamino)crotonamides (**3**) break down in a well-defined manner upon electron impact. In either of the two cases, the fragmentation pattern involves hydrogen transfer, similar to the McLafferty rearrangement. The principal ions formed are characterised and the most plausible mechanism of their formation is discussed.

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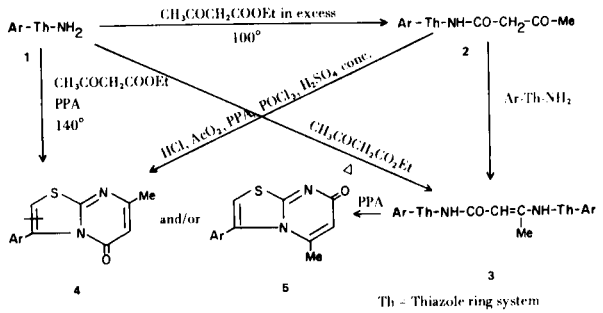
In its reaction with ethyl acetoacetate, 2-aminothiazole as well as its substituted derivatives behave in a manner similar to 2-aminopyridine (1,2). Depending upon the experimental conditions, the reaction may lead either to the cyclic compounds **4** or **5** or to the linear products **2** or **3** (3-6). These different possibilities are summarized in the Scheme 1. It is particularly noticeable that **2** or **3** can be considered as intermediates in the formation of the thiazolo[3,2-*a*]pyrimidine ring system.

Our interest in the study of the behaviour of these compounds under electron impact in a mass spectrometer stemmed from a motive of eventually comparing their stability under the influence of other factors *viz.* heat, chemical reagents, *etc.* Although the decomposition path of the thiazole ring system under electron impact has been well established (7-10), the derivatives of the 2-aminothiazole, to our knowledge, has not yet been properly studied, in this respect.

Six acetylacetamidothiazoles (Ar = H, Me, Ph, tolyl, *p*-ClPh) and two crotonamides (Ar = *p*-ClPh and *p*-xenyl) have been our object of study. The results obtained show that the nature of the aryl substituent plays only a minor role in the fragmentation process in either of the two

Scheme 1



series. Mass spectral data of the most representative members of these series are summarized in Table I and Figures 1-2. Peaks, having relative intensities > 5% have only been reported. Those with values lower than that have been ignored since these are practically of no importance for the interpretation of the fragmentation pattern.

Table I

Compounds	Ar						
2	*p*-$MeOC_6H_4$	m/e	291	290(M)	270	248	232
		I%	23	88	6.2	9.4	15
		m/e	208	206	293	192	191	165
		I%	43	100	15	31	71	14
		m/e	164	163	151	150	149	135
		I%	80	50	17	31	97	43
		m/e	134	133	132	121	120	
		I%	43	38.5	13	76	7.7	
		m/e	103	95.5	77			
		I%	43	17	52.3			
3	*p*-ClC_6H_4	m/e	487	486(M)	452	450	280	
		I%	13	27	12	16	98	
		m/e	279	278	277	276	251	250
		I%	98	79	70	100	60	57
		m/e	249	238	236	235	212	211
		I%	63	26	66	80	51	76
		m/e	210	209	168			
		I%	72	82	52			

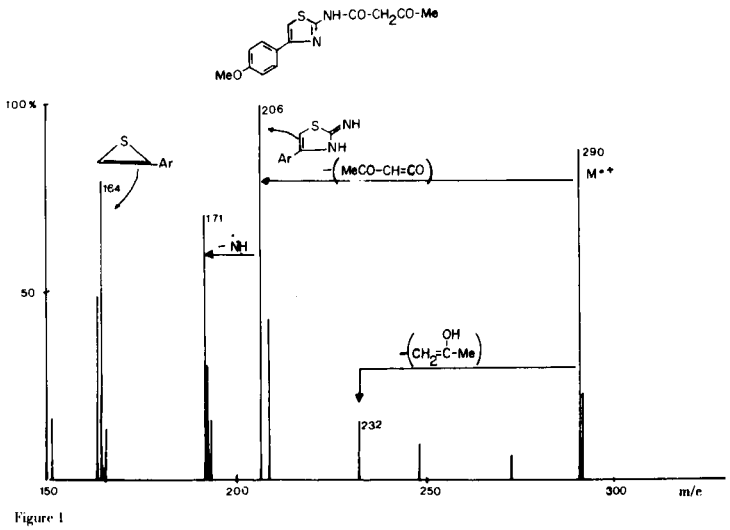


Figure 1

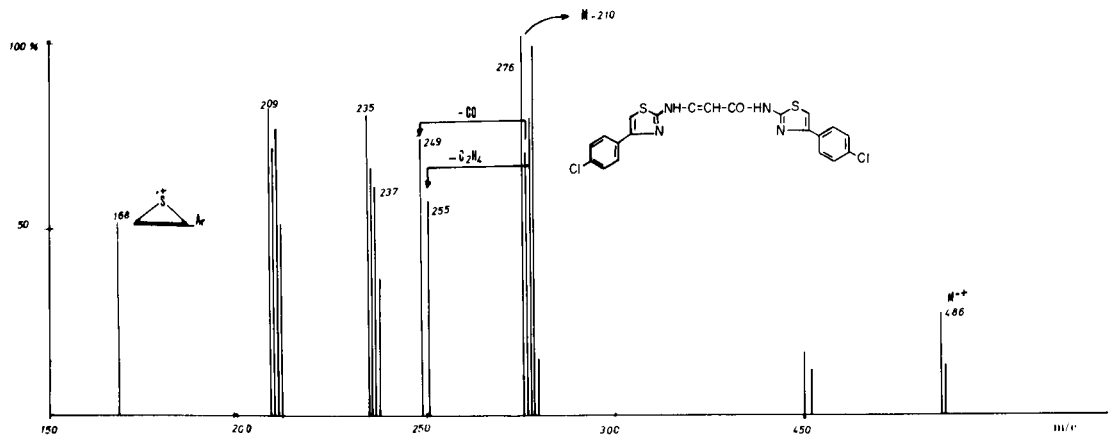
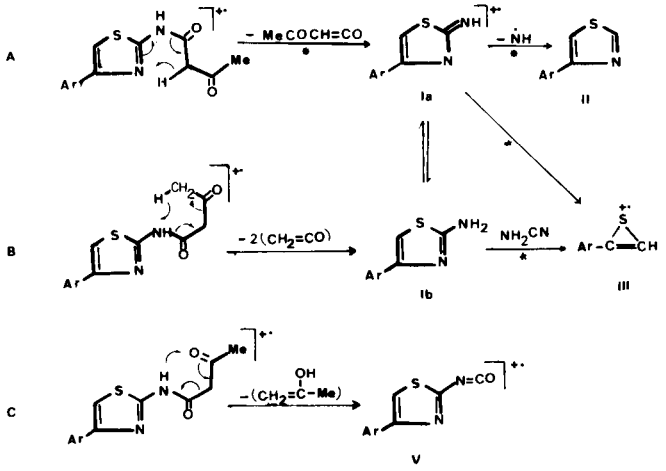


Figure 2

I. 2-Acetylacetamidothiazoles (**2**).

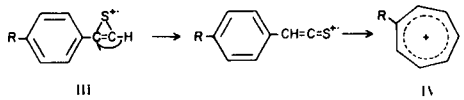
The stability of these compounds under electron impact is manifested by the high relative intensity of the molecular ion peak, which is greater than 50% and even attains 100% in the case of the chloro derivative. The principal fragmentation process involves the loss of a neutral fragment $CH_3COCH{=}C{=}O$ from the molecular ion leading to the ion Ia, which also constitutes the base peak in most of the cases. The mechanism involved is identical with that of a McLafferty rearrangement (11) consisting of a hydrogen transfer.

Scheme 2



* Transition corroborated by a metastable peak.

It can be noted that the hydrogen is transferred to the nitrogen in the ring, which acts as a nucleophile (Path A, Scheme 2). A second mechanism (Path B) can also be envisaged which will involve the loss of two molecules of vinylketone from the molecular ion leading to Ib, the hydrogen being transferred to the amide nitrogen. Considering the high nucleophile character of the cyclic nitrogen, path A seems more plausible. The ion Ia, notwithstanding its pronounced stability, can lose either the NH* radical to give the arylthiazole II or NH_2CN leading to the ion III. The latter can also be formed from II by the loss of HCN. All these transitions are corroborated by appropriate metastable peaks. This breaking of 1-2 and 3-4 bonds of the nucleus, which was evidenced by Clarke (7) and Metzger (10) in the cases of thiazoles, methylthiazoles and phenylthiazoles, can be noticed in all the spectra we have studied. Like the other phenylthiazoles, the ion III, in its turn, undergoes the familiar process of fragmentation already described by Metzger (10), leading the ion IV, particularly important in the case of the *p*-anisyl derivative.



Path C embodies another fragmentation process, which the molecular ion may undergo and which will lead to the ion V. Less important than the other two paths (A and B), it can nevertheless be noticed in all the spectra. It involves the loss of the enol $CH_2{=}C(OH){-}CH_3$, equally followed by a McLafferty rearrangement. This type of hydrogen transfer is quite common in α- and β-diketones (11-13).

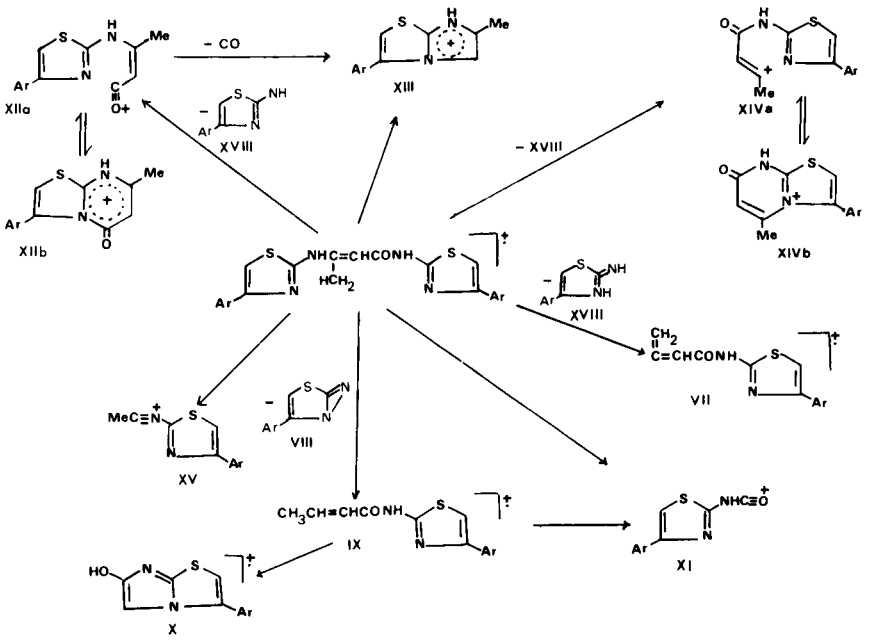
II. *N*-(2-Thiazolyl)-β-(2′-thiazolylamino)crotonamides (**3**).

The electron-impact fragmentation of these compounds becomes an interesting subject of study by virtue of the number and the variety of fragments formed.

Scheme 3 shows the fragmentation pattern of the *p*-chloro derivative as a typical example.

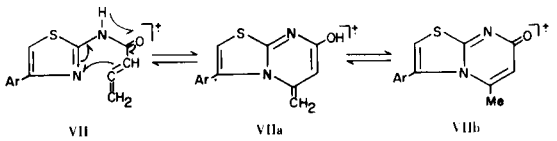
a) The most abundant ion (M-210) is formed by the loss of an iminothiazoline molecule preceeded by a hydrogen transfer from the methyl group to the nearest cyclic

Scheme 3



nitrogen atom. The ion VII thus obtained, probably undergoes rearrangement to the cyclic ion VIIa or VIIb.

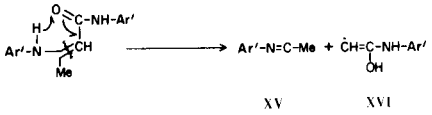
b) A second interesting ion is noticed at m/e 278 (79%



of the base peak) formed by the loss of diazathiazolocyclopropene (VIII) from the molecular ion. This ion, in turn, may undergo a rearrangement and lose a molecule of ethylene leading to the cyclic ion X. Alternatively, loss of an acrylic radical may result in the positive ion XI, which also may be formed by the breaking of the CH-CO bond in the molecular ion. A loss of hydrogen from XI may lead to the ion V, which we have already noticed in Scheme 2.

c) Loss of the Ar-ThNH$^{\bullet}$ radical may lead to the third important peak of the spectrum at m/e 277 (77% of the base peak). This loss of ArTHNH$^{\bullet}$ may occur in two ways: (i) Breaking of the NH-CO bond will lead to the ion XII, capable of existing as either *a* or *b*. This ion may lose CO, in its turn, to give the positive ion XIII, a transition corroborated by the appropriate metastable peak. Fragment XIII is also capable of being formed by the breaking of CH-CO bond in the molecular ion, but there is no appropriate metastable peak to support it. (ii) The second possibility is the breaking of the NH-C(Me) bond leading to the ion XIV, which undergo further fragmentation with the loss of CO and Me-C=CH.

d) Lastly, a peak of very high intensity (80% of the base peak) at m/e 235 probably corresponds to the ion XV, resulting from the breaking of -C(Me)=CH- bond, preceded by a McLafferty rearrangement consisting of a hydrogen transfer from NH to the amide carbonyl function. The other fragment (enol ion XVI) is also quite important (60%).



Besides these, the fragments XVII and XVIII also give peaks of quite high intensity in the spectrum.

It should be noted that most of the transitions indicated in Scheme 3 are justified by appropriate metastable peaks. These are summarized in Table II.

Table II

Transition	m* Calcd.	m* Found
$M^+ \rightarrow 278$	159	161
$278 \rightarrow 250$	224.8	224
$278 \rightarrow 237$	202	200
$277 \rightarrow 249$	223.8	224
$237 \rightarrow 236$	235	236

In both of the series, the 2-iminothiazolines ions are formed with remarkable ease. It is, undoubtedly, the conjugation between the benzene nucleus and the thiazole

ring which is responsible for the relative stability shown by these compounds under electron impact. On the other hand, the various McLafferty type rearrangements noticed in the fragmentation processes with the participation of the cyclic nitrogen can be explained by the highly basic character of this atom.

EXPERIMENTAL

Mass spectra were recorded with an Atlas CH4 mass spectrometer at an ionizing potential of 70 eV. Samples were analysed by direct introduction through a heated inlet system at *ca.* 50° for the acetylamidothiazoles and 250° for the crotonamides. Elemental compositions were obtained by the peak matching method.

The compounds studied are already described in the literature (3-6).

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