Mass Spectra of some 5*H*-Thiazolo[3,2-*a*]pyrimidin-5-ones (1)

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The mass spectra of some 7-methyl, 7-chloro and 6-carbethoxythiazolo[3,2-*a*]pyrimidin-5-ones were studied (**2,3,4**). The electron impact fragmentation patterns of these compounds showed their relatively high stability and their similar mode of decomposition. Certain differences were observed among the three classes of compounds, due to the nature of the substituent on the pyrimidine ring.

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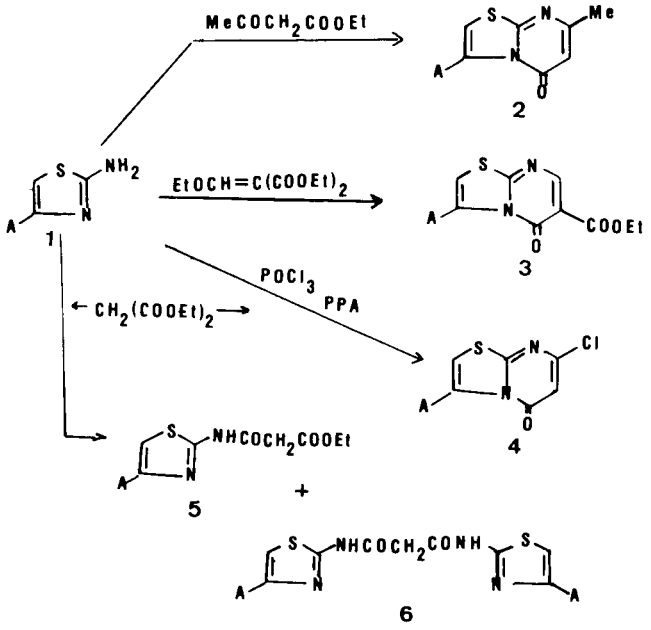
The physico-chemical properties of the open-chain condensation products of 2-aminothiazole and its 4-substituted derivatives with ethyl acetoacetate, ethyl malonate and ethyl ethoxymethylene malonate were previously reported by us (1,2). The present report describes the mass spectra of the cyclic reaction products obtained with the same esters and either 2-aminothiazole or its 4-aryl derivatives.

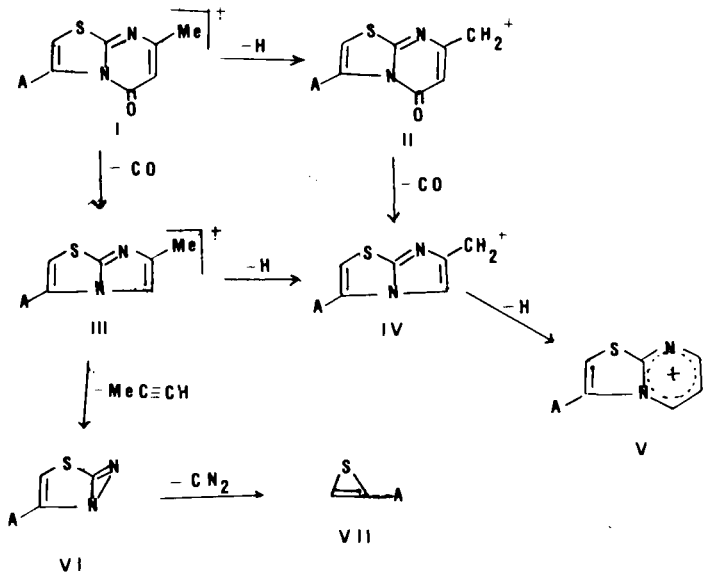
In addition to yielding open-chain compounds, the reaction between 2-aminothiazoles and ethyl acetoacetate and ethyl ethoxymethylene malonate also yields thiazolo-[3,2-*a*]pyrimidin-5-ones (**2** and **3**), whose structures have been confirmed with chemical and physico-chemical techniques (3,7). Apart from ultraviolet spectral data (4,5), however, their physico-chemical properties have not yet been systematically studied.

The major reaction products of 2-aminothiazoles with ethyl malonate under standard conditions are the open-chain compounds **5** and **6** (1,9.10). By heating the two compounds in phosphorus oxychloride in the presence of catalytic amounts of polyphosphoric acid we were able to obtain the bicyclic chloro reaction products. This conclusion is based on elemental analyses and the nmr spectra of the products (Table 1). A higher yield of compounds **4** could be obtained by reacting phosphorus oxychloride with malonamate **5**.

The mass spectra data of the ten products studied are shown in Tables 2-4. Only those peaks with a relative intensity >5% have been included for the sake of simplicity. Relative intensities >5% were ignored, since they are not directly relevant to the fragmentation process.



Scheme 1



Scheme 2

0022-152X/79/081535-05$02.25

Table 1

Characteristics of Compounds **4**

A	Formula	M.p. °C	Yield (%)	% Calculated C	H	N	% Found C	H	N	Nmr Data: Ppm (deuteriochloroform)
Me	$C_7H_5ClN_2OS$	135	42	42.0	2.5	14.0	42.0	2.6	14.0	2.8 (d (a), *Me*), 6.21 (s, *H*6), 6.62 (d (a), *H*2)
p-ClPh	$C_{12}H_6Cl_2N_2OS$	238	17	48.5	2.0	9.4	48.3	2.2	9.2	6.27 (s, *H*6), 6.8 (s, *H*2) 7.35 (s, 4H, arom)
p-MePh	$C_{13}H_9ClN_2OS$	240	60	56.6	3.2	10.1	56.5	3.2	9.8	6.22 (s, *H*6), 6.76 (s, *H*2), 7.21 (s, 4H, arom)
p-MeOPh	$C_{13}H_2ClN_2O_2S$	189	15	53.5	3.1	9.6	53.7	3.2	9.7	6.27 (s, *H*6), 6.75 (s, *H*2), 6.91 (s, 4H, arom), 7.35 (d, 4H, arom)
p-PhPh	$C_{18}H_{11}ClN_2OS$	220	10	63.9	3.3	8.3	63.7	3.4	8.2	6.3 (s, *H*6), 6.85 (s, *H*2), 7.55 (m, 9H, arom)

(a) $J_{H_2'Me}$ = 0.6 cps.

Table 2

Relative Intensity Data for Compounds **2** (a)

Compound No.	A	
2a	H	m/e: 166 (M^+) 151 138 (III) 137 (IV) I%: 100 12 53.4 48.8
2b	*p*-C_6H_4	m/e: 257 256 (M^+) 255 (II) 254 240 238 229 228 (III) 227 (IV) 266 (V) 215 213 I%: 35.3 96 100 95.3 5.9 5.9 17.6 54.11 99 99 34 17.6 m/e: 212 189 188 (VI) 171 168 148 (VII) 147 146 I%: 27 17.6 75.3 10.6 16.5 10.7 59 98
2c	*p*-ClC_6H_4	m/e: 279 278 277 276 (M^+) 275 (II) 251 250 249 248 (III) 247 (IV) 236 235 I%: 35 85 85 85 60 19 85 83 100 83 38 14 m/e: 234 233 211 210 209 170 269 268 (VII) I%: 18 27 26 15 63 35 13 85

(a) Figures in parentheses indicate the nature of the ion.

Compound No.	Transition	Metastable Peaks m* Calculated	m* Found
2a	$M^+ \rightarrow 138$	115	115
2b	$M^+ \rightarrow 228$	203	203
	$228 \rightarrow 227$	226	225-226
	$228 \rightarrow 188$	155	152
	$188 \rightarrow 148$	116.5	114.5
2c	$M^+ \rightarrow 248$	223	222-224
	$248 \rightarrow 247$	246	246

7-methylthiazolo[3,2-*a*]pyrimidin-5-ones (**2**).

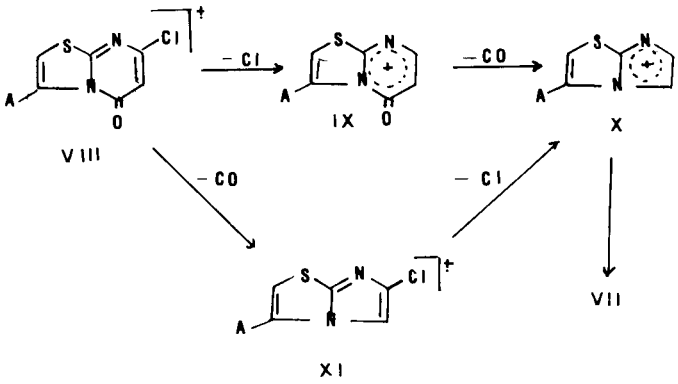
Compound 2 (A = H) was found to be highly stable under electron impact. Aside from the molecular ion, which is also the base peak, the only other peaks of considerable magnitude were (M^+-28) (53%) resulting from the loss of CO, (M^+-29) (49%) resulting from the loss of H and (M^+-15) (12%) resulting from the loss of CH_3.

Fragmentation appears to be facilitated by the introduction of *p*-chlorophenyl or *p*-methylphenyl on position 3. The mass spectrum of the *p*-methylphenyl compound contains a greater number of peaks, the largest of which are indicated in scheme 2. In addition to the molecular ion peak, fragmentation occurs according to two pathways. The first involves the loss of H to form ion II which in turn loses CO to yield ion IV. The second pathway involves the loss of CO to form ion III, followed by the loss of H to form ion IV; the latter loses a second hydrogen to form the positive ion V. The validity of these proposed transitions is supported by the correspond ing metastalbe peaks (Table 2).

The mass spectra of the *p*-chlorophenyl and *p*-methylphenyl compounds also indicate the presence of the thiazolodiazacyclopropene ion, VI, which is formed directly from III by the loss of Me-C≡CH; this is supported by the presence of the appropriate matastable peak. The presence of a peak corresponding to ion VII is also to be noted. This ion probably arises from the decomposition of VI, a process involving the loss of CN_2.

7-chlorothiazolo[3,2-*a*]pyrimidin-5-ones (**4**).

These compounds were also highly stable under electron impact, as shown by the high relative intensity of the molecular ion peak in the mass spectrum, as well as by the presence of a large peak corresponding to the doubly charged ion. The major fragmentation pattern corresponds to the loss of 7-Cl to form ion IX, which yields the base peak in all cases. Ion XI is formed by a second pathway, involving the elimination of CO from the molecular ion, but this mechanism is of minor importance, since the relative intensity of the corresponding peak never exceeds 30%. Ion X can arise by either the loss of CO from IX or the loss of Cl from XI, but unlike the above cases, there is no metastable peak which can confirm this



Scheme 3

Table 3

Relative Intensity Data for Compounds **4**

Compound No.	A	
4a	*p*-MeC_6H_4	m/e: 278 277 (M^+) 275 249 (XI) 244 243 242 (IX) 241 214 (X) 191 174 I%: 60 100 11.7 16.5 11.7 36.5 100 21.2 6 15.1 9.4 m/e: 160 150 149 148 (VIII) 138 I%: 17.6 10 61.2 65.9 11
4b	*p*-$MeOC_6H_4$	m/e: 294 293 292 (M^+) 276 264 (XI) 259 258 257 (IX) 256 241 299 (X) I%: 97 44.7 100 12 14 11 35.3 100 68.2 23.5 9.4 m/e: 206 175 164 (VII) 147 146 I%: 5.9 29.4 93 12 12
4c	*p*-ClC_6H_4	m/e: 300 299 298 297 296 270 268 264 262 261 260 235 210 198 I%: 29.4 22.3 100 37.6 100 21.2 29.4 17.5 53 100 21.2 11 11 12 m/e 193 170 168 I%: 9.4 38.8 62.3

Metastable Peaks

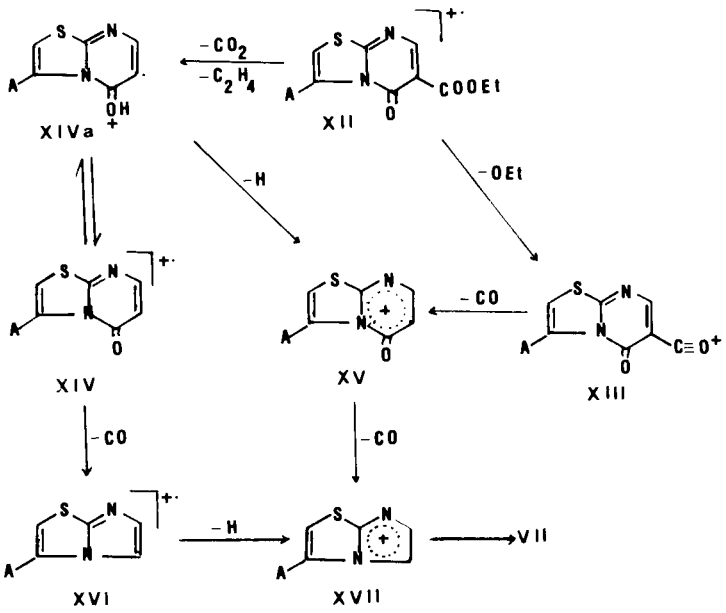
Compound No.	Transition	m* Calculated	m* Found	Transition	m* Calculated	m* Found
4a	$M^+ - CO$	224	224	$M^+ - Cl$	211.4	211.5
	$(M^+ - Cl)$-CO	189	189			
4b	$M^+ - CO$	239	239	$M^+ - Cl$	226	226
	$(M^+ - Cl)$-CO	204	204			
4c	$M^+ - CO$	245	242-244	$M^+ - Cl$	230	230
	$(M^+ - Cl)$-CO	210	208			

transition. Ion VII is also formed by the breaking of the thiazole ring of ion X.

6-carbethoxythiazolo[3,2-*a*]pyrimidin-5-ones (**3**).

The carbethoxy group is affected first by electron impact. Three peaks are present in all spectra at M^+-45, M^+-72 and M^+-73. They correspond to ions XIII, XIV and XV and are formed, respectively, by the loss of OEt, (CO_2 + C_2H_4 or CO + OC_2H_4) and CO_2Et. Ion XIV is formed by a double rearrangement, probably *via* the intermediate XIVa. Both XIV and XV lose CO, yielding XVI and XVII, whose peaks are more or less prominent in the spectra. Finally, the spectra contain a peak corresponding to ion VII, which could have been formed by the decomposition of either XVI or XVII.

Based on the above findings, we may conclude that all three compounds behave quite similarly under electron impact. They all exhibit more or less prominent molecular ion peaks which, in most cases, are also the base peaks. The common fragmentation pattern involves the loss of CO to form the thiazolo[3,2-*a*]imidazole ion (III, XI or XVI). This ion then undergoes a decomposition involving



Scheme 4

Table 4

Relative Intensity Data for Compounds **3**

Compound No.	A	
3a	H	m/e: 225 224 (M^+) 196 181 180 179 (XIII) 154 153 152 (XIV) 151 (XV) 124 (XVI) 111 58 (VII) I%: 6.4 45 12.5 7 25 100 5 10 95 12.5 25 50 15
3b[c]	C_6H_5	m/e: 301 300 (M^+) 271 256 255 (XIII) 228 (XIV) 227 (XV) 226 226 211 201 200 (XVI) I% 18.6 100 4.6 11.6 70 14 93 23 7 7 7 39.6 m/e: 199 (XVII) 187 173 134 (VII) 21 23 11.8 40.5
3c	*p*-$MeOC_6H_4$	m/e: 332 331 330 (M^+) 329 301 287 286 285 (XIII) 260 259 258 (XIV) 257 (XV) 256 I%: 25 68 100 8 8 8 22.8 99 6.8 22.6 99 37 12.6 m/e: 241 231 230 (XVI) 229 (XVII) 217 214 213 206 186 175 165 164 (VII) 149 I%: 22.6 11.5 66 31 22 11.5 13.8 7 11.5 12 22.5 7 62.5
3d	*p*-ClC_6H_4	m/e: 336 335 334 (M^+) 291 290 289 (XIII) 264 263 262 (XIV) 261 (XV) 260 245 I%: 55.5 28 100 33 15.5 74 31 19 80 19 7.5 4.8 m/e: 236 235 234 (XVI) 233 (XVII) 221 168 (VII) I%: 13.8 13.8 34 18 20 48

Metastable Peaks

Compound No.	Transition	m* Calculated	m* Found	Transition	m* Calculated	m* Found
3a	$M^+ \rightarrow 179$	143	144-145	$179 \rightarrow 151$	127.4	128.4
3b	$M^+ \rightarrow 255$	217	218	$M^+ \rightarrow 228$ 173	173	173
	$M^+ \rightarrow 227$	172	173			
3c	$M^+ \rightarrow 285$	248	246	$M^+ \rightarrow 258$	201.7	201-202
	$M^+ \rightarrow 257$	200.1	201-202	$258 \rightarrow 230$	205	202
3d	$M^+ \rightarrow 262$	205.5	205	$M^+ \rightarrow 261$	204	205
	$262 \rightarrow 234$	209	206			

VII, which is the normal pathway of electronolysis of thiazole derivatives (2,11). The only significant differences among these compounds result from the presence of different substituents (Me, Cl, CO_2Et) on the pyrimidine ring.

As with the linear derivatives (1,2), the remarkable stability of substituent A on the thiazole ring is to be noted. No loss nor modification of any type could be detected at any stage of the fragmentation process.

EXPERIMENTAL

Nmr spectra were recorded with a Perkin Elmer R 12 Spectrometer. Mass spectra were recorded with an MS 50 Mass Spectrometer at an ionizing potential of 70 eV. Sample analysis was by direct introduction through a heated inlet system at about 150-230°. Elemental analyses were performed with the peak matching metod.

Compounds **2** and **3** were prviously described (3-9).

7-Chloro-3-(alkyl or aryl)-thiazolo[3,2-*a*]pyrimidin-5-one (**4**).

A mixture of the amine (0.05 mole), ethyl malonate (0.06 mole) and phosphorus oxychloride (0.15 mole) was heated in the presence of 2 g. of polyphosphoric acid at 120° for 3 hours. Absolute ethanol was then carefully added and the resulting precipitate was filtered and washed with ether. It was neutralized with sodium bicarbonate and recrystallized from an aceton-hexane mixture.

The yield of the same products with the malomates (**5**) was slightly higher (Table 1).

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