N,N-Coupled Heterobicycles from Cyclic Hydrazine Derivatives. Part 6 [1]. Electron Ionization Mass Spectrometry of Some Substituted 1-Thiocarbamoyl and 1-Carbamoylpyrazolidines

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The electron ionization mass spectra of six substituted 1-thiocarbamoyl and four substituted 1-carbamoylpyrazolidines were measured and carefully analyzed. The fragmentation pathways were elucidated by metastable ion analysis and exact mass measurement. The principal fragmentations were the same for all the compounds studied. The related importance of different decomposition channels, however, varied according to the structure of the compounds. Some substituents also prompted fragmentations unique to them. The most important reaction was the loss of the thiocarbamoyl or carbamoyl substituent with simultaneous hydrogen atom migration from the (thio)carbamoyl nitrogen to the ring nitrogen giving rise to ionized pyrazolidine at m/z 72. In this process for 1-(*N*-arylthiocarbamoyl)pyrazolidines the charge tended to remain with the substituent part of the molecule. Moreover for all the compounds studied $[M-2H]^{+\cdot}$ ion peaks formed by dehydrogenization of the original compounds were observed.

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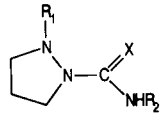
The 1-thiocarbamoyl and 1-carbamoylpyrazolidines whose mass spectrometric behavior is reported in this paper can be synthesized by reaction of pyrazolidine with isothiocyanates and isocyanates, respectively [2]. These pyrazolidines and their cyclization products like related pyrazolo[1,2-*a*][1,2,4]triazoles or pyrazolo[1,2-*c*][1,3,4]thiadiazoles [3,4,5] are potentially biologically active substances. For example, many differently substituted pyrazolidine derivatives have been reported to act as bactericides [6], inflammation inhibitors [7], herbicides [8] or pesticides [5,9].

Relatively little is known about the mass spectrometry of pyrazolidine derivatives [10-12]. However, mass spectrometry is one of the most useful analytical tools in synthetical organic chemistry. For a full utilization of this method it is important to know how different types of compounds behave under mass spectrometric conditions. In this work the electron ionization mass spectra of six substituted 1-thiocarbamoyl and four substituted 1-carbamoylpyrazolidines, compounds **1-10**, have been recorded and carefully analyzed. Our aim was to find fragmentations that could assist in structural determination with these types of compounds. Fragmentation pathways were verified by metastable ion analysis and collision induced dissociation techniques. Exact mass measurement was used to confirm the elemental composition of the principal fragment ions.

The structure of the compounds is given in Scheme 1 and their mass spectral data in Tables 1 and 2. Only 1-(*N*-methylthiocarbamoyl)pyrazolidine (**1**) gave rise to an intense molecular ion peak. For all the other compounds the intensity of the molecular ion peak was relatively low and the peak was totally absent in the spectrum of compound **6**. All the compounds examined showed the $[M-2H]^{+\cdot}$ ion peak. Its absolute intensity was always small but in some cases, however, relatively large compared to the intensity of the molecular ion peak. Pyrazolidines as derivatives of hydrazine are known to have a tendency to undergo oxidation (dehydrogenization) to pyrazolines [13] and in accordance with that fact the $[M-2H]^{+\cdot}$ ions represent the related dehydrogenization products. It is not, however, unambiguously clear whether the oxidation was a real mass spectrometric process or did the conditions in the ion source induced it to take place. Some molecular ions gave rise to an exceptionally intense $[M-2H]^{+\cdot}$ ion peaks in their daughter ion (B/E) spectra. This indicates that the oxidation was the

Scheme 1



Compound	X	R_1	R_2
1	S	H	CH_3
2	S	H	CH_2=$CHCH_2$
3	S	H	4-Br-C_6H_4
4	S	H	4-Cl-C_6H_4
5	S	H	(4-Cl-2-C_6H_5CO)C_6H_3
6	S	$CO_2C_2H_5$	4-Br-C_6H_4
7	O	H	C_6H_5
8	O	H	4-Cl-C_6H_4
9	O	H	3-Cl-C_6H_4
10	O	H	1-naphthyl

real mass spectrometic process. The ^{1}H-nmr spectra showed that no pyrazolines were present in the original samples [2]. Some of the compounds were also studied by liquid chromatography (hplc). The results obtained verified that the original samples did not exist as a mixture of compounds [14].

Table 1

Principal Fragment Ions (Intensity ≥ 7%) in the Mass Spectra of the 1-Thiocarbomoylpyrazolidines Studied. The Relative Intensities for the Pairs of Ions Refer Only to the ^{79}Br or ^{35}Cl Isotope, m/z (% Relative Intensities)

1	145 (77) $M^{+\cdot}$, 75 (13), 74 (33), 72 (100), 71 (51), 57 (10), 56 (7), 44 (72), 43 (19), 42 (16), 41 (7), 30 (37), 27 (8)
2	171 (4) $M^{+\cdot}$, 142 (10), 141 (9), 138 (8), 128 (27), 116 (15), 115 (23), 101 (9), 99 (7), 86 (9), 72 (100), 71 (53), 60 (9), 57 (8), 56 (34), 44 (60), 43 (19), 42 (14), 41 (59), 39 (19), 30 (34), 27 (10)
3	285/287 (10) $M^{+\cdot}$, 214/216 (8), 213/215 (56), 155/157 (16), 134 (34), 90 (11), 76 (16), 75 (21), 74 (8), 72 (100), 71 (30), 67 (9), 63 (7), 50 (17), 44 (48), 43 (11), 42 (8), 41 (7), 30 (12)
4	241/243 (19) $M^{+\cdot}$, 170/172 (11), 169/171 (69), 134 (7), 111/113 (34), 75 (23), 72 (100), 71 (35), 50 (9), 44 (42), 43 (11), 42 (9), 30 (12)
5	345/347 (7) $M^{+\cdot}$, 274/276 (10), 273/275 (43), 272 (9), 196/198 (28), 133 (12), 106 (8), 105 (100), 77 (54), 72 (26), 7(8), 51 (17), 44 (26), 40 (14), 29 (8)
6	357/359 (-) $M^{+\cdot}$, 311/313 (17), 214/216 (8), 213/215 (81), 155/157 (17), 144 (43), 134 (36), 114/116 (15), 90 (13), 76 (15), 75 (20), 74 (8), 72 (9), 71 (100), 67 (9), 63 (8), 50 (16), 45 (7), 44 (20), 43 (8), 42 (17), 31 (11), 30 (19), 29 (19), 29 (11)

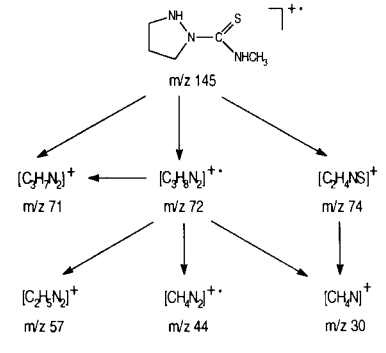
Table 2

Principal Fragment Ions (Intensity ≥ 7%) in the Mass Spectra of the 1-Carbamoylpyrazolidines Studied. The Relative Intesities for the Pairs of Ions Refer Only to the ^{35}Cl Isotope, m/z (% Relavive Intensities)

7	191 (17) $M^{+\cdot}$, 119 (14), 77 (7), 72 (100), 71 (30), 44 (34), 43 (10), 30 (8)
8	225/227 (14) $M^{+\cdot}$, 153/155 (27), 125/127 (11), 90 (9), 72 (100), 71 (36), 44 (33), 43 (9), 30 (8)
9	225/227 (20) $M^{+\cdot}$, 223/225 (14), 153/155 (20), 140/142 (8), 127/129 (20), 125 (7), 90 (8), 72 (100), 71 (44), 70 (85), 69 (35), 63 (8), 44 (34), 43 (15), 42 (13), 41 (7), 30 (10), 29 (13), 27 (7)
10	241 (16) $M^{+\cdot}$, 170 (10), 169 (74), 141 (21), 140 (17), 115 (9), 114 (12), 72 (100), 71 (22), 44 (30), 43 (8)

The principal fragmentation pathways for 1-(*N*-methylthiocarbamoyl)pyrazolidine (**1**) are presented in Scheme 2. As typical of nitrogen compounds, most of the decompositions can be rationalized to be initiated by different nitrogen atoms in the molecule. In principle, these fragmentations were the same for all the compounds examined. The related importance of different decomposition channels, however, varied according to the structure of the compounds. Some substituents also prompted fragmentations unique to them.

Scheme 2



With the exception of compound **5** the most important fragmentation was the charge site (nitrogen 1) initiated rearrangement reaction where the substituent was lost with a simultaneous hydrogen atom migration from the substituent nitrogen to the ring nitrogen 1. The reaction leads to the formation of pyrazolidine and substituted isothiocyanate or isocyanate with thiocarbamoyl and carbamoyl derivatives, respectively, therefore being the reverse reaction for the synthesis of the compounds studied. In this process the charge mostly remained with the pyrazolidine ring giving rise to the $C_3H_8N_2^{+\cdot}$ fragment ion at m/z 72 which almost always represented the base peak in the spectra. The fragmentation pathways of the $C_3H_8N_2^{+\cdot}$ ion (Scheme 2) were the same as those of the pyrazolidine molecular ion measured in our laboratory. The origin of the hydrogen atom migrated was verified by studying the 70 eV fragmentations of dideuterated 1-[*N*-(*N*-$^2H_1$)-methylthiocarbamoyl]-(2-$^2H_1$)-pyrazolidine. In this case the base peak shifted to m/z 74 representing the molecular ion of (1,2-$^2H_2$)-pyrazolidine (Figure 1). It was, however, relatively favorable in this rearrangement reaction that the charge remained with the isothiocyanate or isocyanate part when the nature of the substituent allowed it to stabilize the positive charge. This was the case with thiocarbamoyl compounds when the substituent was aromatic, **3-6**, but not with the aliphatic substituents, compounds **1** and **2**. Also with carbamoyl derivatives **7-10** it was much less favorable although they had an aromatic substituent with exception of compound **10** with a naphthyl substituent. This is reasonable because an aromatic structure can much better stabilize the positive charge than an aliphatic one as can sulfur better than oxygen. Isothiocyanate ions formed decomposed further losing NCS or halogen atom giving rise to fragment ion peaks absent with compounds **1** and **2**.

Another relatively important fragmentation was the loss of the substituent at the ring nitrogen leading to the $C_3H_7N_2^+$ ion at m/z 71. This process can be considered to be an α-cleavage reaction with respect to the ring nitrogen 2. The same bond rupture took place also so that the charge remained with the substituent representing α-cleavage reaction with respect to the substituent nitrogen or thiocarbonyl or carbonyl group. It is noteworthy, that ring cleavage reactions with respect to the nitrogen atoms did not generally take place directly from the molecular ions although the elimination of C_2H_4 from pyrazolidine itself is very favorable. The only exception from this behavior was compound **2** having an allyl substituent in thio-

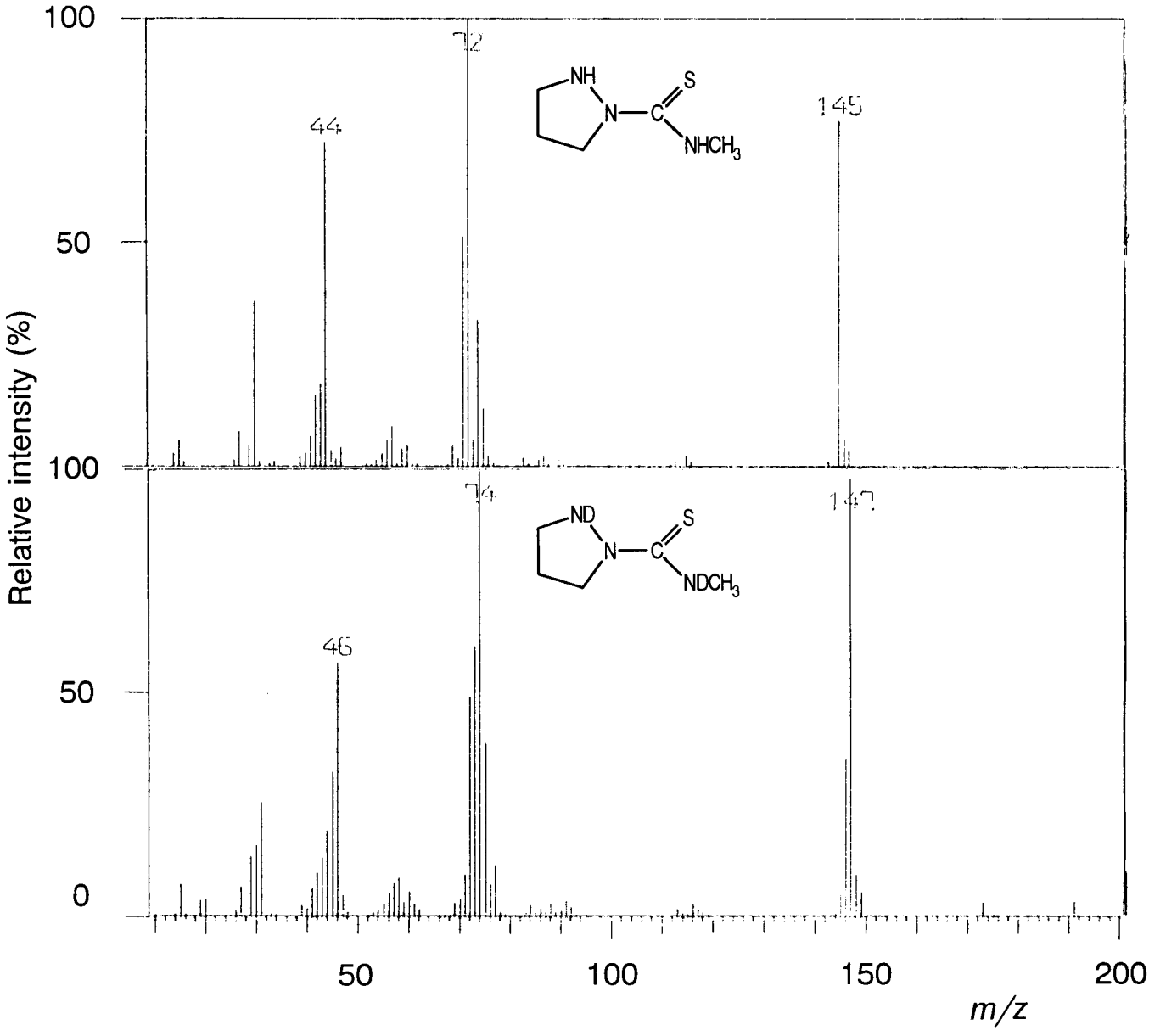


Figure 1. The 70 eV mass spectra for a) 1-(*N*-methylthiocarbamoyl)pyrazolidine (**1**) and b) 1 [*N*-(*N*-$^2H_1$)-methylthiocarbamoyl]-(2-$^2H_1$)-pyrazolidine.

carbamoyl group. This compound lost both C_2H_5N and CH_3N directly from its molecular ion giving rise to the $[C_5H_8N_2S]^{+\cdot}$ and $[C_6H_{10}N_2S]^{+\cdot}$ ions, respectively. If these losses originated from somewhere else than the ring very extensive rearrangements were needed although it is true that pyrazolidine itself does not decompose this way.

At first sight the spectra of compounds **5** and **6** looked very different from those of the other compounds studied. With compound **5** this difference was real due to the benzoyl substituent at the *ortho* position of the phenyl ring. The most intense fragment ion peaks in the spectrum were caused by this substituent. The base peak existed at m/z 105 representing the benzoyl, $[C_7H_5O]^+$, ion. However, all the typical fragment ion peaks mentioned above can also be found in the spectrum although their intensities are relatively weak. Instead, compound **6** behaved analogously to the other compounds. Due to the ethoxycarbonyl substituent at the ring nitrogen 2 the ion at m/z 144 now corresponds to the m/z 72 ions with other compounds. When the m/z 144 ion lost the ethoxycarbonyl substituent the $C_3H_7N_2^+$ ion at m/z 71 was formed representing the base peak in the spectrum.

EXPERIMENTAL

Measurements were made with a Jeol JMS D300 mass spectrometer equipped with a combined EI/CI ion source and con-

nected to a Jeol JMA 2000H data system. Samples were introduced through a direct inlet probe at temperatures 65-130°. Typical source conditions were: temperature 170°, electron energy 70 eV, accelerating voltage 3 kV and ionization current 300 μA. Accurate mass measurements were made at resolution 7000 using the data system. Fragmentation pathways were verified with metastable transitions and/or CID spectra using linked scans at constant B/E.

The hplc analysis were made with a HP 1090 instrument using a Bio-Rad column (Bio-Sil 18 HL 90-SS; 150 x 4.6 mm) and water/acetonitrile, 30/70 (volume parts) as the eluent.

The preparation and structural characterization of the compounds studied have been described elsewhere [2]. Dideuterated 1-[*N*-(*N*-$^2H_1$)-methylthiocarbamoyl]-(2-$^2H_1$)-pyrazolidine was synthesized from compound **1** by shaking it in deuteriochloroform/-deuterium oxide mixture several hours. The desired product was obtained after evaporation of the solvent.

Acknowledgements.

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