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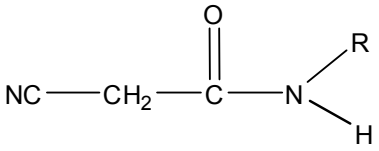
EI/MS/MS SPECTRA OF *N*-MONOSUBSTITUTED CYANOACETAMIDES

The electron-ionization induced mass spectra of twenty six N-monosubstituted cyanoacetamides were recorded and their fragmentation patterns were studied. The effect of N-alkyl and N-aryl substituents to the fragmentation of the investigated compounds was discussed. Mechanistic generalization lead to a conclusion that fission of the carbon-carbon bonds next to carbonyl function or nitrogen were processes common for N-alkyl and N-(4-substituted phenyl) cyanoacetamides. In some amides, the elimination of the acyl group by a ketene fragment gave rise to the more stable ion. Cycloalkyl amides could not fragment by single carbon-carbon bond fission, but subsequent rearrangement resulted in formation of stable even electron ion. N-(4-substituted phenyl) cyanoacetamides were more stable showing also characteristic fragmentation depending on substituent present at phenyl ring.

Key words: N-monosubstituted cyanoacetamides; electron impact; rearrangement; fragmentation.

N-monosubstituted cyanoacetamides are interesting compounds as precursors for the synthesis of certain dyes or dyes developer [1-4]. Moreover, some of the compounds and products from their synthesis exhibit active pharmaceutical or herbicidal activity [5-11] or are used as aids for spectrometric determination [12,13]. Amides were widely studied by EI [14-16] mass spectrometric technique to obtain information regarding structural and stereochemical problems [17]. Also, tautomerisms in solution (amide/imidol) have been studied using ESI technique [18-20] supported with theoretical calculation [19,20] in order to rationalize their chemical behavior.

In order to characterize the structure/fragmentation characteristics of these compounds, the mass spectrometric fragmentations of eleven *N*-alkyl, three *N*-cycloalkyl and twelve *N*-(4-substituted phenyl) cyanoacetamides were described. The investigated compounds were divided in four series depending on the nature of the nitrogen atom substituents: *N*-alkyl, *N*-isoalkyl, *N*-cycloalkyl and *N*-aryl. The general formula of the studied compounds is as follows:



with the following substituents: methyl (**1**), ethyl (**2**), *n*-propyl (**3**), *n*-butyl (**4**), *n*-heptyl (**5**), *n*-octyl (**6**) *n*-decyl (**7**), allyl (**8**), isopropyl (**9**), *sec*-butyl (**10**), isobutyl (**11**), cyclopropyl (**12**), cyclopentyl (**13**), cyclohexyl (**14**), phenyl (**15**), 4-methylphenyl (**16**), 4-methoxyphenyl (**17**), 4-ethylphenyl (**18**), 4-acetylphenyl (**19**), 4-iodophenyl (**20**), 4-bromophenyl (**21**), 4-chlorophenyl (**22**), 4-fluorophenyl (**23**), 4-hydroxyphenyl (**24**), 4-nitrophenyl (**25**) and 4-dimethylaminophenyl (**26**).

Information concerning the fragmentation routes, the effects of overall structure as well as the influence of the amide group substituents to the fragmentation pattern, were obtained by the study of the metastable ions using DA and DADI techniques.

EXPERIMENTAL PART

The synthesis of *N*-monosubstituted cyanoacetamides, where R is an alkyl, isoalkyl or cycloalkyl group, was performed according to literature procedure [21]. *N*-(4-substitutued phenyl)cyanoacetamides were synthesized using different literature procedures

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with some modification for acetyl, nitro and hydroxyl substituted compounds, concerning the choice of the solvent and temperature [22,23]. The structures of the synthesized compounds were confirmed by infrared spectroscopy, ^{1}H- and ^{13}C-NMR and mass spectrometric data.

All mass spectra were recorded on a Thermo Finnigan Polaris Q ion trap mass spectrometer, including TraceGC 2000 (ThermoFinnigan Corp., Austin, TX, USA). GC/MS/MS allows better selectivity than a GC/MS or a MS/MS tandem. Polaris Q is an ion trap GC/MS system with EI, CI, negative CI, MS/MS, with Dip (direct insertion probe) and Dep (direct exposure probe) capability. DIP mode has been used to introduce the sample and EI/MS/MS technique was used to acquire the spectra. The ionization conditions were: ion source temperature 200 °C, maximum energy of electron excitation 70 eV, corona current 150 μA. MS/MS conditions were: collision gas, helium, collision cell pressure, 1 mT, isolation time, 8 ms, *qz* value, 0.30, excitation time, 15 ms, multiplier, 1400 V. The precursor ions were resonantly excited by adjusting voltage in the range 1-2 V, depending on the compound investigated. The data obtained were processed using Xcalibur^{TM} 1.3 software.

RESULTS AND DISCUSSION

The full mass spectra of *N*-monosubstituted cyanoacetamides are given in Table 1. The principal fragmentation and fragment ions characterizing each compounds within the group are noted in form intensities, *m*/*z*, in %.

In order to follow the origin of the ions observed in the full mass spectra, precursor ions were selected and their MS/MS spectra were recorded. The results of MS/MS analyses are presented in Table 2 for some selected cyanoacetamides. The ions of abundance less than 5 % were not given.

The mass spectra of the wide variety of aliphatic amides have been discussed by Gilpin [24], who found that two common processes predominated (Scheme 1). The first process occurs when an acyl group or *N*-alkyl group contains a γ-carbon atom to the carbonyl group, through rearrangement of one hydrogen atom. McLafferty *et al.* [25] found similar rearrangement in the mass spectrum of *sec*-butyl acetate, where most of the hydrogen atoms involved in the transfer came from carbon atoms in the γ-position to the carbonyl group. Pelah *et al.* [26] proved that hydrogen transfer is a complex process during formation of *m*/*z* 60 ion in the spectrum of *N*-cyclohexylacetamide. The analogous reaction in the investigated compounds yields stabilized fragment *m*/*z* 85 given in Scheme 1, path a.

Abundance of the *m*/*z* 85 ion was moderate for lower *N*-alkyl amides, while for long chain amides this peak did not appear probably because of high flexibility of the alkyl chain, as the steric repulsion from the acyl group prevents this kind of rearrangement. Branching at the β-carbon atom (compound **11**) significantly contributed to higher abundance of *m*/*z* 85 ions. Cycloalkyl series, except cyclopropyl, showed high abundances of the *m*/*z* 85 ion as the rigid cycloalkyl groups allow appropriate spatial arrangement, thus higher probability for this fragmentation due to the stable allyl-like radical formed. In this way the proximity of β-ring hydrogen to carbonyl oxygen promotes hydrogen transfer. The *m*/*z* 85 ion further fragments to N=C=O (*m*/*z* 42) or HN=C=O (*m*/*z* 43) ions. *N*-allyl cyanoacetamide did not display fragmentation (Scheme 1, path a) at all, but similar fragmentation without hydrogen rearrangement gave *m*/*z* 84 ion, the most abundant ion in the spectrum. Similar fragmentation to that proposed in Scheme 1, path a, produced cycloalkenyl ion (*m*/*z* 81) for *N*-cyclohexylcyanoacetamide, cyclopentenyl (*m*/*z* 67) ion for *N*-cyclopentyl cyanoacetamide and cyclopropyl (*m*/*z* 39) ion for *N*--cyclopropyl cyanoacetamide.

The second type of fragmentation (Scheme 1, path b) produced the ion $H_2N{=}CH_2$, an *m*/*z* 30 ion, the most abundant in the mass spectra of compounds **3** and **11**. This process corresponded to cleavages of C-N bonds from the amido group with hydrogen rearrangements, and according to labeled analogs the hydrogen originates from the acetyl group [26].

Common ion appearing in the MS/MS spectra of compounds 3-8 was a product of a β-cleavage C-C bond to nitrogen followed by cleavage of α C-C bond to carbonyl group and hydrogen rearrangement giving an *m*/*z* 56 ion (Scheme 2).

Hydrogen transfer followed by α C-C cleavage to nitrogen and cyclization produced 3-oxoaziridne-2--carbonitrile ion (*m*/*z* 82), highly abundant ion in MS^2 spectra of those compounds. By expulsion of either C_2HN or CH_2CN radicals, *m*/*z* 42 and 43 ions were created, respectively.

The fragmentation of compound **1** displayed analogous path to that presented in Scheme 2 producing *m*/*z* 56 ion, while the cleavage of α C-C bond to carbonyl group produced the most abundant methylaminoacylium ion in the spectrum (CH_3NHCO^+, *m*/*z* 58). Analogously to creation of *m*/*z* 56 ion, the losses of acetonitrile and hydrogen radical gave a highly unsaturated ion of the type $CH_2{=}CHCH{=}NCO^+$ (*m*/*z* 82) in MS spectrum of compound **8**. The most abundant

Table 1. Mass spectral data for N-monosubstituted cyanoacetamides (intensities are expressed as % of the base peak)

No.	*m/z*, %
1	98 ($M^{+\cdot}$, 9), 68 (6), 58 (100), 56 (14), 41 (10), 40 (16), 30 (5), 28 (6)
2	112 ($M^{+\cdot}$, 14), 111 (9), 97 (23), 85 (38), 72 (25), 71 (95), 70 (14), 68 (19), 57 (12), 56 (6), 54 (7), 44 (100), 43 (27), 42 (23), 41 (24), 40 (46), 39 (5), 30 (76), 29 (10), 28 (13), 27 (22)
3	126 ($M^{+\cdot}$, 5), 111 (64), 99 (6), 98 (9), 97 (23), 85 (54), 70 (5), 68 (15), 58 (7), 56 (8), 54 (10), 44 (19), 43 (17), 42 (31), 41 (37), 40 (33), 39 (25), 30 (100), 28 (12)
4	140 ($M^{+\cdot}$, 2), 125(7), 111 (17), 101 (6), 100 (100), 98 (18), 97 (28), 93 (5), 85 (5), 68 (16), 58 (9), 57 (7), 56 (39), 54 (10), 44 (26), 43 (16), 42 (40), 41 (52), 40 (24), 39 (31), 30 (86), 29 (6), 28 (9), 27 (11)
5	182 ($M^{+\cdot}$, 0.5), 143 (11), 142 (100), 125 (5), 111 (24), 98 (28), 97 (27), 85 (9), 70 (10),69 (12), 68 (7), 58 (7), 57 (7), 56 (43), 55 (21), 54 (5), 44 (12), 43 (10), 42 (24), 41 (43), 40 (8), 39 (22), 30 (38), 29 (6)
6	196 ($M^{+\cdot}$, 0.3), 157 (10), 156 (100), 111 (20), 98 (23), 97 (16), 85 (5), 83 (7), 70 (8), 69 (12), 56 (25), 55 (16), 44 (9), 43 (12), 42 (15), 41 (27), 39 (19), 30 (20)
7	224 ($M^{+\cdot}$, 0.4), 185 (12), 184 (100), 111 (24), 98 (15), 97 (16), 70 (8), 69 (13), 56 (18), 55 (14), 44 (6), 43 (8), 42 (9), 41 (18), 39 (11), 30 (12)
8	124 ($M^{+\cdot}$, 1.5), 109 (50), 97 (15), 96 (11), 95 (22), 84 (100), 83 (7), 82 (58), 80 (6), 69 (6), 68 (22), 57 (14), 56 (83), 54 (11), 44 (5), 42 (12), 41 (56), 40 (32), 39 (69), 30 (11), 28 (20)
9	126 ($M^{+\cdot}$, 4), 111 (46), 99 (6), 93 (5), 70 (6), 68 (6), 58 (8), 44(100), 43 (5), 42 (14), 41 (17), 40 (11),39 (10)
10	140 ($M^{+\cdot}$, 2), 111 (57), 93 (6), 85 (10), 68 (6), 58 (15), 44 (100), 42 (11), 41 (13), 40 (8), 39 (8)
11	140 ($M^{+\cdot}$, 4), 126 (5), 125 (63), 107 (8), 100 (7), 99 (5), 98 (19), 97 (39), 85 (54), 84 (6), 68 (15), 58 (46), 57 (10), 56 (99), 55 (9), 54 (12), 43 (36), 42 (54), 41 (81), 40 (34), 39 (51), 30 (100), 29 (7), 28 (13), 27 (9)
12	124 ($M^{+\cdot}$, 2), 109 (40), 97 (10), 96 (9), 95 (14), 85 (5), 84 (87), 83 (7), 82 (38), 68 (25), 57 (16), 56 (100), 54 (10), 45 (11), 44 (6), 43 (8), 42 (11), 41 (46), 40 (36), 39 (36), 38 (6), 31 (7), 30 (9), 29 (8), 28 (31), 27 (9)
13	152 ($M^{+\cdot}$, 1.3), 123 (42), 111 (7), 109 (10), 96 (7), 85 (74), 84 (10), 83 (7), 82 (14), 80 (14), 70 (7), 69 (9), 68 (35), 67 (51), 56 (100), 44 (4), 43 (15), 42 (57), 41 (30), 40 (15), 39 (27), 28 (8)
14	166 ($M^{+\cdot}$, 2.3), 123 (41), 85 (62), 82 (37), 81 (17), 80 (14), 79 (8), 70 (11) 68 (14), 67 (100), 57 (6), 56 (91), 55 (17), 54 (6), 43 (12), 42 (34), 41 (15), 40 (11), 39 (26)
15	161 ($M^{+\cdot}$+1, 12), 160 ($M^{+\cdot}$, 100), 120 (37), 94 (32), 93 (68), 92 (40), 91 (6), 77 (16), 66 (25), 65 (17), 64 (6), 63 (8), 51 (10), 39 (14)
16	175 ($M^{+\cdot}$+1, 14), 174 ($M^{+\cdot}$, 100), 134 (13), 133 (15), 108 (34), 107 (38), 106 (70), 105 (5), 104 (6) 91 (9), 79 (17) 78 (6), 77 (24), 51 (7)
17	191 ($M^{+\cdot}$+1, 14), 190 ($M^{+\cdot}$, 100), 150 (7), 149 (43), 134 (8), 124 (35), 123 (14), 122 (52), 109 (9), 108 (43), 95 (17), 80 (10), 65 (7), 52 (8)
18	189 ($M^{+\cdot}$+1, 10), 188 ($M^{+\cdot}$, 66), 187 (7), 174 (11), 173 (89), 132 (16), 120 (7), 108 (8), 107 (100), 106 (29), 91 (7), 79 (6), 78 (6), 77 (16)
19	202 ($M^{+\cdot+}$, 29), 188 (11), 187 (100), 146 (37), 122 (6), 121 (76), 120 (7), 92 (7), 65 (7), 63 (5)
20	287 ($M^{+\cdot}$+1, 12), 286 ($M^{+\cdot}$, 100), 246 (6), 245 (21), 220 (31), 219 (44), 218 (20), 118 (7), 93 (5), 92 (49), 91 (25), 90 (8), 76 (6), 65 (18), 64 (12), 63 (13), 39 (5)
21	241 ($M^{+\cdot}$+3, 9), 240 ($M^{+\cdot}$+2, 79), 238 ($M^{+\cdot}$,81), 200 (14), 199 (23), 198 (15), 197 (24), 174 (72), 173 (96), 172 (76), 171 (100), 170 (28), 92 (79), 91 (45), 90 (18), 75 (8), 65 (26), 64 (16), 63 (38), 41 (16)
22	196 ($M^{+\cdot}$+2, 31), 195 ($M^{+\cdot}$+1, 10), 194 ($M^{+\cdot}$, 100), 156 (7), 155 (9), 154 (21), 153 (24), 130 (19), 129 (32), 128 (61), 127 (93), 126 (29), 102(4), 101(6), 100 (12), 99 (18), 92 (12), 90 (9), 75 (10), 73 (9), 63 (17), 41 (12)
23	179 ($M^{+\cdot}$+1, 11), 178 ($M^{+\cdot}$, 100), 138 (18), 137 (12), 112 (34), 111 (72), 110 (33), 109 (7), 95 (5), 84 (22), 83 (23), 82 (5), 75 (7), 63 (7), 57 (12), 41 (10)
24	177 ($M^{+\cdot}$+1, 11), 176 ($M^{+\cdot}$, 100), 136 (7), 135 (38), 110 (41), 109 (37), 108 (42), 107 (5), 81 (25), 80 (24), 53 (13), 52 (11)
25	207 ($M^{+\cdot}$+2, 7), 206 ($M^{+\cdot}$+1, 15), 205 ($M^{+\cdot}$, 96), 175 (43), 165 (30), 139 (9), 138 (50), 134 (9), 109 (13), 108 (100), 107 (16), 80 (26), 65 (20), 64 (10), 63 (19), 52 (9), 41 (9), 40 (10), 39 (8), 28 (8)
26	204 ($M^{+\cdot}$+1, 17), 203 ($M^{+\cdot}$, 84), 202 (12), 162 (17), 161 (12), 136 (12), 135 (100), 119 (9)

ion in the MS spectrum of compound **8** was *m/z* 84 ion produced by CH_2CN radical loss from molecular ion according to MS^2 spectral data.

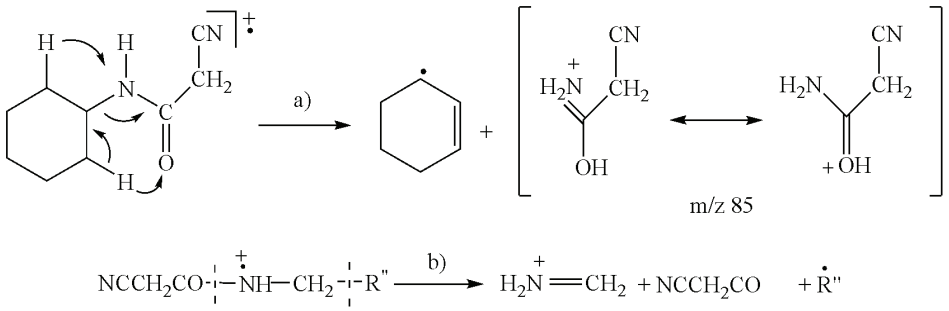
In the mass spectra of compounds **12**-**14**, aside from a very low abundance of molecular ion, substantial peaks at *m/z* 39-43, 56, 67-68 and 123 for compounds **13** and **14** were found. Previous investigations [21] of *N*-cyclohexylacetamide from the study of deuterio acetyl amide derivative and shifts in the spectra, showed that the major constituent of the *m/z* 123 ion contains the acetyl group intact. Since the hydrogen atoms located at C-1 ring carbon are retained

Table 2. MS/MS data for selected N-monosubstituted cyanoacetamides (abundances are expressed as % of base precursor ion)

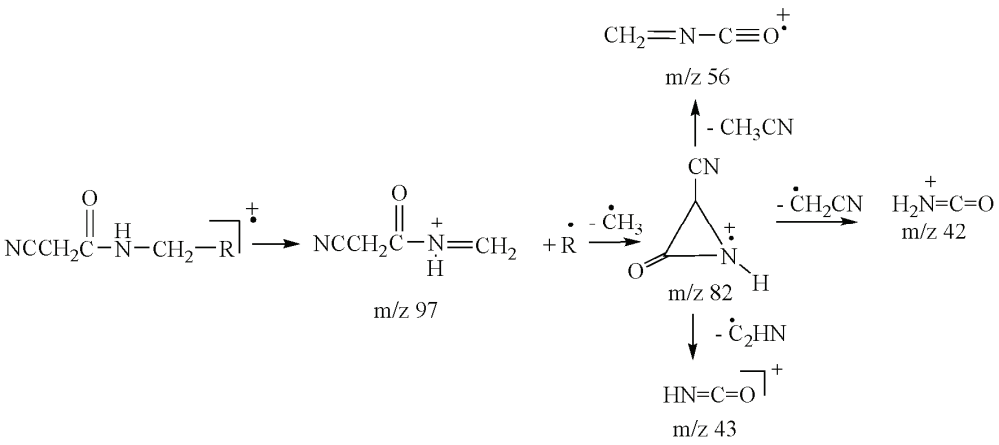
No.	Precursor ion, *m/z*	MS/MS (*m/z*, %)
2	112	112(16), 111(100), 97(13), 85 (18), 72 (6), 71(37)
	111	112(10), 111(100), 97(13), 85(16), 71 (41), 57 (6), 43(10), 42(13)
	97	98(11), 97(100), 79(8), 67(11)
	85	83(7), 57(55), 43(100), 42 (12)
	71	71(46), 70(11), 68(19), 55(100), 53(28), 44(77), 43(86), 42(12), 40(10), 30(14)
	68	68(37), 55(88), 53(41), 43(100), 42(22), 30(15)
	57	58(11), 57(100), 56(62), 55(25), 54(25), 43(5), 42(9)
	44	44(100), 43(60), 42(36), 41(5)
4	140	141(11), 140(100), 125(8), 111(12), 100(60), 97(13), 85(6), 57(7)
	125	126(10), 125(100), 123(12), 107(29), 84(6), 83(9), 80(6), 58(8)
	111	112(10), 111(100), 93(27), 83(13), 70(15), 66(15), 44(60)
	107	107(82), 80(100), 66(16), 53(24)
	100	101(10), 100(100), 82(15), 56(10)
	97	97(35), 93(18), 83(10), 82(100), 56(65), 55(20)
	93	94(12), 93(100), 66(86), 39 (9)
	85	83(7), 57(55), 43(100), 42 (12)
	82	82(34), 56(18), 43(11), 42(100)
	70	70(73), 69(10), 68(100), 44(8), 43(70), 42(9), 40(48), 30(24)
	68	68 (100), 67(18), 43(17), 42(22), 41(21)
	56	56(76), 55(17), 42(9), 41(100), 29(22)
10	140	141(7), 140(80), 125(12), 111(9), 100(6), 97(37), 94 (5), 85(100), 73(11), 55(4)
	125	126(8), 125(100), 108(9), 107(33), 85(10), 58(11)
	111	112(7), 111(77), 93(26), 83(11), 70(16), 66(8), 44(100),
	107	108(20), 107(100), 80(96), 66(12), 53(27)
	100	100(100), 98(22), 82(7), 72(10), 57(22), 56(11), 42(8)
	97	98(30), 97(38), 83(25), 82(100), 66(10), 56(78), 55(10), 44(6)
	93	94(10), 93(100), 66(66), 39(8)
	85	85(15), 84(25), 83(27), 43(13), 42(100)
	82	83(8), 82(80), 56(4), 43(10), 42(100)
	80	80(25), 67(10), 56(11), 55(35), 42(100)
	70	70(100), 68(38), 55(32), 43(12), 41(11), 40(10)
	67	68 (100), 67(18), 43(17), 42(22), 41(21)
	53	54(15), 53(22), 41(100), 39(20), 29(35)
13	152	153(11), 152(100), 123(11), 109(11), 85(71)
	123	124 (5), 123(54), 96(7), 80(17), 56(100)
	109	110(11), 109(100), 82(32), 67(5)
	96	97 (11), 96(100), 95(47), 94(26), 93(26), 78(10), 68(17), 67(12), 66(11), 56(7)
	92	92(100), 78(18), 68(20), 67(40), 66(56)
	85	85(20), 82(19), 81(11), 55(6), 43(10), 42(100)
	82	82(18), 80(12), 55(9), 43(8), 42(100)
	78	79 (10), 78(7), 54(16), 53(100)
	67	68 (12), 67(100), 65(9), 41(24)
17	190	191 (12), 190(100), 149(16), 124(11)
	149	150 (13), 149(100), 134(21), 122(4)
	134	135 (24), 134(100), 133(10), 132(7), 107(8), 106(69), 78(16)
	124	125(12), 124(100), 109(8), 108(22), 95(18)
	122	123(11), 122(100), 109(21), 108(9), 95(15)
	108	109(11), 108(100), 106(7), 80(25)
	95	96 (9), 95(100), 67(9), 65(27), 41(10)

Table 2. Continued

No.	Precursor ion, *m/z*	MS/MS (*m/z*, %)
17	80	81(11), 80(100), 79(21), 78(41), 77(23), 53(15), 52(19), 51(16)
	65	66 (10), 65(100), 64(46), 39(29)
22	194	197(3), 196(31), 195(12), 194(100), 153(7), 130(7), 129(3), 128(20), 127(10)
	153	155(32), 154 (41), 153(100), 152(7), 128(17), 127(4), 126(48), 125(12)
	127	130(17), 129 (32), 128 (49), 127(100), 126(22), 125(5), 101(3), 99(10), 90(5)
	99	102(16), 101(32), 100(50), 99(100), 75(5), 73(15), 65(14), 63(9)
	90	91(81), 90(100), 89(14), 65(45), 63(39)
	73	75(32), 74(19), 73(100), 72(26)
26	204	204(14), 203(100), 202(18), 175(5), 135(6)
	175	176 (10), 175(100), 174(21), 173(33), 172(28), 171(18), 143(9), 107(7),
	162	162(95), 161(100)
	135	136(11), 135(100)
	119	120(12), 119(100), 118(17), 92(11), 91(6),65(4)
	119	120(12), 119(100), 118(17), 92(11), 91(6), 65(4)
	92	94(93), 92(100), 91(86), 90(22), 77(8), 67(6), 66(21), 65(43), 64(6), 63(14), 39(4)
	79	80(54), 79(100), 78(50), 77(80), 76(13), 75(6), 52(11), 51(28), 50(6)



Scheme 1. Two general fragmentation processes in the investigated amides.



Scheme 2. Proposed fragmentation paths through m/z 97 ion.

and so is one of the hydrogens at C-2, the fragment *m/z* 43 came from the ring and it is C_3H_7 radical [26]. Similarly the C_3H_7 radical can be lost from the investigated compounds in the manners presented in Scheme 3. Also, the peak located at *m/z* 56 originating from *m/z* 123 ion (Scheme 3), consists of a single species $C_3H_6N^+$ according to high resolution mass spectrometry, and is shifted to *m/z* 57 in the spectrum of trideuteroacetyl analog [26].

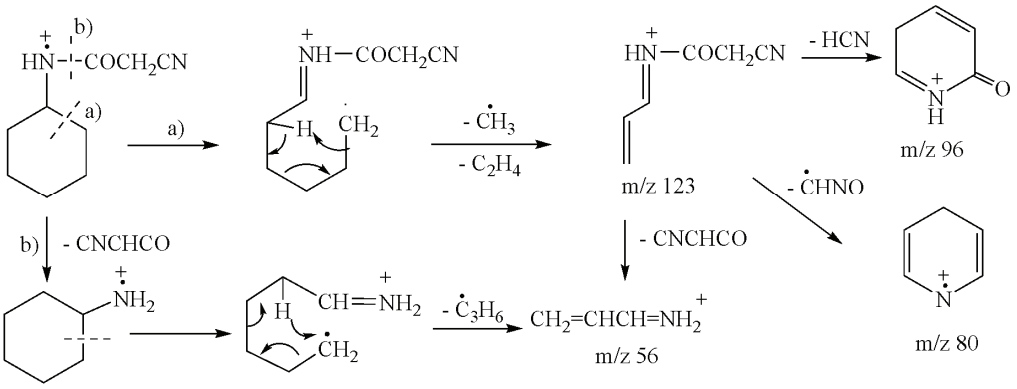
The base peak in the MS spectra of compounds **12** and **13**, and 91% for compound 14 was located at *m/z* 56. Based upon the study of three-deutero ana-

logs [26], it can be visualized as being formed by cyanoketene loss from *m/z* 123 ion or the initial loss of cyanoketene from molecular ion can be invoked (Scheme 3, path b). The cycloaklylamine ion which could be produced by cyanoketene loss from molecular ion, was not observed in MS^2 spectra of compounds **12**–**14** indicating that fragmentation to *m/z* 56 ion from *m/z* 123 ion was highly preferable. Low influences of steric strain on formation of *m/z* 56 ion, and somewhat higher abundance of *m/z* 56 ion for higher strained compounds were observed.

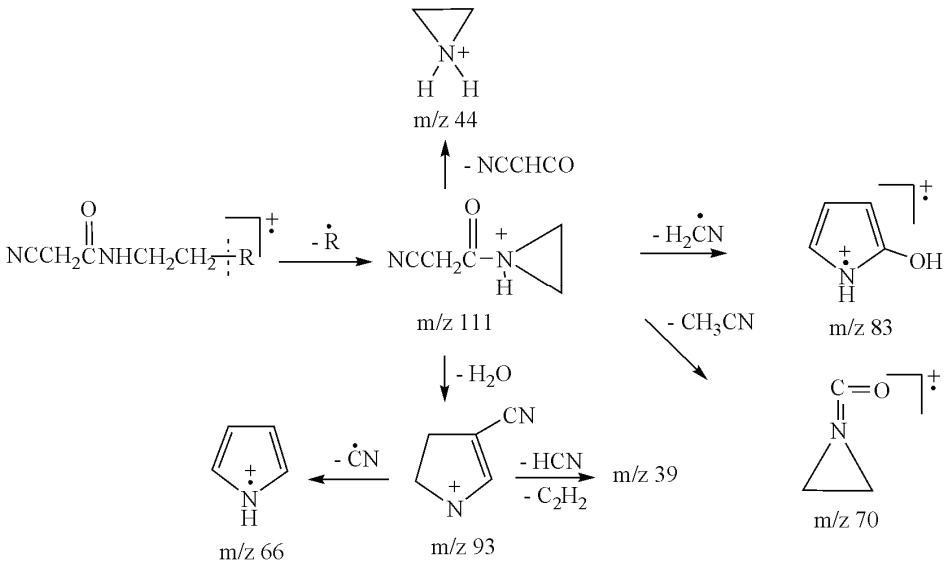
Furthermore, the subsequent double β C-C cleavage to nitrogen and C-N bond to carbonyl with hydrogen rearrangement produced ion *m/z* 44. β C-C cleavage followed by cyclization of *N*-cyanoacetyl aziridine ion (*m/z* 111), which was probably initiated by the inductive effect of the electron-deficient nitrogen and caused fission of the C-N bond with hydrogen rearrangement, giving an energetically favorable three-membered ring. Fragmentation of the d_3-analog of *N*-butyl acetamide was consistent with the fragmentation sequence which includes formation of aziridine ring [27a], and could be analogously applied to the investigated compounds (Scheme 4).

Fragmentation to the *m/z* 44 ion is highly preferable for compounds **9** and **10** with branching at α C atom to nitrogen, thus formed ions were significantly stabilized by neighboring nitrogen. Dehydration of the *m/z* 111 ion gave a low abundant *m/z* 93 ion, a 4,5-dihydropyrrole-3-carbonitrile, which upon elimination of CN radical and HCN and acetylene produced pyrrole (*m/z* 66) and cyclopropenyl (*m/z* 39) ion, respectively.

A very low abundance of peaks corresponding to molecular ions were noticed from the spectra of higher members of a series of aliphatic amides, which indicates easy fragmentation of the alkyl chain of those compounds. A cleavage of the C-C bond closest to the carbonyl group produced corresponding M-40 ions (Scheme 5, path b). The most abundant ions in spectra of compounds **4** (*m/z* 100), **5** (*m/z*



Scheme 3. Two possible paths for formation of m/z 56 ion.

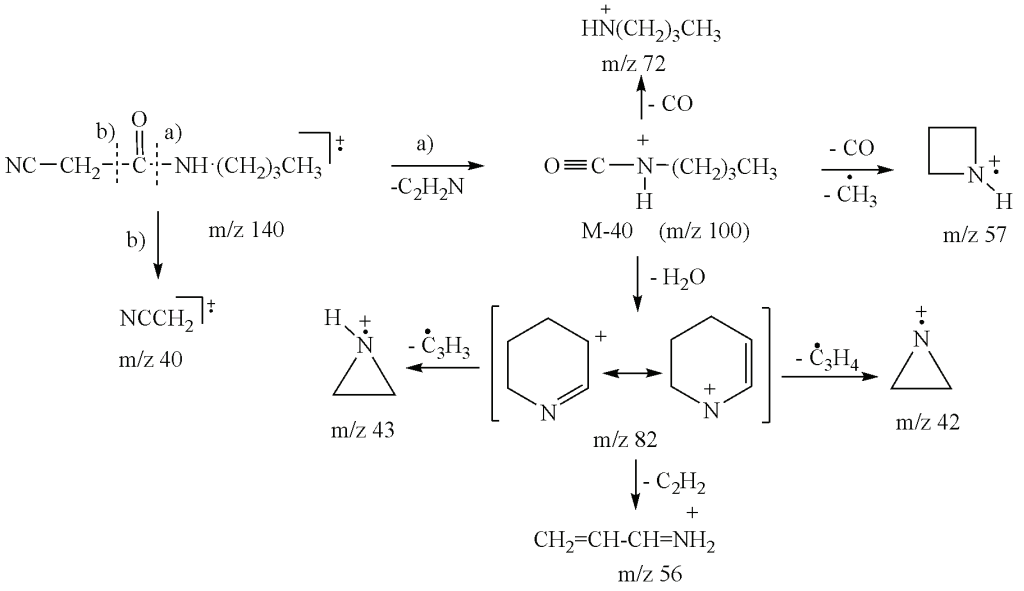


Scheme 4. Proposed fragmentation paths for the creation of m/z 44 ion through m/z 111 ion.

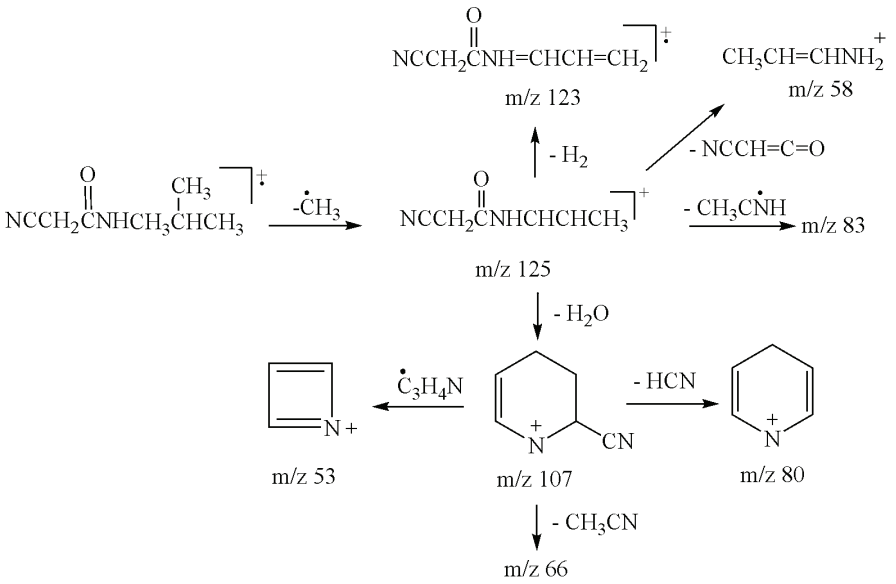
142), **6** (*m/z* 156) and **7** (*m/z* 184) were M-40 ions. Dehydration of the M-40 ion and simultaneous cyclization produced 2,3,4-tetrahydropyridine ion (*m/z* 82), where upon elimination of either cyclopropenyl or cyclopropen radicals, aziridine (*m/z* 43) or deprotonated aziridine (*m/z* 42) were formed, respectively. On the other hand, cleavage of α and γ C-C bonds to nitrogen produced *m/z* 56 ion (Scheme 5).

An abundant peak, formed by expulsion of methyl radical from molecular ion, appeared in mass spectrum of compound **11** (*m/z* 125, Scheme 6), which is low abundances for compounds **4**, **5** and **10** in corresponding MS spectra. It was formed by expulsion of methyl radical from molecular ion. Furthermore, dehydration of the *m/z* 125 ion, followed by cyclization produces 1,2,5,6-tetrahydropyridine-2-carbonitrile ion (*m/z* 107). A low abundant 1,2-dihydroazete ion (*m/z* 53) was produced by expulsion of C_3H_4N radical from *m/z* 107 ion. Alternatively losses of acetonitrile or hydrogen-cyanide from *m/z* 107 ion produces 4*H*-pyridine (*m/z* 80) and deporotnated pyrrole (*m/z* 66), respectively. Elimination of cyanoketene from *m/z* 125 gave propenamine ion (*m/z* 58), and by elimination of acetaldimine like radical *m/z* 83 ion has been created.

Some discrepancy of similar fragmentation to that presented at Scheme 6, for cyclic substituents

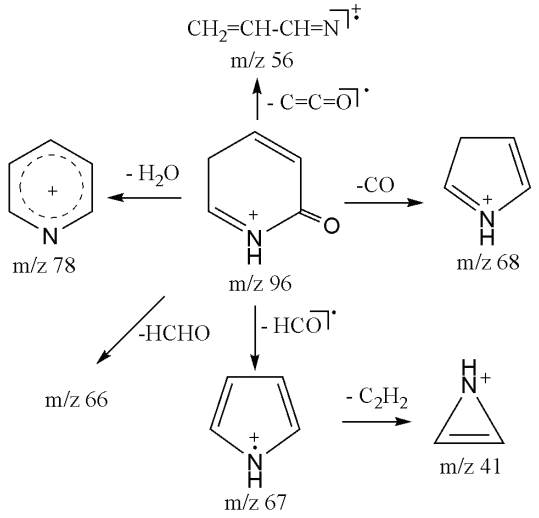


Scheme 5. Proposed fragmentation paths through intermediary M-40 ion.



Scheme 6. Proposed fragmentation paths through intermediary m/z 125 ion.

was observed for compounds **13** and **14**, where the *m*/*z* 123 ion (Scheme 3) was produced directly from the molecular ion. Expulsion of HCN from that ion gave *m*/*z* 96 ion (2-oxo-2,3-dihydropyridinium ion), and after dehydration of that ion, an *m*/*z* 78 ion was created. Alternatively, loss of carbon monoxide or formaldehyde like fragments produced *m*/*z* 68 (3*H*-pyrrole) and *m*/*z* 67 ions (pyrrole), respectively (Scheme 7).



Scheme 7. Proposed fragmentation paths through intermediary m/z 96 ion.

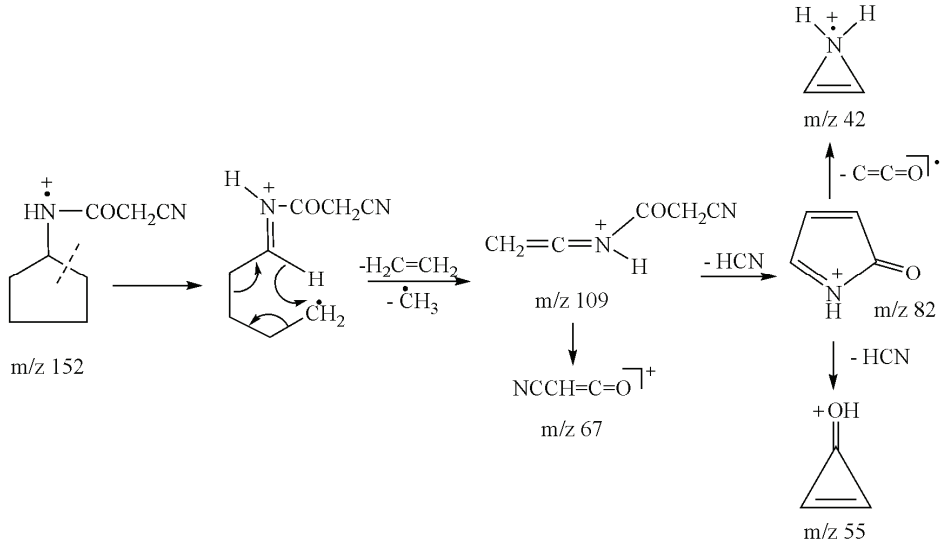
It has been shown that the peak M-43 of *N*-ethyl-*N*-acetylcyclopentylamine [26] from a study of the corresponding deuterio analogs is a complex process. It is a composite peak obtained by the expulsion of acetyl with and without rearrangement that accounts for about 60% of the peak. The remainder involved loss of the C_3H_7 from the ring. Analogously, the double β and γ C-C-cleavage with hydrogen rearrangement, resulted in elimination of a methyl radical and ethylene (Scheme 8), give *m*/*z* 109 ion for compound **13**. This fragmentation path could be also ascribed to the compounds **8** and **12**. The formation of the *m*/*z* 82 was achieved by the loss of HCN and cyclization from *m*/*z* 109 ion, while further loss of either HCN or C=C=O fragments produced *m*/*z* 55 and 42 ions, respectively.

The formation of *m*/*z* 67 ion from *m*/*z* 109 ion was the most preferred fragmentation for compound **14** (Table 1). It is less pronounced for compound **13** and was not observed for compound **12**. Steric strain in cyclic systems for compounds **12** is the largest, lower for compound **13** and the lowest for compound **14**. That is reflected in higher abundances of ion *m*/*z* 109 for more strained compounds. The opposite trend is true for the values of the abundance of *m*/*z* 67 ion in the MS spectra of these compounds.

N-aryl series of cyanoacetamides displayed higher stability under applied fragmentation conditions; molecular ions were the most abundant ions in MS spectra of compounds **15**-**17**, **20** and **22**-**24**, compared to *N*-alkyl series.

Substituents present at the phenyl ring caused contribution of *n*,π- or π,π-conjugation, electron-acceptor substituents achieve better interactions through *n*,π-conjugation with the lone electron pair at the nitrogen thus influencing twisted spatial arrangement of the *N*-aryl part of molecule. The opposite was true for electron-donor substituents which contribute more to π,π-conjugation and consequently more to planar conformation [28].

Elimination of acetonitrile or CH_2CN radical produced corresponding substituted phenylisocyanate



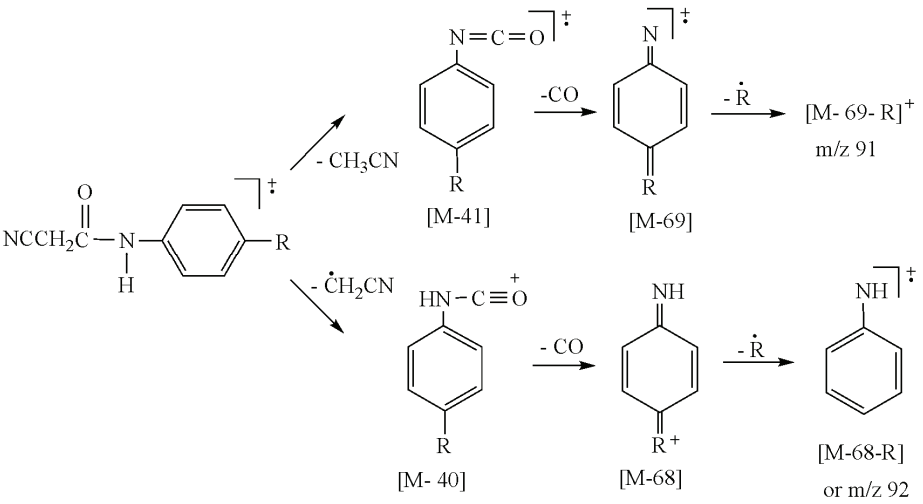
Scheme 8. Proposed fragmentation paths through intermediary m/z 109 ion.

ion [M-41] or 4-substituted-1-aminoacylium ion [M-40], which were of low to moderate abundances. After elimination of carbon monoxide from both [M-40] and [M-41] ions, 1-substituted-4-iminocyclohexa-2,5-diene type ions, [M-68] and [M-69] were formed. Significant stabilization of this ion was observed for compounds with electron-donor substituent: dimethylamino group (compound **26**), *m*/*z* 135 (100%), methoxy (compound **17**) *m*/*z* 122 (52%) and hydroxyl (compound **24**) *m*/*z* 110 (41%). Oppositely for strong electron-acceptor (compound **25**) the peak M-41 disappears (Scheme 9).

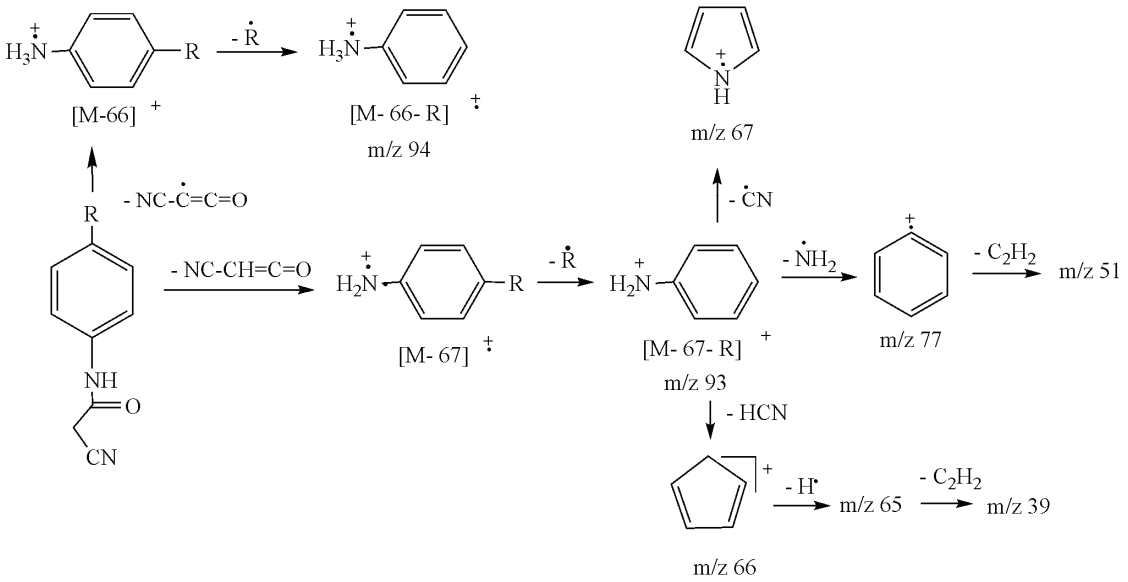
Important fragmentation of all *N*-aryl cyanoacetamides were exemplified by C-N amide bond cleavage with formation of protonated substituted anilines [M-66] or deprotonated anilines [M-67], which further shows characteristic fragmentations for substituted anilines (*m*/*z* 66, 65 and 39 ions, Scheme 10).

The characteristic cleavage of alkyl substituted benzenes [27b] occurs either through hydrogen loss which is β to the aromatic ring (compound **17**) or β C--C bond rupture of the benzylically activated bond (compound **18**) to yield tropylium (benzyl) ion which after expulsion of acetylene gave cyclopentadienyl ion (*m*/*z* 65).

Fragmentations of *N*-(4-hydroxyphenyl) and *N*--(4-methoxyphenyl) cyanoacetamides are affected by strong positive resonance character of hydroxyl and methoxy substituents. Expulsion of methylene radical from *O*-methoxy-4-imino-cylohexa-2,5-dienone ion (*m*/*z* 122) gave 4-imino-cyclohexa-2,5-dienone ion (*m*/*z* 108). Further elimination of CO led to an ion $C_6H_5N^+$



Scheme 9. General proposed fragmentation paths for N-arylcyanoacetamides through [M-41] and [M-40] ions.



Scheme 10. General proposed fragmentation paths for N*-arylcyanoacetamides through [M-66] and [M-67] ions.*

of mass 80, which was assumed to be the pyridinium ion [29]. Two formulas have been proposed for the $C_6H_5N^+$ ion, the pyridinium [29] and aminocyclopentadienyl [30], but no experimental evidence has been presented to differentiate between them. On the other hand, elimination of HCN from *m/z* 122 ion gave *O*-methyl-2,4-cyclopentadienyl ion (*m/z* 95; Scheme 11), which after expulsion of formaldehyde produced cyclopentadienyl ion (*m/z* 65).

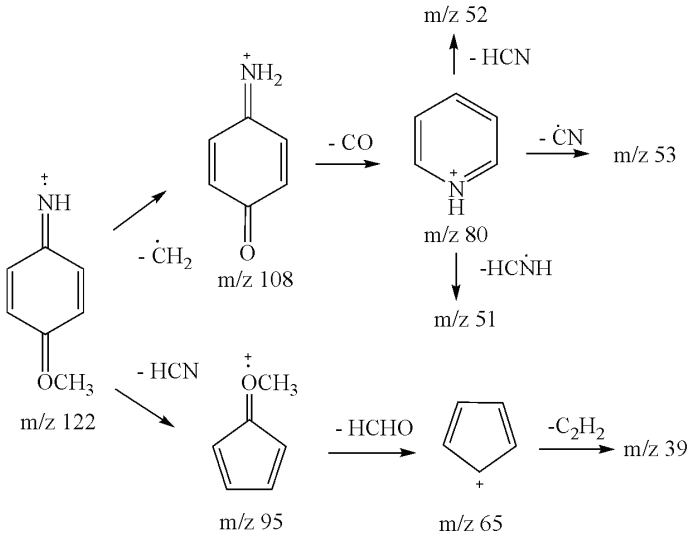
Halogen substituted cyanoacetamides followed fragmentation paths depicted on Schemes 9 and 10, and similarly to compounds **17** and **24** (Scheme 11), after loss H_2CN radical a 1-chloro-2,4-cyclopentadienyl ion have been created (*m/z* 100).

Regardless of the strong electron-acceptor character of the nitro goup, fragmentation of *N*-(4-nitrophenyl)cyanoacetamide showed similar fragmentations to other *N*-(substituted phenyl)cyanoacetamides (Schemes 9 and 10). The loss of nitrosyl radical either from the molecular ion (*m/z* 175) or from *m/z* 138 ion is well known in literature [27c]. The produced 4-imino-cyclohexa-2,5-dienone ion (*m/z* 108) expels CO forming $C_6H_5N^+$ ion (Scheme 12).

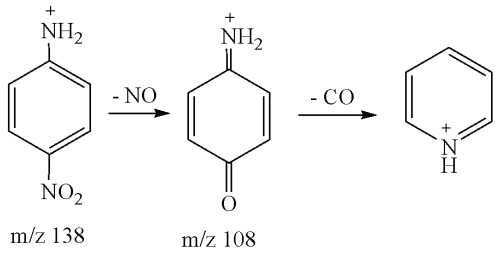
N-(4-*N*-dimethylaminopheny)cyanoacetamide showed fragmentation which largely depends on strong electron-donor nature of dimethylamino group and also ability of its easy fragmentation. The most abundant ion in the spectra of this compound was a *m/z* 135 a 1-*N*-dimethylamino-4-imino-cyclohex-2,5-diene ion (M--69; Scheme 9) being stabilized by the strong electron-donor character of the dimethylamino group.

CONCLUSION

Based on EI MS/MS data of investigated compounds, mechanistic paths of their fragmentation were established. It could be stated that cleavage of bonds β or α to a nitrogen will occur readily. The presence of an electron-withdrawing carbonyl group will not stabilize the ion, so if an acyl group can be lost by ketene elimination, a much more favored ion will result. This was reflected in the high intensity of the peaks of *m/z* 30, 44, 56 and M-40. The flexible long alkyl chain gave the most abundant peaks corresponding to loss of cyanoketene. In the case of *N*-cycloalkylcyanoacetamides a single cleavage β to nitrogen could not fragment the molecule, but it was usually the initial step in the formation of the most stable ion. Loss of side chain of cyclic systems, a competing process, gave a common fragmentation which was explained. *N*-(substi-



*Scheme 11. Characteristic fragmentation paths for compounds **17** and **24**.*



Scheme 12. Characteristic fragmentation of nitro substituted compound.

tuted phenyl) cyanoacetamides showed significant stability under applied fragmentation condition with a two dominant processes: loss of side chain of aromatic ring with or without carbonyl function. Fragmentation of substituted anilines significantly depended on the electronic character of substituents present and also on substituent fragmentation.

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NAUČNI RAD

EI/MS/MS SPEKTRI *N*-MONOSUPSTITUISANIH CIJANOACETAMIDA

U ovom radu su proučavani fragmentacioni putevi dvadeset šest N-monosupstituisanih cijanoacetamida dobijenih jonizacijom izazvanom bobardovanjem elektronima. Na osnovu definisanih fragmentacionih puteva diskutovan je uticaj prisutnih N-alkil i N-aril supstituenata. Sagledavanjem mehanizama fragmentacija ispitivanih N-monosupstituisanih cijanoacetamida uočava se da je cepanje veze ugljenik-ugljenik susedne karbonilnoj grupi ili azotu proces uočen i kod N-alkil i N-(4-supstituisanih fenil) cijanoacetamida. Kod nekih amida, eliminacija acil grupe u vidu fragmenta ketena dovodi do nastajanju stabilnijih jona. Cikloalkil amidi ne mogu da se fragmentišu samo cepanjem veze ugljenik-ugljenik, već u narednom koraku pregradnje daju stabilnije parne jone. N-(4-supstituisani fenil) cijanoacetamidi se stabilni u primenjenim jonizacionim uslovima i pokazuju karakteristične fragmentcije na koje utiče prisutni supstituent na fenilnom jezgru.

Ključne reči: N-monosupstituisani cijanoacetamidi; elektron impakt; pregradnja; fragmentacije.