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MASS SPECTROMETRIC IDENTIFICATION OF RING–CHAIN TAUTOMERS OF 4-CYANO-3-PYRAZOLIDONES IN THE GAS PHASE

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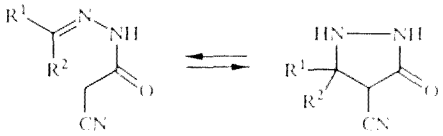
Analysis of the electron impact mass spectra of a series of 4-cyano-3-pyrazolidones, which manifest ring–chain tautomerism in polar solvents, showed that these compounds also exist in the gas phase as a mixture of tautomers, which undergo characteristic fragmentation. The quantitative tautomer ratio in this series is a function of electronic and steric substituent effects. The fragmentation pathways for each of the tautomers were determined using high-resolution mass spectrometry.

We have already established that the reaction of the hydrazide of cyanoacetic acid with carbonyl compounds, which proceeds readily at room temperature in ethanol, leads to 4-cyano-3-pyrazolidones as the result of an intramolecular cyclization of the initially formed hydrazones [1]. This reaction was later found to be reversible. ^{1}H NMR spectroscopy was used to show a tautomeric equilibrium in polar solvents such as DMSO and acetonitrile between pyrazolidones and linear cyanoacetyl hydrazones of aliphatic carbonyl compounds [2]. This reaction is still another case of the ring–chain tautomerism of azomethines involving the C=N group, previously studied for substituted thiosemicarbazones [3, 4]. Feasibility was demonstrated for identifying ring–chain tautomers of N-substituted thiosemicarbazones in the gas phase by analysis of the electron impact mass spectra.

The mass spectrometric study of ring–chain tautomers often reveals electronic and steric effects of the substituents since the solvent effect is eliminated in the gas phase and there are no intermolecular interactions. The applicability of mass spectrometry for the study of tautomeric structures may be considered completely demonstrated at least for prototropic tautomerism [5]. The use of mass spectral analysis in the case of ring–chain tautomers is especially convenient since the corresponding structures, as a rule, have specific fragmentation pathways and may be readily identified.

In the present work, we studied the electron impact mass spectra of a series of aliphatic (Ia-Id) and aromatic carbonyl compounds (IIa-IIf).

Products I and II were prepared by the reaction of equimolar amounts of the corresponding aldehydes and ketones with the hydrazide of cyanoacetic acid in yields above 95%. Products Ia-Id were characterized in our previous work [2]. The physical indices and ^{1}H NMR spectra of II are given in Table 1.



IA IB

Ia-d

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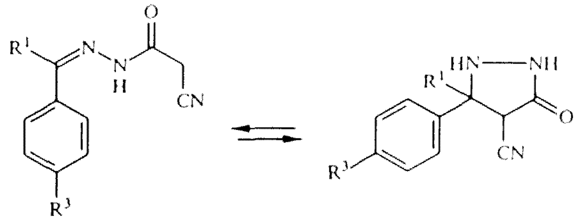

IIA IIB

IIa–f

IIa–c R^1 = H, Ia–c, IId–f CH_3, Id C_2H_5; Ia R^2 = CH_3, Ib C_2H_5, Ic,d C_4H_9; IIa,d R^3 = H, IIb OH, IIc $(CH_3)_2N$, IIe Cl, IIf NO_2

We should note that the ^1H NMR spectra of II supply only slight information relative to the tautomeric forms. Thus, the tautomers may be reliably distinguished only in the case of aldehyde derivatives relative to the signals of the CH=N fragment and the AB system of protons at $C_{(4)}$ and $C_{(5)}$ of the ring form. For example, the finding of signals of the CH=N group protons at 7.71-7.88 ppm indicates the formation of a linear form of benzaldehyde derivatives IIa-IIc in $CDCl_3$ and DMSO-d_6 (Table 1). The integral intensities of the CH_2CN group signals indicate that IIc-IIe exist in solution predominantly in the linear form, while nitro derivative IIf exists predominantly in the cyclic form. This finding is in accord with the electron-withdrawing capacity of the nitro group. Comparison of the structure of aliphatic Ia-Id [2] and aromatic derivatives IIa-IIf in solution using NMR spectroscopy indicates the predominance of linear structures in the latter case. This behavior may be attributed to the conjugation effect of the CH=N group of the linear tautomer with the aromatic ring, which stabilizes the linear form. Such an effect has already been noted for substituted thiosemicarbazones of aromatic carbonyl compounds [6].

FRAGMENTATION OF I UPON ELECTRON IMPACT

Analysis of the mass spectra of I (Table 2) indicates greater stability for the molecular ions of Ia and Ib, which possess short substituents (Table 3) since the molecular ions of Ic and Id readily undergo a McLafferty rearrangement with loss of a propene molecule and formation of Φ_6 ions (see scheme below), whose peaks have greatest intensity in the spectra of Ic and Id. The maximum peaks in the spectra of Ia and Ib correspond Φ_3 ions formed upon the loss of substituents R^1 or R^2. The presence of two $M^{+\cdot}$ isomers in the gas phase for Ia and Ib is indicated by the finding of peaks for characteristic fragment ions Φ_1 and Φ_2. A study of the metastable transitions showed that Φ_1 ions are formed exclusively from $M^{+\cdot}$ with loss of the CH_2CN fragment as indicated by high-resolution mass spectral data, which may occur only from the linear form of $M^{+\cdot}$ (IA), while Φ_2 are formed predominantly from $M^{+\cdot}$ upon the loss of HNCO, which characterizes the cyclic $M^{+\cdot}$ form (IB). Although the metastable spectra and high-resolution mass spectra show that Φ_5 ions (isobaric to Φ_2 ions) arise in small amounts from $(M - CH_3)^+$ ions (Φ_3) as the result of the loss of CO, this process may occur only from cyclic Φ_3 forms and, thus, the total intensity of the (M − 43) peaks, corresponding to the Φ_2 and $\Phi_5$ions show the contribution of the cyclic form of $M^{+\cdot}$.

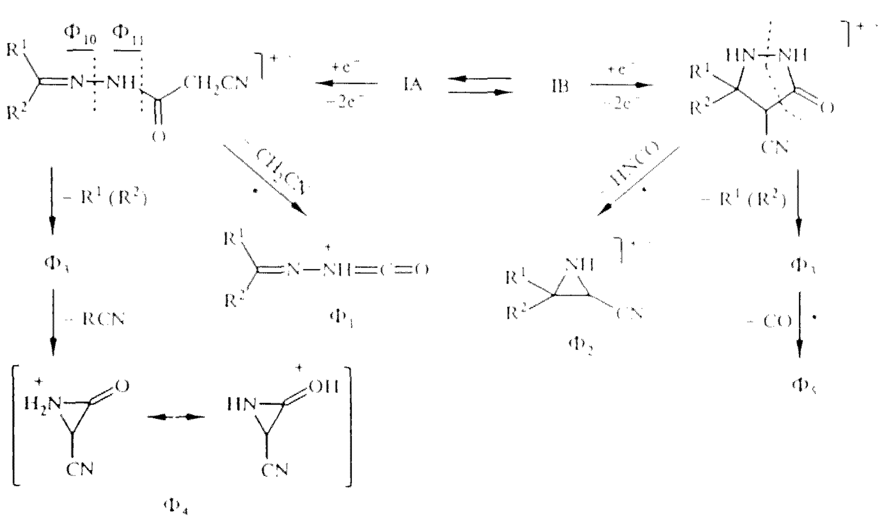

TABLE 1. Physical Indices of II

Compound	Chemical formula	mp, °C	^{1}H NMR spectra (100 MHz), δ, ppm, $CDCl_3$					Yield, %
			R^1	CH=N	CH_2CN	NH (br.s)	arom	
IIa	$C_{10}H_9N_3$	174	—	†	3,93 s (1H)	9,42, 9,73	7,42...7,83 m	95
IIb	$C_{10}H_9N_3O_2$	188...190	—	7,88* s	4,14* s (<2H)	9,93*, 11,58	6,78...7,54* d.d	96
IIc	$C_{12}H_{14}N_4O$	154	—	7,71 s	3,91 s (2H)	9,26	6,67...7,55 d.d	95
IId	$C_{11}H_{11}N_3O$	123...124	2,35 s	—	3,95 s (2H)	9,95	7,39...7,77 m	96
IIe	$C_{11}H_{10}ClN_3O$	187...188	2,30 s	—	3,91 s (2H)	9,53	7,36...7,70 d.d.	96
IIf	$C_{11}H_{10}N_4O_3$	225...226	2,33 s	—	3,90 s, 4,29* s (1H)	11,28*	7,89...8,32 d.d	96

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*In DMSO-D_6.

†Signal located in the aromatic proton region.

TABLE 2. Mass Spectra of I and II

Compound	m/z (rel. intensity, % of max)
Ia	139 (25) M, 124 (100), 99 (10) , 96 (49), 83 (10), 72 (37), 71 (88), 68 (18), 57 (37), 56 (24), 55 (27)
Ib	153 (10) M, 138 (19), 124 (100), 113 (10), 110 (17), 85 (26), 68 (27), 57 (20), 56 (17), 55 (16), 42 (42), 42 (26)
Ic	181 (0,4) M, 152 (22), 139 (100), 124 (19), 99 (17), 98 (20), 96 (10), 71 (40), 70 (48), 68 (21), 58 (31), 55 (35)
Id	195 (3) M, 166 (31), 153 (100), 113 (21), 110 (9), 98 (31), 85 (41), 70 (80), 68 (28), 58 (45), 56 (59), 55 (72), 54 (31)
IIa	187 (29) M, 119 (11), 104 (100), 103 (35), 92 (19), 90 (8), 89 (10), 77 (15), 65 (18), 63 (7), 51 (12)
IIb	203 (58) M, 163 (3), 135 (17), 120 (100), 119 (65), 108 (12), 105 (11), 104 (38), 90 (10), 77 (20), 68 (16), 65 (17), 51 (19)
IIc	230 (100) M, 190 (6), 162 (21), 148 (37), 147 (22), 146 (29), 145 (17), 120 (13), 119 (26), 118 (11), 77 (10), 65 (6), 51 (6)
IId	201 (100) M, 200 (94), 186 (30), 161 (12), 158 (20), 133 (78), 118 (26), 104 (18), 103 (32), 92 (72), 78 (20), 77 (61), 65 (25), 51 (29)
IIe	237 (36) M, 236 (34), 235 (100) M, 234 (63), 220 (24), 200(24), 195 (16), 192 (18), 169 (21), 167 (60), 152 (22), 126 (32), 111 (23), 103 (24), 90 (14), 77 (22), 75 (27), 51 (16)
IIf	246 (67) M, 231 (44), 229 (41), 206 (11), 203 (20), 199 (42), 179 (22), 178 (26), 132 (100), 131 (39), 77 (50), 75 (25), 68 (24), 51 (27)

The loss of CH_2CN and HNCO directly from $M^{+\cdot}$ is not observed for Ic and Id. However, rearranged Φ_6 ions (isomeric to $M^{+\cdot}$ ions of Ia and Ib) decompose analogously with the loss of CH_2CN and formation of Φ_{12} ions, which are isomeric to Φ_1 ions.

Although the McLafferty rearrangement leading to Φ_6 ions is more likely for the linear $M^{+\cdot}$ form, cyclic $M^{+\cdot}$ ions also probably exist in the gas phase since $(M - Bu)^+$ ions (Φ_7) subsequently lose CO, which indicates their cyclic form.

FRAGMENTATION OF IIa-IIf UPON ELECTRON IMPACT

The molecular ions of these compounds are rather stable and, in some cases, give the strongest peak in the mass spectra (Table 2). In the remaining cases, the strongest peaks correspond to Φ_{10} ions formed upon cleavage of the N–N bond of the linear $M^{+\cdot}$ form (IIa and IIb). The Φ_{11} ion ($M - COCH_2CN$) is also characteristic for all II. The characteristic Φ_1 and Φ_2

TABLE 3. Peak Intensities of Characteristic Fragment Ions in the Mass Spectra of I (%Σ_{50})

Compound	w_M	$(M-H)^+$	Φ_1	Φ_2	Φ_3	Φ_4	Φ_6	Φ_7	Φ_8	Φ_{10}	Φ_{11}	Φ_{12}	Φ_{13}
Ia	5,0	0,2	1,6	9,8	17,8	1,7	—	—	—	5,7	18,0	—	—
Ib	3,1	0,1	2,2	3,6	3,8(-Me), 20,2(-Et)	1,5	—	—	—	1,1	4,3	—	—
Ic*	0,1	—	—	—	0,2(-Me)	3,6	22,4	4,2	2,2	4,6	0,3	3,9	9,0
Id*	<0,1	—	—	—	3,5(-Et)	2,0	29,3	3,4	1,4	3,8	0,3	3,8	6,2

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*Intensity in % Σ_{70}.

TABLE 4. Peak Intensities of the Characteristic Fragment Ions in the Mass Spectra of II (%Σ_{50})

Compound	w_M	$(M-H)^+$	Φ_1	Φ_2	Φ_3	Φ_{10}	Φ_{11}
IIa	7,4	—	0,5	—	—	49,5	4,1
IIb	15,9	—	0,8	—	—	24,3	4,1
IIc	27,8	1,0	2,0	0,3	—	7,4	5,3
IId	16,8	14,2	1,8	3,0	4,4 (-Me)	3,9	11,7
IIe	18,5	10,4	2,1	2,4	3,5 (-Me)	3,2	8,7
IIf*	9,6	1,5	1,4	2,5	5,5 (-Me)	—	3,3

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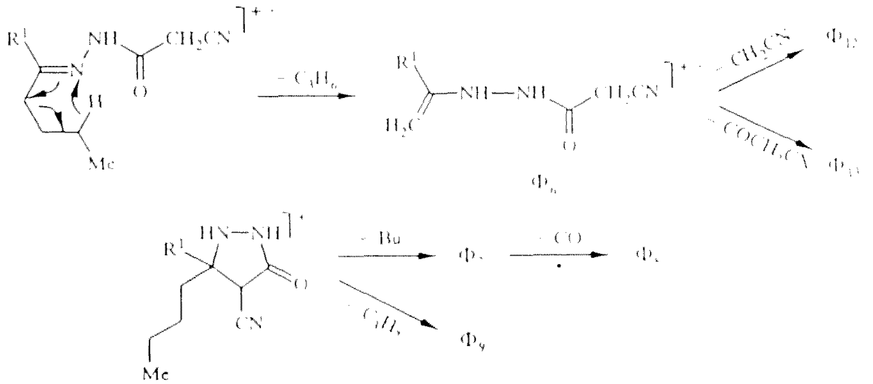
*The following ion peaks are found: $[M-OH]^+$ (5.1%), $[M\text{-}HNO_2]$ (5.3%), $[\Phi_{11}\text{-}NO_2]$ (12.6%), $[\Phi_{11}\text{-}HNO_2]$ (4.9%).

ions observed in the mass spectra of aliphatic derivatives Ia-Id are also formed in the case of II. However, only peaks for Φ_1 ions are found in the mass spectra of benzaldehyde derivatives IIa-IIc, which indicates a predominantly linear form of these compounds in the gas phase. The cyclic form of the $M^{+\cdot}$ ions predominates for acetophenone derivatives IId-IIf. The Φ_2 peaks in the spectra of IId-IIf are stronger than the Φ_1 peaks. This difference in molecular ion structure is indirectly indicated by the finding that strong peaks are found for $(M - H)^+$ ions in the mass spectra of IId-IIf, which are lacking in the spectra of IIa-IIc. If the $M^{+\cdot}$ ions of the benzaldehydes existed in cyclic form, they should readily lose a proton from $C_{(5)}$ of the pyrazoline ring. The analogous loss of a substituent from this position leads to rather stable $(M - CH_3)^+$ ions (Φ_3) in the spectra of IId-IIf. On the other hand, the loss of the $R^3C_6H_4$ substituent is not observed in the spectra of IIa-IIc. The existence of linear and cyclic forms of $M^{+\cdot}$ in the case of acetophenone derivatives IId-IIf is indicated by the finding that Φ_{11} ions, which are characteristic for the decomposition of linear structures, are observed in the mass spectra of all compounds IIa-IIf.



Unfortunately, we were unable to determine the effect of the R^3 substituent on the ratio of the linear and cyclic forms of the molecular ions of IId-IIf by comparison of the peak intensities of ions Φ_1 and Φ_2. Thus, the Φ_2 ions are more stable in the case of IId (R^3 = H) and IIf ($R^3 = NO_2$) but the peaks of the Φ_1 and Φ_2 ions have almost the same intensity in the spectrum of IIe (R^3 = Cl).

The total intensity of the peaks of the characteristic ions given in Tables 3 and 4 comprise 40-60% of the total ion current for each of these compounds, which indicates high selectivity in the fragmentation. However, the presence of the nitro group in IIf leads to additional fragmentation channels related to the loss of OH, NO_2, and HNO_2 fragments from the molecular and other ions (Table 4).

Thus, the results of analyzing the electron impact mass spectra show that derivatives of aliphatic ketones Ia-Id exist in the gas phase as in solution as a mixture of linear and ring tautomers. In the gas phase, benzaldehyde derivatives IIa-IIc have predominantly linear structure, while derivatives of acetophenones IId-IIf exist as a mixture of tautomeric forms.

EXPERIMENTAL

The direct inlet electron impact mass spectra were obtained on Kratos MS-25 and MKh-1321A mass spectrometers at 50 and 70 eV, respectively. The mass spectra of the metastable peaks for Ia were obtained on the Kratos MS-25 spectrometer with V/E and V^2/E coupled scanning. The high-resolution mass spectra were taken on a VG ZAB spectrometer using PFC as the standard.

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