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INVESTIGATION OF THE MASS-SPECTROMETRIC BEHAVIOR OF AMINOMETHYL AND AMINOMETHYLENE DERIVATIVES OF TETRAHYDROFURAN

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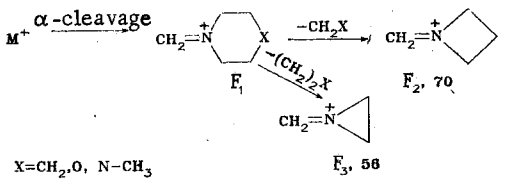
The principal pathway in the mass-spectrometric fragmentation of aminomethyltetrahydrofurans is cleavage of the α-C—C bond, in which a tetrahydrofuranyl radical is eliminated in the form of a neutral fragment, and the charge is retained on the amino fragment. This process is completely absent in methylene derivatives, for which one of the characteristic fragmentation pathways is cleavage of the β bond with retention of the charge on the hydrofuran fragment. The established mass-spectrometric principles makes it possible to reliably distinguish aminomethyl- and aminomethylenetetrahydrofurans.

New amino derivatives of the tetrahydrofuran series have been obtained by the reaction of 2-formyltetrahydrofuran with secondary amines, and some of their transformations have been studied [1, 2]. In the present research we studied the mass-spectrometric behavior of the following compounds under the influence of electron impact:

Ia-c IIa-c

a R=piperidyl, b R=morpholyl, c R=N N—CH_3

Compounds Ia-c give low-intensity molecular-ion peaks, and this constituted evidence for low stabilities of the molecules with respect to electron impact. In the case of Ic the the molecular-ion peak has a somewhat higher intensity (2.8%) as compared with the molecular-ion peaks of Ia, b (1.4%); this is due to the greater basicity of the substituent. The principal pathway in the fragmentation of Ia-c involves cleavage of the α bond of the substituent and the formation of F_1 ions, which have the same structure:



X=CH_2,O, N-CH_3

This sort of fragmentation pathway is extremely characteristic for alkylamines [3]. The peaks of these ions have considerable intensities (100, 100, and 70%, respectively).

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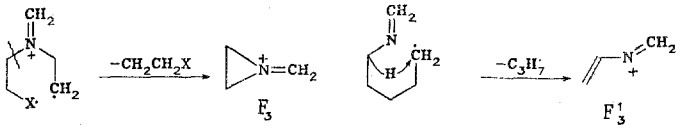
TABLE 1. Mass Spectra of Ia-c and IIa-c

Compound	m/z values (relative intensities, %)*	W_M, %
Ia	169 (4), 99 (14), 98 (100), 70 (17), 69 (10), 55 (26), 44 (19), 43 (18), 42 (30), 41 (34), 39 (9)	1,4
Ib	171 (3), 101 (7), 100 (100), 71 (6), 70 (9), 56 (27), 55 (5), 43 (15), 42 (14), 41 (11), 39 (6)	1,4
Ic	184 (10), 113 (72), 98 (10), 71 (25), 70 (100), 58 (10), 56 (12), 55 (7), 43 (37), 42 (43), 41 (14)	2,8
IIa	167 (36), 111 (100), 110 (25), 96 (54), 84 (26), 83 (18), 69 (28), 55 (41), 42 (51), 41 (78), 39 (26)	3,6
IIb	169 (22), 113 (96), 111 (32), 98 (22), 83 (61), 57 (26), 56 (36), 55 (100), 43 (55), 41 (89), 39 (21)	2,8
IIc	182 (58), 126 (25), 111 (24), 97 (33), 83 (20), 70 (100), 58 (38), 55 (40), 43 (75), 42 (77), 41 (38)	7,8

*The 10 most intense peaks in the mass spectra are presented.

Proceeding from Stevenson's rule [4], according to which in the case of simple cleavage the charge in the ion is retained on the fragment with the lower ionization potential (IP), it may be asserted that the IP of the tetrahydrofuranyl radical is higher than the IP of any of the F_1 fragments, since $C_4H_7O^+$ ion peaks are completely absent in the mass spectra. The fragmentation of the F_1 ions determines the mass spectra of Ia-c, and the common pathway of their fragmentation consists in elimination of CH_2X molecules to give common ion F_2.

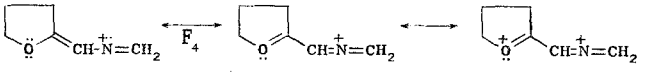
Another common pathway in the fragmentation of the F_1 ions is splitting out of CH_2CH_2X fragment (to give F_3 ions). A similar process occurs in the case of Ia with migration of a hydrogen atom to the eliminated fragment (to give F_3^1 ions). The formation of F_2 and F_3 ions in this case evidently suggests prior cleavage of the C–N bond in the heteroring, whereas these processes are due to cleavage of the C–X bond in the case of Ib, c:



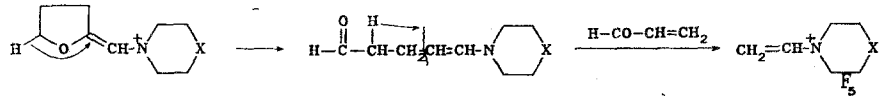
Although peaks of tetrahydrofuranyl cations are not observed in the mass spectra of Ia-c, the presence of this fragment in the molecules is confirmed not only by the difference in the m/z values of the molecular ions and the F_1 ions but also by the ion peaks with m/z 43, 41, and 39, which are characteristic for tetrahydrofurans [5].

In contrast to aminomethyl derivatives of tetrahydrofuran Ia-c, the molecular-ion peaks in the mass spectra of IIa-c have considerably higher intensities. The W_M values range from 2.8 to 7.8%; as in the first series of compounds, IIc has the highest stability with respect to electron impact.

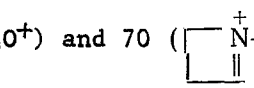
Two common fragmentation pathways, viz., elimination of a $CH_2CH_2XCH_2$ molecule and splitting out of a fragment with a mass of 56 amu, are observed. The first fragmentation pathway involves cleavage of the heteroring of substituent R to give ion F_4, which can be stabilized through resonance:



The elimination of a fragment with a mass of 56 amu does not depend on X and is consequently due to cleavage of the hydrofuran ring with the loss of a C_3H_4O particle. This process should be accompanied by migration of two hydrogen atoms from the hydrofuran part of the molecule to the charged fragment and can be described by the following scheme:



In addition to the indicated processes, cleavage of the exocyclic C–N bond (β cleavage) occurs in the fragmentation of IIa-c; the charge is retained on the tetrahydrofuran fragment of the molecule in this case, and ions with m/z 83 are formed. In the fragmentation of IIb

and IIc cleavage of the heteroring of the substituent leads to the formation of ions with m/z 55 ($C_3H_3O^+$) and 70 (), the signals of which have the maximum intensities in the spectra. Characteristic peaks of ions with m/z 41 and 39, which are formed in the fragmentation of the furan ring, are also observed.

Thus we have established differences in the mass-spectrometric fragmentation of aminomethyl- and aminomethylenetetrahydrofurans: First, the stabilities of the molecular ions of aminomethylenetetrahydrofurans with respect to electron impact are higher than in the case of the aminomethyl derivatives; second, the principal fragmentation pathway for the aminomethyl derivatives is cleavage of the α bond, which is absent in the case of aminomethylenetetrahydrofurans, for which cleavage of the β bond of the substituent is characteristic. Cleavage of the α bond in this case proceeds with double migration of a hydrogen atom. It follows from the information stated above that the mass-spectrometric characteristics make it possible to reliably distinguish these compounds from their mass spectra.

EXPERIMENTAL

The mass spectra were obtained with a Varian MAT-44-S chromatographic mass spectrometer at an ionizing voltage of 70 eV, a cathode emission current of 800 μA, and an ion-source temperature of 180°C. The substances were introduced into the mass spectrometer through a Varian-3700 chromatograph. The temperature of the capillary column was 110°C, the stationary phase was FFAP, and the length of the column was 25 m.

The investigated IIa, b were previously obtained in [1, 2].

2-(4-Methylpiperazinomethylene)tetrahydrofuran (IIc). A solution of 10 g (0.1 mole) of freshly distilled tetrahydrofuran in 10 ml of benzene was added slowly at 10°C to a solution of 20 g (0.2 mole) of methylpiperazine in 80 ml of benzene, after which the temperature was raised to 30°C, and the reaction mixture was stirred for 30 min. The water was separated, and the benzene extract was dried with sodium sulfate. The benzene was removed, and the residue was distilled in vacuo to give 8.1 g (44%) of a product with bp 81-82°C (1 mm) and n_D^{20} 1.5170. IR spectrum: 1700 cm^{-1}. PMR spectrum ($CDCl_3$): 1.87 (2H, q, 4-CH_2, J = 6.5 Hz), 2.15 (3H, s, N–CH_3), 2.30 (6H, weak m, 3-CH_2, β-CH_2), 2.80 (4H, m, α-CH_2), 3.98 (2H, t, 5-CH_2, J = 6.5 Hz), and 4.55 ppm (1H, s, C=CH, J = 1.0 Hz, Z isomer).

2-Piperidinomethyltetrahydrofuran (Ia). A 0.5-liter autoclave with a glass lining was charged with 5.0 g of IIa, 30 ml of absolute hexane, and 0.25 g of the catalyst (5% Pd/C), and hydrogenation was carried out for 4 h at 50°C at an initial hydrogen pressure of 50 atm. The hexane was removed, and the residue was distilled in vacuo to give 4.8 g (95%) of a product with bp 53-54°C (1 mm) and n_D^{20} 1.4730. PMR spectrum ($CDCl_3$): 1.10-1.20 (10H, weak m, 3,4-β,γ-CH_2), 2.30 (6H, m, N–CH_2), and 3.75 ppm (3H, m, 2-CH, 5-CH_2).

2-Morpholinomethyltetrahydrofuran (Ib). Hydrogenation of 5.1 g of IIb as in the preceding example gave 4.9 g (96%) of Ib with bp 61-62°C (1 mm) and n_D^{20} 1.4745. PMR spectrum ($CDCl_3$): 1.40-2.20 (4H, 3,4-CH_2), 2.50 (6H, m, N–CH_2), 3.70 (4H, m, O–CH_2), and 3.90 ppm (3H, m, 2-CH, 5-CH_2).

2-(4-Methylpiperazinomethyl)tetrahydrofuran (Ic). Tetrahydrofuran Ic, with bp 73-74°C (1 mm) and n_D^{20} 1.4835, was similarly obtained in quantitative yield from 5.46 g of IIc. PMR spectrum ($CDCl_3$): 1.40-2.20 (4H, m, 3,4-CH_2), 2.25 (3H, s, N–CH_3), 2.50 (10H, m, N–CH_2), and 3.80 ppm (3H, m, 5-CH_2, 2-CH).

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