MASS-SPECTROMETRIC IDENTIFICATION OF CERTAIN 2-(e-BENZOYLAMINO-CAPROYLAMINO)BENZOPHENONES AND THEIR DI- AND TETRAAZAMACRO-CYCLIC CYCLIZATION PRODUCTS

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Dissociation occurring during mass-spectrometric measurements of 2-(benzoylaminocaproylamino)benzophenones substituted in the benzene ring and also of 11- and 22-membered di- and tetraazaheterocycles obtained by their intra- and intermolecular cyclization proceeds preferentially at the amide C-N bonds, partially with the transfer of a hydrogen atom to the amino group. The size and character of the heterocycle can be established by analyzing the intensities of the characteristic ions.

We have recently proposed methods for the synthesis of 11- and 22-membered nitrogen heterocycles [1], which are of interest as potential physiologically active compounds. The synthesis of these compounds was effected as the result of intra- or intermolecular cyclization of the corresponding  $2-(\varepsilon$ -benzoylaminocaproylamino)benzophenones (I). A necessity therefore arose of developing a method for a fast and reliable identification of both the starting compounds and the products of their cyclization. For this purpose we studied the mass-spectrometric behavior of a series of compounds Ia-f, and also of 11-methyl-9-phenylbenzo[b]-1,8-diaza-8-undecen-2-one (II) and certain 22-membered heterocycles IIIc-e.



a, b  $R^1 = H$ , c-f  $R^1 = COC_6H_5$ ; a, d  $R^2 = NO_2$ , b, f  $R^2 = Br$ , c  $R^2 = CH_3$ , e  $R^2 = CI$ 

Analysis of the mass spectra obtained (Table 1) shows that the fragmentation of the slightly stable (Table 2) molecular ions  $(M^+)$  of acetylaminobenzophenones I is characterized (scheme 1) by a loss of a hydroxyl radical or a molecule of water, which indicates the high probability of the existence of iminol forms of these compounds in the gaseous phase.

At the same time, similarly to aromatic acylamines [2], the  $M^+$  of compounds I undergoes a cleavage of the amide bond C-N (path A) proceeding both with the transfer (ion  $\phi_1$ ) and without the transfer of the hydrogen atom to the nitrogen atom (ion  $\phi_2$ ). The first of the fragments formed then readily eliminates a radical C<sub>6</sub>H<sub>5</sub> (ion  $\phi_4$ ). Moreover, a cleavage of the exocyclic  $\alpha$ -C-N bond is observed (path B) leading to ion  $\phi_3$ . The peaks of ions  $\phi_1$  and  $\phi_2$ are most intense in the mass spectra of compounds I. The splitting of  $\alpha$ - and  $\beta$ -C-N bonds by paths A and B also proceeds partially with the retention of the charge on the aliphatic part of the molecule with the formation of ions  $\phi_5$  and  $\phi_6$ . During the cleavage of the C-C bonds in the aliphatic radical, ions are also formed, homologous to fragments  $\phi_5$ . As expected (the Stivenson rule), the peak intensity of the  $\phi_6$  ions increases uniformly with increase in the

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TABLE 1. Mass Spectra of Compounds I-III

Com- pound	Values of m/z (relative intensity, ヴァ,)・									
Ia	355 (9), 338 (14), 243 (25), 242 (100), 241 (95), 212 (14), 195 (13), 114 (28), 105 (28), 77 (40), 56 (50)									
Ib	388 (12), 275 (100), 274 (56), 195 (18), 167 (12), 105 (34), 77 (27), 73 (14), 72 (23), 59 (15), 56 (20)									
Ic	(11), 12 (20), 03 (10), 00 (20) (20) (20) (20) (20) (20) (20) (									
Ig4	(41), 13 (30), 31 (11), 33 (10) 242 (32), 241 (24), 226 (20), 218 (62), 176 (32), 134 (23), 112 (23), 106 (46), 105 (100), 77 (02)									
Ie	(40), 105 (100), 17 (32) 448 (2), 231 (100), 230 (40), 218 (10), 213 (12), 212 (54), 211 (36), 176									
Ιf	492 (1), $125$ (67), $274$ (37), $218$ (14), $195$ (9), $176$ (8), $167$ (8), $134$ (5), $1020$ (7), $275$ (67), $274$ (37), $218$ (14), $195$ (9), $176$ (8), $167$ (8), $134$ (5),									
п	105 (100), 77 (33), 73 (10) 306 (16), 290 (25), 289 (59), 287 (21), 234 (33), 229 (92), 214 (17), 213 (100) 96 (21) 77 (29) 73 (29)									
IIIc	(100), 50 (21), 11 (22), 13 (23) (21) (10), 105 (45), 104 (17), 96 (75), 91 (32), 89 (25) 77 (100) 55 (50)									
IIId	(52), (52), (52), (71), (100), (50) (574), (2), (320), (29), (29), (268), (43), (254), (43), (252), (46), (222), (32), (208) (200), (200									
IIIe	(25), 200 (23), 50 (100), 77 (43) (552 (36), 353 (20), 326 (35), 300 (44), 299 (50), 298 (34), 257 (77), 243 (86), 242 (53), 241 (100), 104 (41)									

\*Peaks of M<sup>+</sup> and of 10 most intense peaks are given. The values of m/z, calculated for the light isotope of halogen (<sup>35</sup>Cl or <sup>79</sup>Br) are indicated by italics. †The peak of M<sup>+</sup> is absent.

TABLE 2. Peak Intensity of the Principal Characteristic Ions in Mass Spectra of Compounds Ia-f ( $\%\Sigma_{50})$ 

Com- pound	₩ <sub>M</sub>	[M-OH]+	$[M - H_2O]^*$	$\Phi_1$	Φ2	$\Phi_3$	Φ,	ΣΦ5	$\Phi_6$	<i>m/z</i> 105	<i>m/z</i> 77
Ia Ib Ic Id Ie If	1,1 0,8 1,0  0,5 0,5	1,3 0,2 0,2 0,6 0,5 0,3	0,4 0,2 0,4 0,5 0,2 0,6	9,6 23,2 16,3 3,2 24,1 21,6	9,2 13,0 9,5 2,4 13,3 9,6	3,6 0,1 0,5 2,0 0,1	1,1 2.3 1,8 0,5 1,6 0,7	6,4 3,9 2,2 9,1 3,8 3,5	$2.8 \\ 0.9 \\ 1.4 \\ 6.2 \\ 2.4 \\ 1.6$	2,6 3,9 12,4 10,1 18,1 8,8	3,9 3,1 6,7 9,3 6,0 5,8

electronegativity of substituent  $R^2$ . The peak intensity of the  $\phi_2$  ion is inversely dependent on the electronic properties of this substituent. It should be noted that benzoyl cations are probably formed not only from M<sup>+</sup>, but also as the result of the further dissociation of the  $\phi_5$  or  $\phi_6$  ions, since the peak intensity of the ion with m/z 105 sharply increases on transition from compounds Ia, b to compounds Ic-f. The overall proportion of ions in mass spectra of compounds Ia-f listed in Table 2 is 32-69% of the total ionic current, which indicates a fairly high selectivity of their dissociation from M<sup>+</sup>.

The dissociative ionization processes of compounds II and IIIc-e are also characterized by primary splitting of the amide C-N bond, leading either to fragments having possibly the structure of an ll-membered heterocycle (path AA, ion  $\phi_7$ ) or an open form of an aminoketone (ion M<sub>1</sub><sup>+</sup>) (Scheme 2).

TABLE 3. Peak Intensity of Characteristic Ions in Mass Spectra of Compounds II, IIIc-e  $(\%\Sigma_{50})$ 

Com- pound	W <sub>M</sub>	Φ7	[Φ <sub>7</sub> -H]*	[Φ7-OH]-	$[\Phi_7 - H_2O]^*$	[Φ7−H, −H2O]*	Ф	ΣΦ,	ΣΦ10	ΣΦ11	m/2 96	m/2 77
    c    d     e	1,7 4,9 0,3 3,3	(1,7) 0,2 0,9 2,4	0,4 0,3 1,5 0,5	4,7 1,3 1,7 0,5	0,4 0,7 0,6 0,4	1,7 1,1 0,6	0,8 -1,3	9,2 0,8 7,4 13,2	0,4 0,6 4,0 10,8	0,4 1,8 6,9 11,4	1,7 11,0 5,7 3,7	1,8 14,7 2,5 0,8



The first of these  $(\Phi_7)$ , similarly to the derivatives of benzodiazepinone [3-6] and benzodiazocinone [7], eliminates the H', OH', or H<sub>2</sub>O particles. The dissociation of ions M<sup>+</sup> and M<sub>1</sub><sup>+</sup> is also accompanied by splitting of the C-C bonds by paths AB, AC, AD, AE, AF, and AG with the retention of charge preferentially on the fragment with the smaller mass (ions  $\Phi_8 - \Phi_{11}$ ). Ion  $\Phi_8$  also undergoes dissociation of the C-N bond with the formation of an ion with m/z 96. The overall peak intensity of the above ions in the mass spectra of compounds II and IIIc-e (Table 3) is, in general, 23-48% of the overall ion peak, so that these ions can be considered characteristic. A similar type of decomposition of the macrocycle was noted in the study of the mass spectra of the macrocyclic esters in [8].

Thus the analysis of the mass spectra of both the intermediates and the final macrocyclic compounds makes it possible to confidently establish the size of the ring and also the character and structure of fragments included in it.

## EXPERIMENTAL

The mass spectra were run on a MAT-112S spectrometer at an ionization energy of 70 eV with direct introduction of the compounds into the ionization field at temperatures of 20-30°C



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below the melting point of the samples. The synthesis of most of the compounds (except for Ib) was described in [1].

5-Bromo-2-(e-aminocaproylamino)benzophenone Ib. A 27.6 g portion (0.1 mole) of 5-bromo-2-aminobenzophenone and 18.6 g (0.1 mole) of a freshly prepared 2-aminocaproyl chloride hydrochloride in 150 ml of absolute chloroform are placed in a flask fitted with a stirrer and a calcium chloride tube. The contents of the flask are stirred at 20°C for 60 h. The precipitate is filtered and washed with 100 ml of acetone and 20 ml of ether. Recrystallization of the reaction product from acetonitrile gives 41.4 g (97%) of hydrochloride of compound Ib, mp 155-156°C. Rf 0.40 (methanol:25% aqueous NH<sub>3</sub>, 10:25). UV spectrum,  $\lambda_{max}$  204, 241, 320 nm. IR spectrum: 1725, 1695 (C=O), 3300-3200 cm<sup>-1</sup> (N-H). Found, %: C 52.8, H 5.1, N 6.5. C19H21BrN2O2. Calculated, %: C 53.6, H 5.2, N 6.6. A 4.3 g portion (0.01 mole) of the hydrochloride obtained is dissolved in 50 ml of distilled water and the solution is passed slowly through a glass column (100 × 10 mm) filled with an EDE-10P anion exchanger in basic form. The column is washed with 100 ml of distilled water, and then with 100 ml of acetone. The acetone solution is evaporated and 20 ml of water and 50 ml of  $CHCl_3$  are added to the residue. The chloroform layer is separated, dried over anhydrous sodium sulfate, evaporated, and the residue is recrystallized from a mixture of benzene and hexane. The yield of base Ib is 2.7 g (70%), mp 77-78°C. Rf 0.65 (acetone-hexane, 1:1). UV spectrum,  $\lambda_{max}$  208, 238, 325 nm. IR spectrum: 1670, 1645 (C=0); 3300 cm<sup>-1</sup> (N-H). Found, %: C 58.5, H 5.3, N 7.4. C<sub>19</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>2</sub>. Calculated, %: C 58.6, H 5.4, N 7.2.

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