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International Journal of Mass Spectrometry 240 (2005) 7–15
International Journal of Mass Spectrometry
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Fragmentation and skeletal rearrangements of products of the reaction between fluorobenzenes and bicyclic N-bases studied by electron ionization mass spectrometry

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Received 31 August 2004; accepted 5 October 2004
Available online 11 November 2004

Abstract

The electron ionization (EI) induced mass spectrometric fragmentation pathways of the titled compounds were studied by electron ionization mass spectrometry. It was found that in the case two isomers are formed in one reaction, the substantially different fragmentation patterns enable to discriminate between them. All of the compounds studied have shown simple bond ruptures in the alkyl chain, some of them were accompanied by H-shift. Moreover, complex rearrangements, depending on compound structure, were also observed. In order to better understand the latter processes, mass spectra of isotope-labeled compounds, B/E mass spectra of metastable ions and high resolution mass spectra were recorded.

Keywords: Fluoronitroaniline derivatives; Electron ionization; Fragmentation pathways

1. Introduction

Bicyclic N-bases, namely 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) have found wide application as very effective catalysts (due to their basic properties) in organic synthesis [1–11]. These compounds are considered relatively unreactive and there is little data in the literature on their use as substrates in chemical reactions [12]. In our previous papers, the reactions between fluorobenzenes and the above bases were reported with special emphasis being put on the mechanism of these unusual reactions [13–15] which led to the formation of fluoroaniline conjugates (**1**–**11**, Scheme 1).

From the point of view of the reaction product structure determination (including discrimination between isomers), that is of crucial importance to the elucidation of reaction mechanism, studies of mass spectrometric fragmentation pathways of these compounds can provide interesting information. Therefore, the electron ionization (EI) induced decompositions of the above compounds were the subject of this study. As it will be discussed in the further part of this paper, some of the compounds revealed unexpected rearrangements, which are of interest with respect to gas phase ion chemistry.

2. Experimental

The EI mass spectra were recorded on an AMD-402 two-sector mass spectrometer (AMD Intectra, Germany) of B/E geometry with an acceleration voltage of 8 kV, an electron energy 70 eV and an ion source temperature 200 °C. The B/E linked scan mass spectra of metastable ions and exact mass measurements (high resolution data) were performed on the same instrument. High resolution data were obtained

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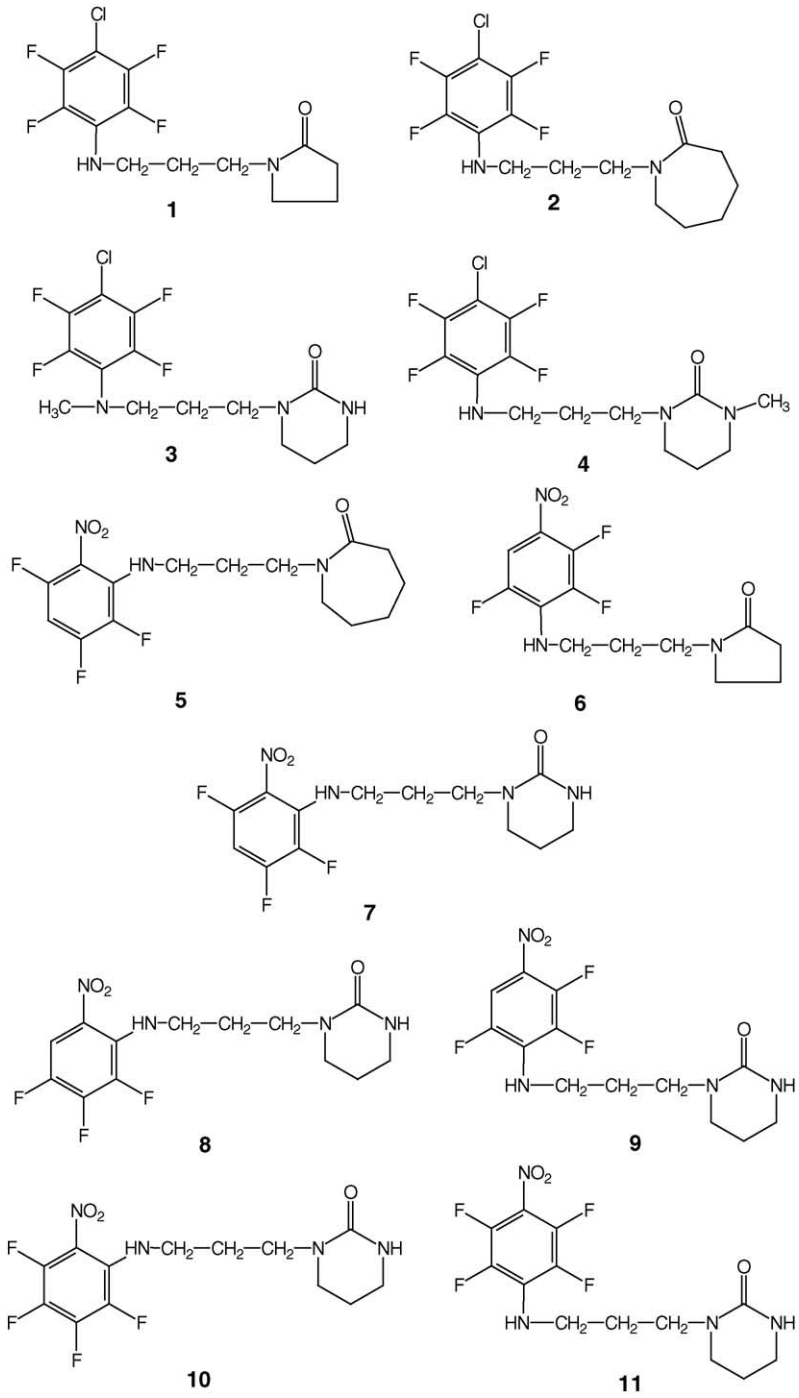
doi:10.1016/j.ijms.2004.10.001



Scheme 1. Compounds studied.

by using *V*/*E* high resolution scan in relation to perfluorokerosene, with an error less than 10 ppm for all ions discussed. Compounds studied were introduced by using direct insertion probe or, if indicated in the text, by gas chromatograph (Hewlett–Packard 5890II) equipped with fused silica capillary column DB-5.

The isotope-labeled compounds were obtained by dissolving the parent compounds in CH_3OD/D_2O (3/1).

3. Results and discussion

Compounds **1** and **2** were formed by the reaction of chloropentafluorobenzene with DBN and DBU, respectively [13]. Their EI mass spectra and fragmentation patterns are shown in Fig. 1.

Decompositions of molecular ions correspond to simple bond ruptures in the alkyl chain. The ruptures accompanied

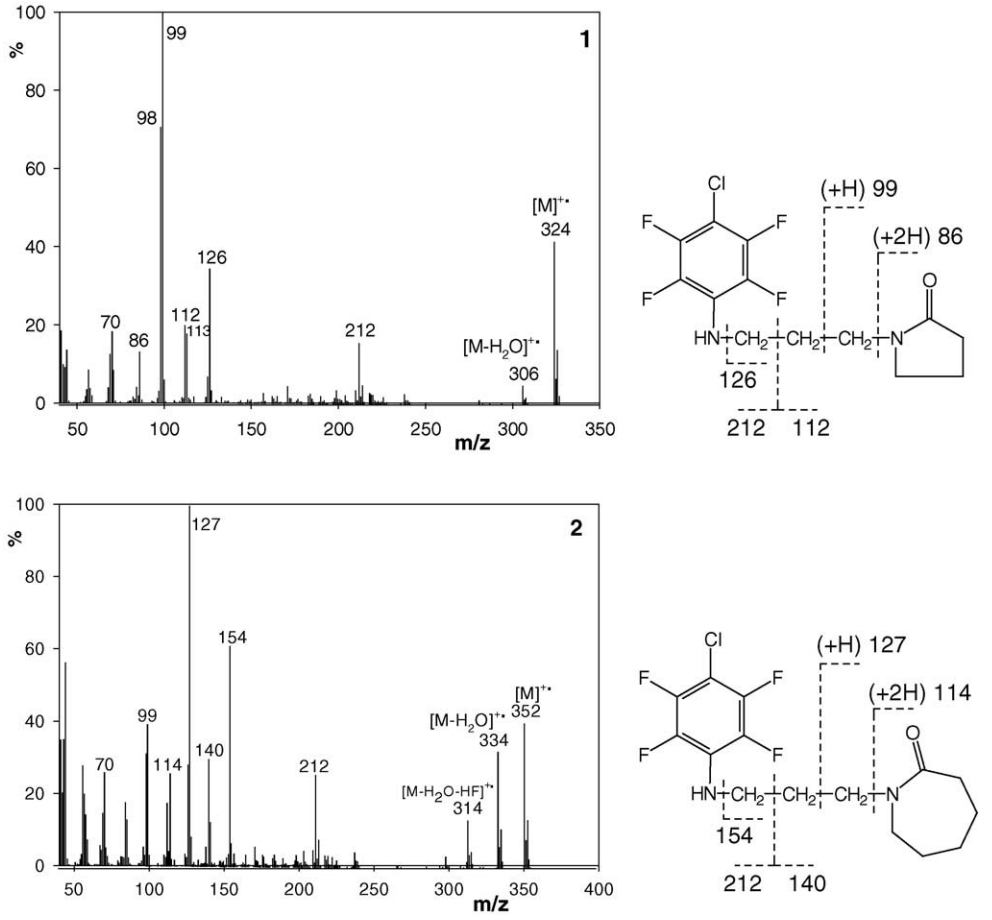
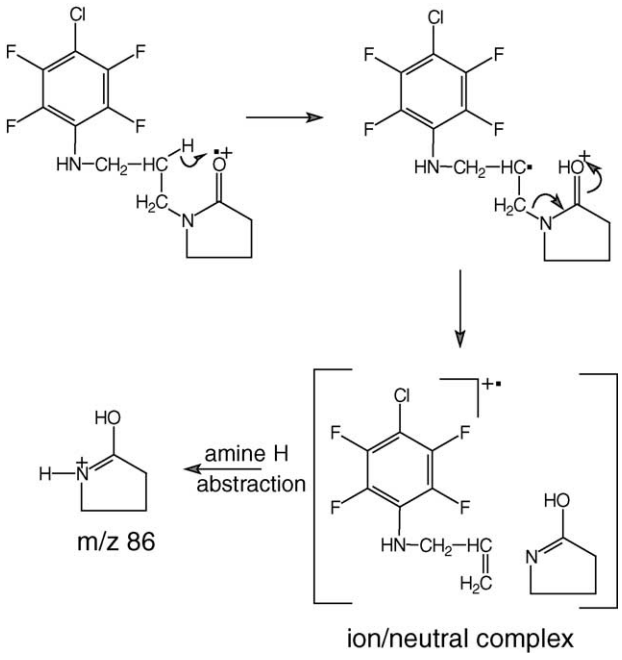


Fig. 1. The EI mass spectra and fragmentation patterns observed of **1** and **2**.

by H-shift (ions at *m*/*z* 99 and 113) can be regarded as examples of McLafferty's rearrangements [16]. There are also fragment ions formed by the transfer of two hydrogen atoms, namely of *m*/*z* 86 for **1** and of *m*/*z* 114 for **2**. Analogous fragmentation pathways have been observed for all remaining compounds studied. Double and even triple hydrogen rearrangements are well-known in EI mass spectrometry and they can occur via differently sized transition states, although the six-membered state is the most common [16,17]. Recently, Yamaoka et al. have described in detail the formation of *m*/*z* 102 ion from *N*-(5-phenylvaleryl)-1-azacyclopentanone-2-thione, which is a thio analog of the *m*/*z* 86 fragment ion originated from **1** [17]. This excellent paper describes a novel type of double hydrogen rearrangement yielding a protonated γ-thiobutyric lactam. The above authors have established that this process proceeds through the ion/neutral complex. Therefore, we suggest that the formation of the *m*/*z* 86 ion (protonated γ-butyric lactam) from **1** (and *m*/*z* 114 ion from **2**) also proceeds through the ion/neutral complex as shown in Scheme 2.

The abstraction of amino hydrogen atom (in fact, a proton abstraction) seems to be favored since the alkanyl/alkenyl hydrogen atoms are less acidic. The formation of the *m*/*z* 102 ion occurs via abstraction of benzylic hydrogen which is also less



Scheme 2. The plausible mechanism of the *m*/*z* 86 ion formation from **1**.

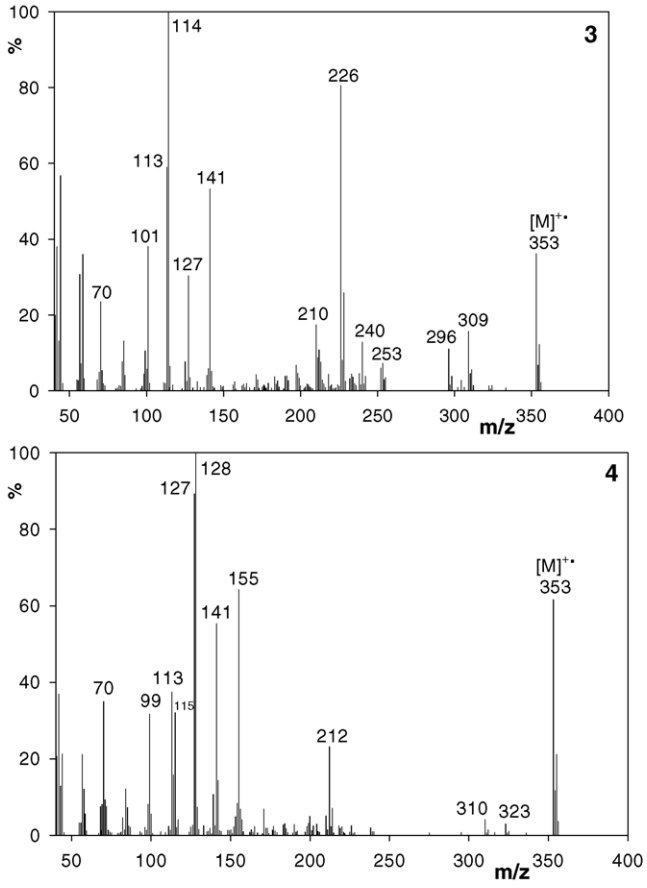


Fig. 2. EI mass spectra of **3** and **4**.

acidic than amino hydrogen. Therefore, the ion/neutral complex, besides of the *m/z* 102 ion formation, can also dissociate yielding the fragment ion $[M-101]^{\bullet+}$ of *m/z* 160 [17]. Among the compounds studied in this work, only **3** has methyl group instead of amine hydrogen atom (Scheme 1). For **3,** the fragment ion formed through the double H-shift (analogous to that of *m/z* 86 for **1**) is observed at *m/z* 101 (Fig. 2). Because **3** does not have the acid amine hydrogen atom, the dissociation of ion/neutral complex yields the ion $[M-100]$ of *m/z* 253 (Fig. 2, Scheme 3).

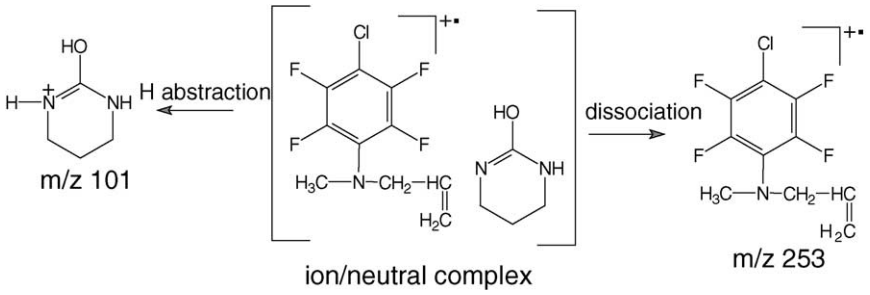
For **2**, which contain a seven-membered lactam ring, the loss of water (followed by the loss of HF) occurs with a higher yield than for **1**, which contains a five-membered lactam ring. The release of HF molecule can be explained by the existence of hydrogen bond, which can be formed due to the polarity of C–F bond and most likely the eliminated fluorine originates from *ortho* position [18]. However, it is difficult to elucidate why the HF loss proceeds as a consecutive fragment after water loss.

Isomers **3** and **4** are formed by the reaction of chloropentafluorobenzene with MTBD [13]. Their EI mass spectra are shown in Fig. 2.

In the mass spectrum of **3,** the above discussed ion at *m/z* 253, which was not observed in the spectrum of **4**, is present (Fig. 2). On the ground of B/E linked scan spectrum we can say that the ion of *m/z* 253 is formed directly from molecular ion (Fig. 3) and high resolution data show that the elemental compositions of this ion is $C_{10}H_8NF_4C$. These findings confirm that the *m/z* 253 ion is formed through the dissociation of ion/neutral complex shown in Scheme 2. The ions analogous to that of *m/z* 253 were not observed for any other compound studied, thus it seems reasonable to assume that this ion was formed due to the presence of methyl group on amino nitrogen. In other words, the presence of acidic amino hydrogen atom favors the H-abstraction process over the dissociation of the ion/neutral complex.

In the EI mass spectrum of **3** (Fig. 2), there is also an abundant ion of *m/z* 210; analogous ions are not observed for any other compound studied. High resolution data has indicated that this ion has elemental composition C_7HNF_4Cl and was formed from the *m/z* 253 ion as it was shown by B/E mass spectrum of the latter. The plausible structure of ion 210 is shown in Scheme 4.

In the mass spectrum of **3** there are significant peaks at *m/z* 309 and 296. Exact mass measurement has shown that these ions are formed by loss of C_2H_6N and C_3H_7N fragments, respectively. The formation of these ions is an unusual rearrangement because we have deduced that cleaved fragments do not originate from piperimidone ring but they contain tertiary nitrogen attached to fluorophenyl ring. First, in the mass spectrum of **4** the respective peaks are by 14 *m/z* units higher (*m/z* 323 and 310, characterized by lower intensities, Fig. 2); note that **4** has hydrogen instead of methyl at the nitrogen atom attached to fluorophenyl ring. Second, the mass spectrum of isotope-labeled **3** (Fig. 3),



Scheme 3. Formation of the *m/z* 101 and 253 ions through the ion/neutral complex from **3**.

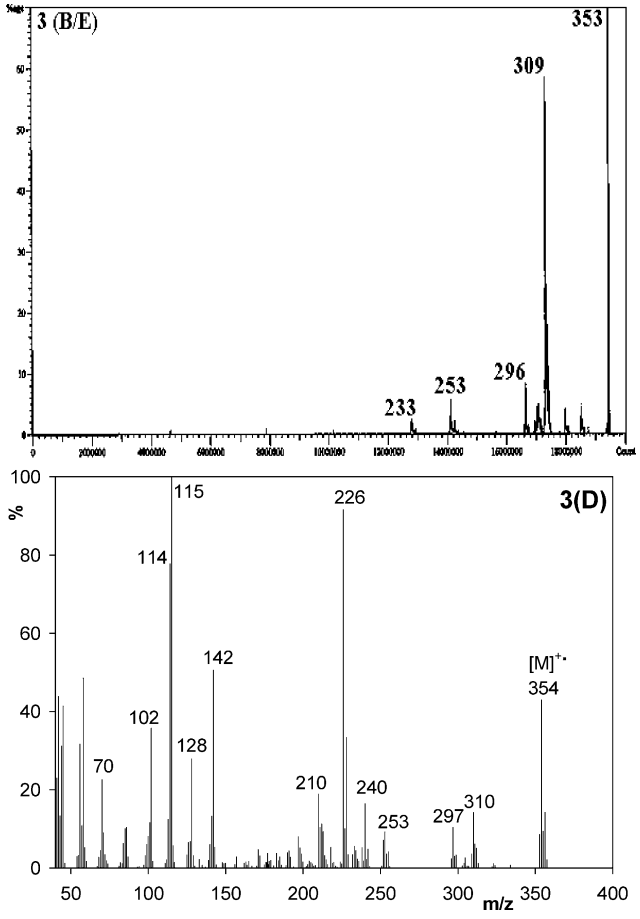
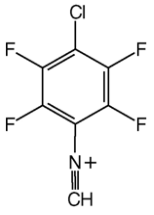


Fig. 3. B/E linked scan mass spectrum of molecular ion of **3** and EI mass spectrum of isotope-labeled **3**.

having amide hydrogen atom exchanged for deuterium, shows that this hydrogen is not cleaved during formation of these fragment ions. The B/E linked scan mass spectra of the *m*/*z* 309 and 296 fragment ions are shown in Fig. 4. The ion of *m*/*z* 296 is an odd-electron ion, thus we have compared its decomposition to the EI induced fragmentation pathway of the compounds for which the *m*/*z* 296 ion can have an analogous structure. First, we put forward the hypothesis that ion of the *m*/*z* 296 corresponds to 1-(2,3,5,6-tetrafluoro-4-chlorobenzyl)-tetrahydro-pyrimidin-2-one. However, the decomposition of the *m*/*z* 296 does not resemble that of 1-benzyl-tetrahydro-pyrimidin-2-one [19]. For example, in the EI mass spectrum of the latter, there was an abundant



Scheme 4. The plausible structure of ion 210 for **3**.

tropylium ion of *m*/*z* 91, as expected for a compound containing benzyl moiety [16,20]. For 1-(2,3,5,6-tetrafluoro-4-chlorobenzyl)-tetrahydro-pyrimidin-2-one, *m*/*z* of this ion would be shifted to 197 (tetrafluorochloro derivative) but it was not detected. Loss of formyl radical (loss of mass 29) also does not occur for the *m*/*z* 296 ion but it was observed for 1-benzyl-tetrahydro-pyimidin-2-one [19]. Therefore, the 1-(2,3,5,6-tetrafluoro-4-chlorobenzyl)-tetrahydro-pyimidin-2-one structure has to be rejected as concerns the ion of *m*/*z* 296. Taking into account the above examples, it is reasonable to assume that the *m*/*z* 296 ion contains neither benzyl moiety nor tetrahydro-pyrimidin-2-one ring. The next structure which we propose for the *m*/*z* 296 ion is inserted in its B/E mass spectrum (Fig. 4). For this structure features of EI induced decomposition of both *N*-alkyl-*N*-methyl-anilines and alkyl isocyanates should be observed and they are, indeed. In the EI mass spectra of *N*-alkyl-*N*-methyl-anilines there is the base peak of the *m*/*z* 120 ion [21–23]. For the *m*/*z* 296 ion, this fragment ion is shifted to the *m*/*z* 226 because of the presence of four fluorine atoms and chlorine atom on aromatic ring (Fig. 4). In the EI mass spectra of alkyl isocyanates, there are significant peaks of fragment ions formed as a result of the rupture of the β-bond in relation to nitrogen atom [24,25]. For the *m*/*z* 296 ion, this fragmentation pathway has led to the formation of the *m*/*z* 240 fragment ion (Fig. 4). Thus, the structure of the *m*/*z* 296 ion proposed in Fig. 4 seems to be reasonable, although it is difficult to propose a plausible mechanism for its formation. It appears that we deal with a very complex skeletal rearrangement. Other fragmentation pathways of the *m*/*z* 296 ion correspond to the halogen atom loss (*m*/*z* 277, 261 and 207) and are not structurally informative. The ion of *m*/*z* 309 is an even-electron one, thus an analogous consideration as that for the *m*/*z* 296 ion cannot be performed. The only informative fragment ion observed in B/E linked scan mass spectrum of the former ion is that of *m*/*z* 113. In Fig. 4 the intact tetrahydro-pyrimidin-2-one ring is proposed for this ion, however, other structures cannot be ruled out.

The above skeletal rearrangements discussed for **3** and **4** does not proceed for any other compound studied. Their absence in the case of **1** and **2** indicates that they are related to the presence of tetrahydro-pyrimidin-2-one moiety in **3** and **4** since **1** and **2** contain lactam rings instead of tetrahydro-pyrimidin-2-one ring (Scheme 1). Other compounds studied, which contain tetrahydro-pyrimidin-2-one ring (e.g., **9** and **11**), also did not show these rearrangements because, as described further, their EI decomposition was dominated by the processes related to the presence of nitro group.

Compound **5** was obtained by the reaction of 2,3,4,6-tetrafluoronitrobenzene with DBU (unpublished data from our laboratory); its EI mass spectrum is shown in Fig. 5.

Molecular ion (*m*/*z* 345) was not detected. Peaks of ions formed by the loss of water molecule(s) and hydroxyl group (*m*/*z* 327, 310, 392) are present in the spectrum. This is a characteristic feature of *N*-alkyl-*ortho*-nitroanilines [26], while most of other fragment ions (*m*/*z* 251, 215, 199) originate

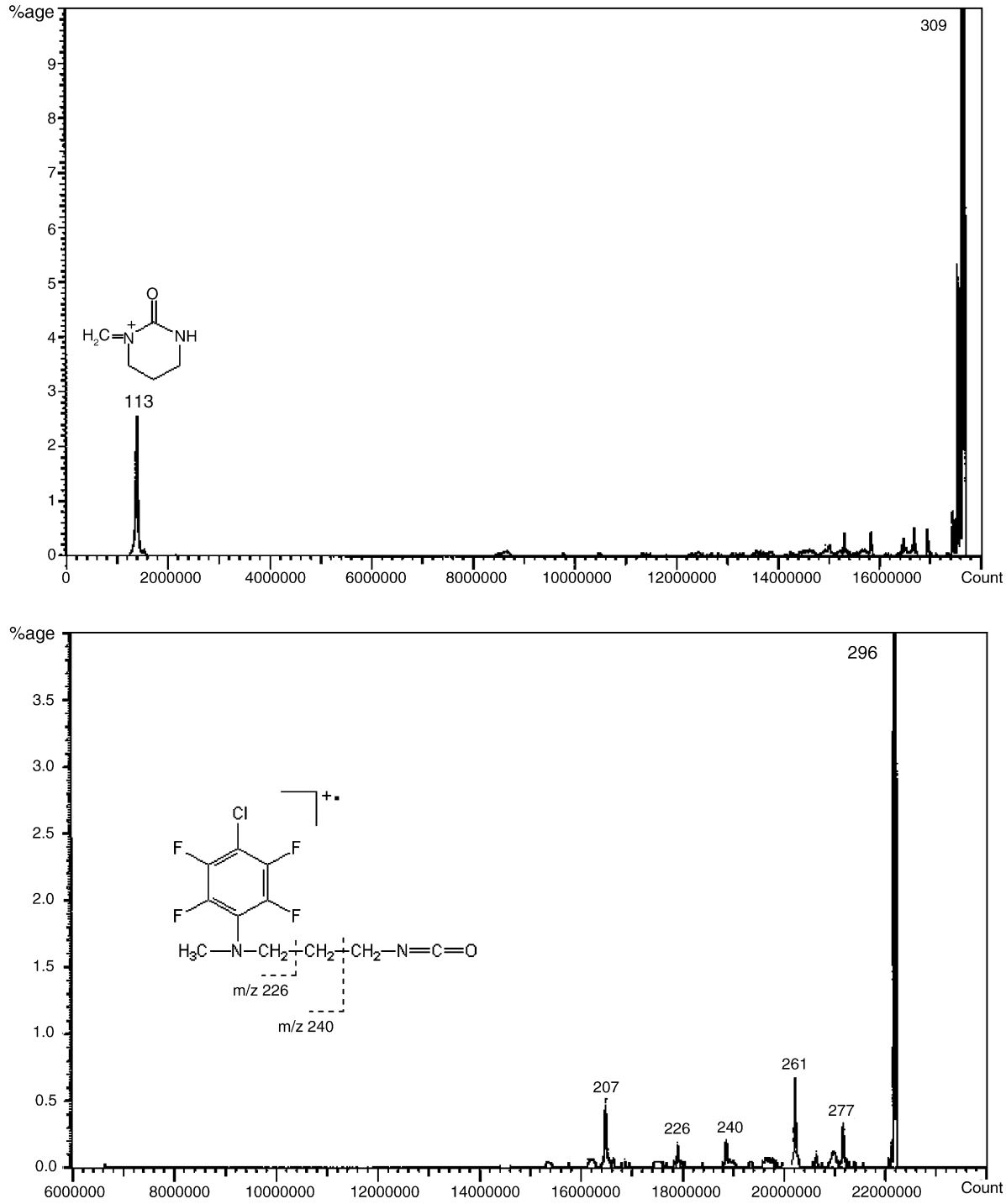


Fig. 4. The B/E mass spectra of fragment ions 309 and 296 derived from **3**.

from 310 ion. As it is usually in the case of *N*-alkyl-*ortho*-nitroanilines, the decomposition of **5** is quite a complex process. In the EI mass spectra of the *N*-alkyl-*ortho*-nitroanilines the peaks of fragment ions formed as a result of alkoxy radical loss have significant abundances [26]. For **5**, we have also observed this process, however, the charge remains on the opposite side. The fragment ion of *m*/*z* 170 corresponds to N-substituent having oxygen atom attached. The lack of molecular ion and significant peaks of fragment ions formed as a result of hydrogen abstraction by nitro group or transfer of oxygen from nitro group to N-substituent indicate that these processes proceed in a very easy way. They are more efficient than for *N*-alkyl-*ortho*-nitroanilines and this is a result of evident influence of fluorine atoms substituted on phenyl ring (*N*-alkyl-*ortho*-nitroanilines exhibit abundant molecular ions).

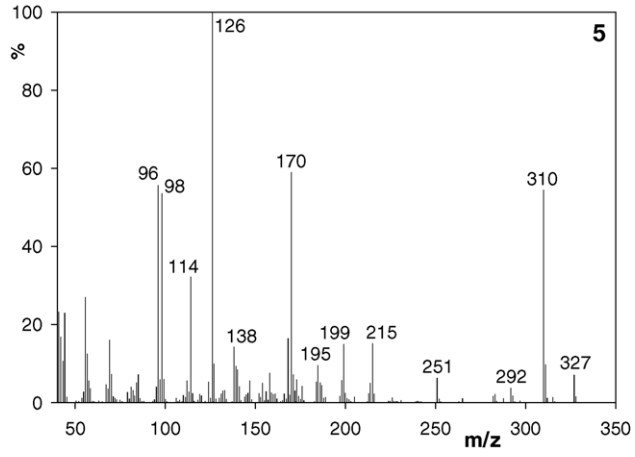


Fig. 5. EI mass spectrum of **5**.

Compound **6** was obtained by the reaction of 2,3,4,5-tetrafluoronitrobenzene with DBN (unpublished data from our laboratory) and its EI mass spectrum and B/E mass spectrum are shown in Fig. 6.

The abundant fragment ion at *m*/*z* 299, formed as a result of water elimination, is unexpected. For low-energy decompositions this is the only observed process as indicated by B/E mass spectrum of molecular ion of **6** (Fig. 6). The eliminated

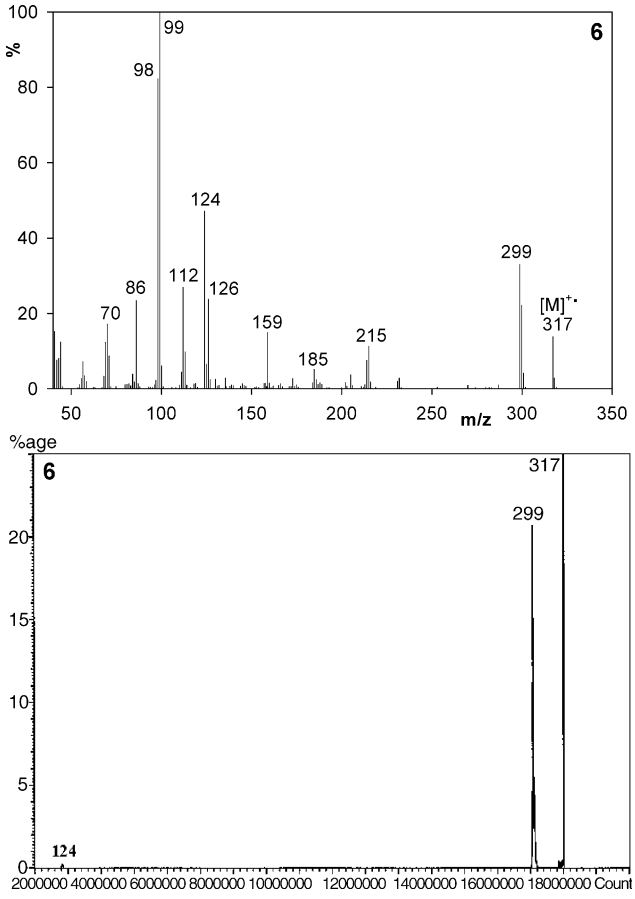


Fig. 6. EI mass spectrum of **6** and B/E mass spectrum of molecular ion of **6**.

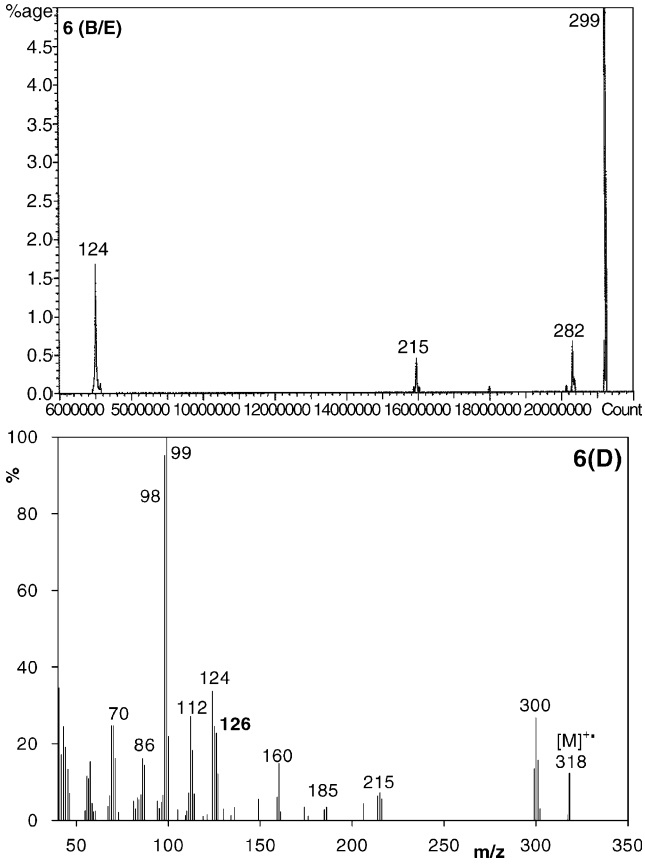


Fig. 7. B/E mass spectrum of ion 299 derived from **6** and EI mass spectrum of isotope-labeled **6** (bottom).

H_2O does not originate from lactam ring because, first, for **1** the water loss is a minor process (Fig. 1) and, second, ion 299 loses lactam moiety (loss of mass 84) leading to the formation of ion at *m*/*z* 215 as shown by B/E mass spectrum of ion 299 (Fig. 7). For isotope-labeled **6** (Fig. 7), having amino hydrogen atom exchanged for deuterium, loss of water occurs either as H_2O or HDO elimination. This is in contrast to the *N*-alkyl-*ortho*-nitroanilines since in the case of these compounds hydrogen atom in the eliminated water molecule always originated from amino group [26]. As it was mentioned above for **5**, hydrogen abstraction by nitro group or transfer of oxygen from nitro group to N-substituent occurs easily due to the presence of fluorine atoms on phenyl ring and, therefore, is observed even for *N*-alkyl-*para*-nitroaniline (**6**). It seems reasonable to suppose that these processes proceed according to the "ring-walking" mechanism, similarly as it was proposed for HF molecule loss from fluorophenols and fluoroanilines [27]. Loss of lactam moiety from ion 299 leads to the formation of ion 215. Further decomposition of the latter corresponds to NO loss (ion 185) followed by C_2H_2 loss (ion 159) as concluded from B/E mass spectra of ions 215 and 185 and confirmed by high resolution data obtained for each of the above fragment ions. Second fragmentation pathway of ion 299 consists in the formation of ion 124 (Fig. 7). As evidenced by elemental composition

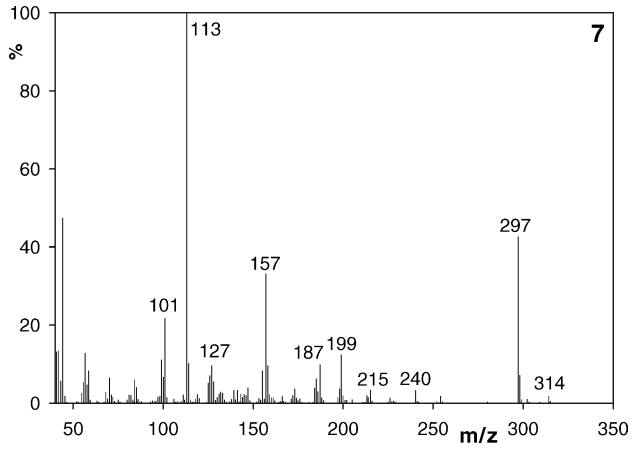


Fig. 8. EI mass spectrum of **7**.

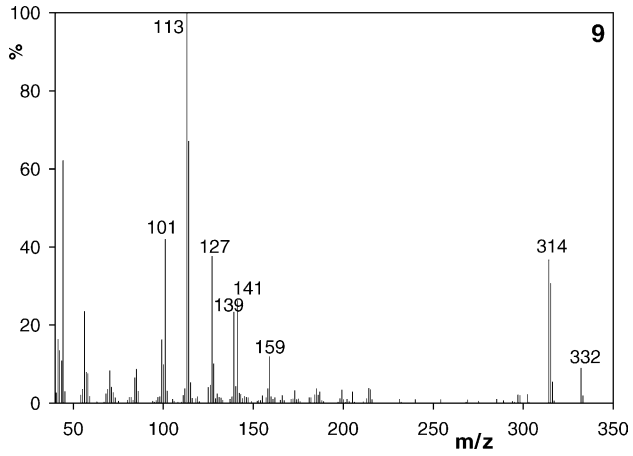


Fig. 9. The EI mass spectrum of **9** obtained by GC/MS.

determined for ion 124, it corresponds to N-substituent deprived of two hydrogen atoms. Third fragmentation pathway of ion 299 consists in hydroxyl radical loss (ion 282). This fragment ion is very unstable and it is not observed in EI mass spectrum of **6** (Fig. 6), thus it can be observed only in mass spectra of metastable ions, which are formed just above the decomposition energy threshold. As indicated by EI mass spectrum of isotope-labeled **6** (Fig. 7), the decomposition of **6** proceeds with random exchange of amino and alkyl hydrogen atoms.

Compound **7** was formed by the reaction of TBD with 2,3,4,6-tetrafluoronitrobenzene [14]. Its EI mass spectrum is shown in Fig. 8.

The fragmentation pattern of **7** resembles this discussed above for **5**. The molecular ion was not detected. In Fig. 8 abundant fragment ion 297, formed by the loss of water molecule and hydroxyl radical, can be seen, whereas most of other fragment ions (240, 199, 187) originate from 297 ion. Another fragment ion seen in Fig. 8 is that at *m*/*z* 157, which corresponds to N-substituent having oxygen atom attached.

Isomers **8** and **9** were formed by the reaction of TBD with 2,3,4,5-tetrafluoronitrobenzene [14]. These compounds could not be separated, therefore they were introduced into mass spectrometer through a gas chromatograph. The relative amounts of these compounds depend on the reaction conditions. Therefore GC/MS technique can be used for the investigation of this reactions carried out provided that we know which of peaks on a chromatogram corresponds to a given compound. The EI mass spectrum of **8** was practically identical to that of **7** (Fig. 8), therefore its presentation is not necessary. The EI mass spectrum of **9** is shown in Fig. 9.

The fragmentation pattern observed for **9** is very similar to that discussed above for **6**; no essential influence of piperimidone ring (tetrahydro-pirimidin-2-one ring) was observed. The discrimination between isomers **8** and **9** can be performed on the basis of the following EI mass spectrometric features: molecular ion is observed only for **9** (*m*/*z* 332), significant fragment ion of *m*/*z* 157 corresponding to N-substituent having oxygen atom attached and fragment ion formed by the loss of water molecule and hydroxyl group (*m*/*z* 297) are observed only for **8**. Obviously, the fragment ions formed from the *m*/*z* 297 ion (*m*/*z* 187, 199, 240) are also present only in the EI mass spectrum of **8**.

Isomers **10** and **11** were formed by the reaction of pentafluoronitrobenzene with TBD [14]. Their EI mass spectra were also recorded after the introduction through gas chromatograph, since these compounds could not be separated as well. The fragmentation pattern of **10** was exactly the same as those of **7** and **8** and, analogously, the EI induced decomposition of **11** resembled very well those observed for **6** and **9**. Therefore, the discrimination between isomers **10** and **11** can be done in the way analogous to that described above for **8** and **9**; of course the respective *m*/*z* values are shifted by 18 units. Also in this case, the effect of reaction conditions on relative amounts of isomeric products formed can be evaluated by using GC/MS.

4. Conclusions

The EI mass spectra of products of the reaction between fluorobenzenes and bicyclic N-bases were found to be useful for the discrimination between isomers. This can be performed on the ground of the presence/absence of molecular ions as well as by the determination of fragmentation pathways characteristic of a given isomer. This is of importance to establishing how the reaction conditions affect the relative amounts of isomeric products formed. Some of the compounds studied have shown unexpected rearrangements. Rearrangement of two hydrogen atoms for **1** and **2**, very likely proceeding through the ion/neutral complex, leads the protonated lactam; in the case of **1** it is protonated γ-butyric lactam. The fragments C_2H_6N and C_3H_7N, which were eliminated from molecular ion of **3,** contain tertiary nitrogen attached to fluorophenyl ring. Analogous fragmentation pathways were also observed for **4**, although with a lower

yield. Loss of water molecule from molecular ions of **6**, **9** and **11** is an unusual process which, most likely, proceeds according to the "ring-walking" mechanism.

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