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Chemical ionization of amino and hydroxy group containing arylalkyl compounds with ions in a nitromethane plasma

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Dedicated to Professor Jack Beauchamp on the occasion of his 60th birthday and in recognition of his many important contributions to gas-phase ion chemistry.

Abstract

The gas-phase ion/molecule reactions of organic molecules containing several functional groups, including amino, hydroxy and carboxy groups, have been investigated under nitromethane chemical ionization conditions. Three main reaction channels are observed in the ion source: (a) proton transfer, (b) electron transfer and (c) hydride abstraction. The product ion $[M+NO]^+$ is also formed, but in a very low abundance. Initial electrophilic attack of the nitrosonium ion on the aromatic ring is postulated to explain the elimination of HNO from the $[M+NO]^+$ adduct ions, observed for all substrates studied. Elimination of water is a characteristic fragmentation pathway for all substrates possessing a benzylic hydroxy group. Fragment ions resulting from cleavage of the molecular ions of the amines, formed by charge transfer, react with the neutral molecules forming two types of adduct ions: $[M+\text{immonium}]^+$ and $[M+C_7H_7]^+$, which have been characterized through the study of their unimolecular decompositions. The latter provide strong evidence for the existence of two types of structures: a covalent and an ion/molecule complex, that is a non-covalent structure. (Int J Mass Spectrom 222 (2003) 101–116)

Keywords: Chemical ionization; Arylalkylamines; Nitromethane plasma; Covalent and non-covalent ion structures; Adduct ion formation

1. Introduction

The use of the nitrosonium ion, NO^+, as a reagent ion in chemical ionization mass spectrometry was first reported by Hunt and Ryan [1]. In general, the nitrosonium ion reacts with neutral molecules M via three different pathways: charge exchange ($M^{\bullet+}$), hydride abstraction ($[M-H]^+$) or addition ($[M+NO]^+$), depending on the substrate. The substrate molecules which have been studied in chemical ionization mass spectrometry with NO^+ include a variety of compounds [2] namely olefins [3,4], alkenic compounds [5–7], substituted benzenes [8], alcohols, aldehydes, ketones [9], amino acids [10] and dipeptides [11]. Ion cyclotron resonance spectrometry has also been used in the study of the reactions of NO^+ with various organic molecules [12]. With aromatic molecules the main reaction products are $M^{\bullet+}$ or $[M+NO]^+$ depending on the ionization energy of the neutral molecule. For aromatic molecules [8] with ionization energies higher than ~8.7 eV, adduct ions will be favored, while for molecules with lower ionization energies, charge

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exchange processes will dominate. Carboxylic acids and secondary and tertiary alcohols undergo a formal hydroxide ion abstraction, while for the primary alcohols hydride ion abstraction is the dominant process. With the amino acids glycine, alanine, valine and their *N*-methyl derivatives, two products are observed in all cases: the formation of an immonium ion and an $[M-H]^+$ ion. Studies concerning the mechanism and structure of nitrosated benzene using ion cyclotron resonance spectrometry have been published [13], as well as the NO^+ affinities towards several bases [14,15]. Various problems associated with the use of nitric oxide as a reagent gas for the production of the NO^+ ion have been reported, namely the short lifetime of the rhenium filament and the occurrence of secondary oxidation reactions of the substrate. To overcome these problems the use of a mixture of 5%NO/95%H_2, or N_2O [16] as reagent gases has been described. More recently, Vairamani [17] has shown that nitromethane could be used instead of nitric oxide as a source of nitrosonium ions. Under chemical ionization conditions the NO^+ is the base peak in the spectrum, with ions such as *m*/*z* 62, 76, 91 and 123 being also present. He has compared the chemical ionization mass spectra of some alkenes, alkynes and alcohols obtained using nitromethane with those obtained using nitric oxide and concluded that the two spectra are quite similar.

In this work we describe the ion/molecule reactions under nitromethane chemical ionization conditions of amino and hydroxy group containing arylalkyl compounds. It will be shown that besides the formation of $[M + NO]^+$ adduct ions, in which we were primarily interested, other adduct ions such as $[M + \text{immonium}]^+$ and $[M + C_7H_7]^+$ are formed in the nitromethane plasma.

2. Experimental

The compounds were commercially available and most of them were used without further purification, in the form of their corresponding hydrochloride salts. The salts of 3-phenylpropylamine, 4-phenylbutylamine, and 2-phenyl-*N*-methylethylamine were recrystallized from acetone/hexane. Mass spectrometric measurements were performed with use of a Micromass Autospec Q Mass Spectrometer of EBEqQ geometry, equipped with a chemical ionization source. Nitromethane (Aldrich) was introduced into the mass spectrometer through the PFK inlet at a pressure giving a reading of $\sim 7.4 \times 10^{-5}$ Torr and a source temperature of 200 °C. The electron energy was 70 eV and the accelerating voltage 8 kV. Samples were introduced with an unheated direct insertion probe. The nature of the reagent gas ions and the composition of the reaction mixtures were analyzed by means of the chemical ionization mass spectra. The ions of mass-to-charge ratio corresponding to the relevant adducts formed with the compounds, were selected with the magnetic sector and their unimolecular fragmentations were analyzed through scanning of the second electrostatic analyzer of the mass spectrometer (MIKES). The deuteration of the amines was performed by shaking their hydrochloride salts with D_2O at room temperature and drying under N_2, prior to reaction with trimethyl borate.

3. Results and discussion

3.1. Chemical ionization mass spectra

The chemical ionization mass spectrum of nitromethane at a source pressure of $\sim 7.4 \times 10^{-5}$ Torr is shown in Table 1. Although the decrease of ion source pressure has the effect of increasing the relative

Table 1
CI mass spectrum of nitromethane (source pressure $\sim 7.4 \times 10^{-5}$ Torr)

m/*z*	Relative abundance (%)	Proposed composition
15	5	CH_3^+
30	100	NO^+
45	18	$CH_3NO^{\bullet +}$
46	49	NO_2^+
61	7	$CH_3NO_2^{\bullet +}$
62	41	$[CH_3NO_2 + H]^+$
76	71	$[CH_3NO_2 + CH_3]^+$
91	11	$CH_3NO_2NO^+$

abundances of ions *m*/*z* 15 and 61, and decreasing those of the ions *m*/*z* 62 and 91, the nitrosonium ion, NO^+, is always the most abundant, as mentioned in an earlier publication on the use of nitromethane in chemical ionization [17].

The chemical ionization mass spectra of the compounds studied using nitromethane as ionizing reagent (Table 2) show a marked dependence on the functional groups present in the neutral molecules. For compounds with only oxygenated functional groups, the base peak in the mass spectra corresponds to the formation of the molecular ion, $M^{\bullet +}$, through an electron transfer between the neutral molecule and NO^+. This can be explained by the lower ionization energy of the neutral molecule when compared with the effective recombination energy of NO^+ which is estimated [18] to be ∼8.7 eV (IE(NO) = 9.3 eV [19]). Although the ionization energies of the majority of the compounds studied are not known, they are estimated to be lower than 8.7 eV due to the presence of aromatic rings activated with electron-donating substituents, such as the hydroxyl and methoxyl groups. For the amines, the most abundant ion in the mass spectra is, in general, the ion $[M + H]^+$ because the proton affinities of the amines [20] ($\geq$907 kJ mol^{-1}) are considerably higher than the proton affinity of nitromethane [19] (755 kJ mol^{-1}). The exceptions to this general behavior are the following: (a) benzylamine for which the base peak corresponds to the ion $[M-H]^+$ where hydride abstraction from the benzylic position will generate a resonance stabilized cation; (b) hordenine and adrenaline for which the immonium ion $CH_2{=}NR^1R^{2+\bullet}$ (R^1 and R^2 = H and/or CH_3) formed by α-cleavage from the corresponding molecular ions, is the most abundant ion; (c) octopamine with a benzylic hydroxyl group, for which the base peak in the spectrum corresponds to an ion resulting from loss of the radical $^{\bullet}CH_2NH_2$ from the molecular ion by α-cleavage relative to the hydroxyl group (not given in Table 2).

The immonium ion $CH_2{=}NR^1R^{2+\bullet}$ is observed in the mass spectra of all compounds that have a $–CH_2NR^1R^2$ moiety with relative abundances ranging from 1 to 100%. When the amine is primary, the immonium ion has the same mass-to-charge ratio as NO^+ also being present in the spectra. However, using a mass resolution of ∼1300 it has been possible to separate the two ions and to measure their relative abundances (exact mass NO^+ = 29.998; $CH_2{=}NH_2^+$ = 30.034).

The formation of an unexpected adduct ion, $[M + 91]^+$ is observed for all unsubstituted phenylalkylamines (benzylamine, 2-phenylethylamine, 3-phenylpropylamine, 4-phenylbutylamine and 2-phenyl-*N*-methylethylamine). The origin of the ion *m*/*z* 91 could be the ionizing reagent (see Table 1); however, this assumption cannot explain why only the unsubstituted amines, mentioned above, would form the adduct ion. It is well known that the molecular ions of the unsubstituted amines fragment by α-cleavage relative to the aromatic ring generating the benzyl or tropylium ion, $C_7H_7^+$. Because the molecular ions of these amines are formed in the reaction with nitromethane, it is possible that both $CH_3N_2O_3^+$ and $C_7H_7^+$ ions are formed in the ion source. This hypothesis is confirmed by increasing the mass resolution of the mass spectrometer to a value of ∼5000 that allows the separation of the two ions (exact mass $CH_3N_2O_3^+$ = 91.01142; $C_3H_7^+$ = 91.05477). The analysis of the MIKE spectra of both ions confirms the presence of $CH_3N_2O_3^+$ and $C_7H_7^+$ ions in the ion source of the mass spectrometer. This conclusion is based on the observation of the fragmentation 91 → 65 in the MIKE spectra of one of the ions, and by comparison of the spectrum of the other ion with the MIKE spectrum of the $CH_3N_2O_3^+$ ion (Fig. 1) generated in the nitromethane plasma. The structure proposed for this latter ion, based on the fragmentations observed, is shown in Scheme 1.

The formation of an $[M + 91]^+$ ion in the electron ionization mass spectrum of dibenzylsulfoxide has been reported previously [21].

As a general conclusion, the data discussed so far show that, in the presence of nitromethane, the main reactions of the compounds reported in this study, are the following: (a) proton transfer, (b) electron transfer and (c) hydride abstraction. The abundance of the ions $[M + NO]^+$ is, in all cases, very low.

Table 2
Nitromethane chemical ionization mass spectra

		$[M + 91]^+$	$[M + 30]^+$	$[M + 15]^+$	$[M + H]^+$	$M^{\bullet +}$	$[M - H]^+$	$CH_2{=}NR^1R^{2+}$
$C_6H_5CH_2NH_2$	Benzylamine	10	<1	<1	78	91	100	14
$C_6H_5(CH_2)_2NH_2$	2-Phenylethylamine	3	<1	<1	100	1	2	18
$C_6H_5(CH_2)_3NH_2$	3-Phenylpropylamine	4	<1	1	100	24	3	31
$C_6H_5(CH_2)_4NH_2$	4-Phenylbutylamine	3	<1	1	100	22	9	1
$C_6H_5(CH_2)_2NHCH_3$	2-Phenyl-*N*-methylethylamine	1	<1	1	100	1	3	56
$HOC_6H_4(CH_2)_2NH_2$	Tyramine	–	<1	1	100	12	6	61
$HOC_6H_4(CH_2)_2N(CH_3)_2$	Hordenine	–	<1	<1	19	2	2	100
$HOC_6H_4CH(OH)CH_2NH_2$	Octopamine	–	<1	<1	31	9	4	20
$HOC_6H_4CH(OH)CH_2NHCH_3$	Synephrine	–	<1	<1	100	<1	<1	18
$(HO)_2C_6H_3CH(OH)NHCH_3$	Adrenaline	–	<1	2	29	19	6	100
$HOC_6H_5(OCH_3)CH(OH)CH_2OH$	4-Hydroxy-3-methoxy-phenylethylenoglicol	–	<1	<1	15	100	3	–
$HOC_6H_5(OCH_3)CH(OH)COOH$	4-Hydroxy-3-methoxy-mandelic acid	–	<1	<1	13	100	5	–

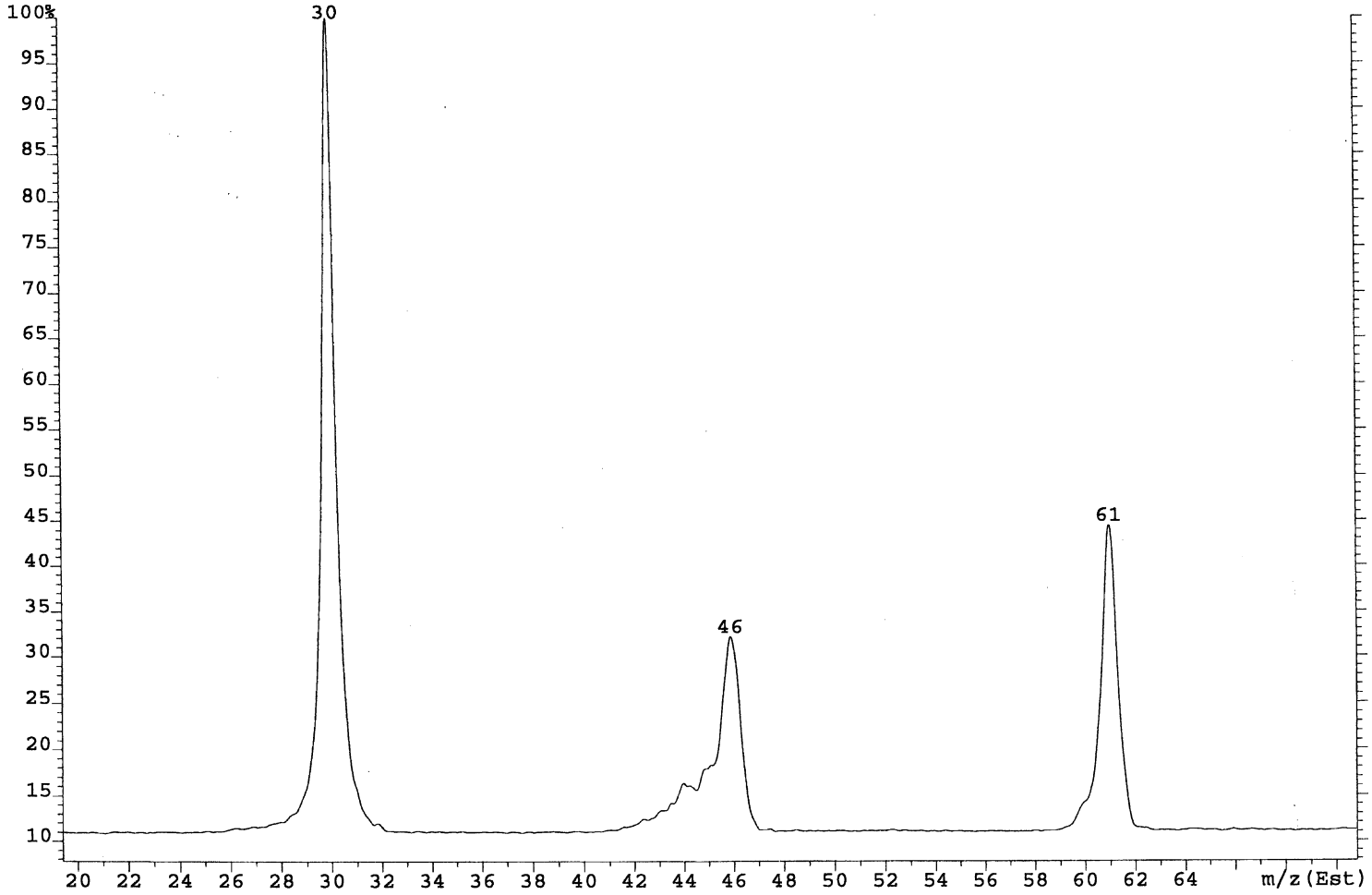
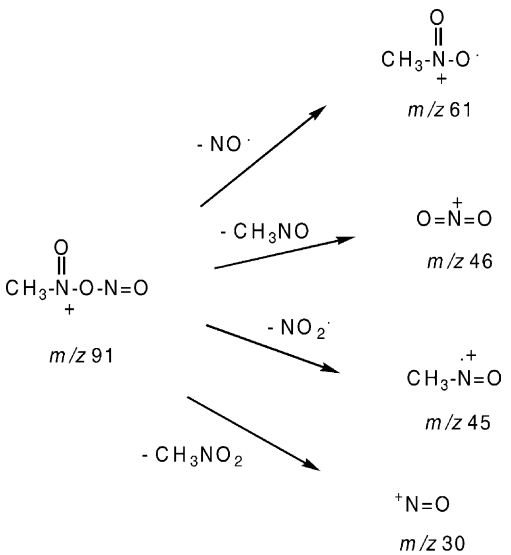


Fig. 1. MIKE spectrum of ion $CH_3N_2O_3$ (m/z 91) of nitromethane.



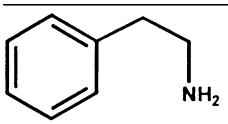
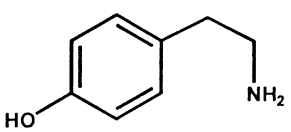
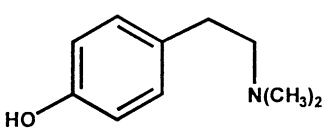
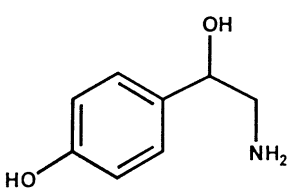
Scheme 1.

3.2. Unimolecular decompositions of ions $M^{\bullet+}$, $[M + 15]^+$, $[M + 30]^+$, $[M + immonium]^+$ and $[M + 91]^+$

3.2.1. $M^{\bullet+}$ ions

The main fragmentation pathways of the metastable radical cations of arylalkylamines generated upon EI, are the following [22]: (a) α-cleavage for the secondary and tertiary amines without any substituents in the aromatic ring, (b) McLafferty type of rearrangement involving the aromatic ring, for the primary amines with substituents in the aromatic ring and (c) formation of ions $CH_3NH_3^+$ and $(CH_3)_2NH_2^+$ for the amines with a benzylic OH through a mechanism which probably involves the formation of an ion/molecule complex as an intermediate. Table 3 presents the MIKE spectra of the molecular ions, formed under CI conditions with nitromethane, of four amines considered to be representatives of all

Table 3
Relative abundance[a] of fragment ions in the MIKE spectra of the molecular ions, $M^{\bullet+}$, produced by electron impact (EI) and chemical ionization with nitromethane

Amine	Fragment ions	EI (%)	CI(CH_3NO_2) (%)
	$[M - NH_3]^{\bullet+}$	–	100
	$[M - {}^{\bullet}CH_2NH_2]^+$	–	9
	$CH_2{=}NH_2^+$	100	12
	$[M - NH_3]^{\bullet+}$	–	12
	$[M - CH_2{=}NH]^{\bullet+}$	100	100
	$[M - H]^+$	12	–
	$[M - CH_3]^+$	–	30
	$[M - CH_2{=}NCH_3]^{\bullet+}$	–	20
	$[M - (CH_3)_2NH]^{\bullet+}$	–	100
	$CH_2{=}N(CH_3)_2^+$	100	98
	$[M - H_2O]^{\bullet+}$	–	100
	$[M - CH_2{=}NH]^{\bullet+}$	–	10
	$[M - {}^{\bullet}CH_2NH_2]^+$	–	26
	$CH_3NH_3^+$	100	14

[a] Calculated as percentage relative to the base peak (100%).

arylalkylamines studied together with the fragment ions observed under EI conditions. The data show that, under CI conditions, α-cleavage with respect to nitrogen is no longer a dominant process of fragmentation (except for the tertiary amine) being completely absent for tyramine. Instead, the molecular ions decompose mainly by rearrangement processes involving the aromatic ring (McLafferty type of rearrangement) or the aliphatic chain (loss of NH_3 or $(CH_3)_2NH$ or H_2O). The loss of ammonia will involve rearrangement of a hydrogen atom from the benzylic carbon atom to the amino group, followed by elimination of the neutral molecule. These observations are consistent with a lower internal energy content of the molecular ions formed in nitromethane CI, as compared to EI.

3.2.2. $[M + CH_3]^+$ adduct ions

Because the methyl cation is also generated in the chemical ionization of nitromethane, the MIKE spectra of the $[M + CH_3]^+$ adduct ions of 2-phenylethylamine, tyramine, hordenine and octopamine were recorded to test the possibility of using nitromethane as a methylating agent. The results (Table 4) are similar those obtained with dimethyl ether, i.e., the preferred site of methylation is always the amino group, with a competition between the aromatic ring becoming evident when the ring is activated by substituents such as the hydroxyl group. Elimination of methanol (17%) from octopamine indicates methylation on the benzylic OH.

3.2.3. $[M + NO]^+$ adduct ions

In studying these adducts ions, the first problem to be addressed, is the formation of $CH_2{=}NH_2^+$ (*m/z* 30) ions with all substrates that possess a primary amino group and the possibility of formation of adduct ions $[M{+}CH_2{=}NH_2]^+$ which would be isobaric to the $[M{+}NO]^+$ ions. The second problem is the low abundance of the $[M + NO]^+$ ions, which has as a consequence that the signal-to-noise ratio of the peaks in some MIKE spectra is too low to provide reproducible data. Table 5 shows the MIKE spectra of the $[M + NO]^+$ adduct ions that could be analyzed taken into consideration the above limitations. Loss of 31 Da could be explained by elimination of HNO or CH_3NH_2 from the precursor ion. However, the $[M + NO]^+$ adduct ion of the deuterated (d_1) 2-phenyl-*N*-methylethylamine decomposes by the exclusive loss of a neutral of 31 Da. This provides evidence for HNO elimination without deuterium scrambling prior to the elimination, and also points at the aromatic ring as the initial site of electrophilic attack by the nitrosonium ion.

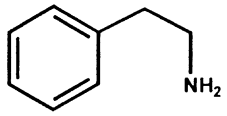
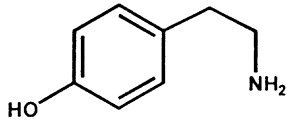
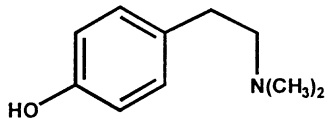
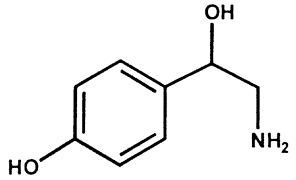
Elimination of water from the $[M + NO]^+$ adduct ions is an important fragmentation pathway for the other four compounds having a benzylic hydroxyl group, generating for all of them the most intense peak with the exception of 4-hydroxy-3-methoxyphenylethyleneglycol. The mechanism proposed is illustrated in Scheme 2 for d_3-synephrine, which eliminates exclusively D_2O without any deuterium scrambling prior to the elimination.

For the two substrates without an amino group, *m/z* 153 is one of the most abundant ions. The precursors of this ion have been established as $[M{+}NO{-}HNO{-}HCHO]^+$ (4-hydroxy-3-methoxy-phenylethyleneglycol) and $[M{+}NO{-}HNO{-}CO_2]^+$ (4-hydroxy-3-methoxy-mandelic acid), on the basis of their B^2/E spectra. D-labeling of the hydroxyl groups of these compounds shows that all the hydroxylic hydrogens are retained in the *m/z* 153 ions, which means that the hydrogen in the HNO loss originates from the benzylic or aromatic ring positions. Although a plausible structure for the *m/z* 153 ions is presented in Scheme 3, in the absence of further D-labeling, no mechanism can be suggested.

3.2.4. $[M +$ immonium ion$]^+$ adduct ions

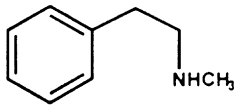
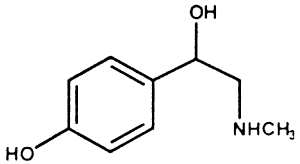
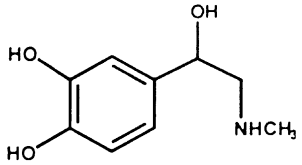
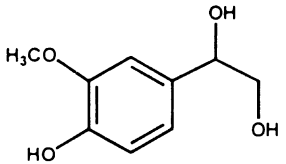
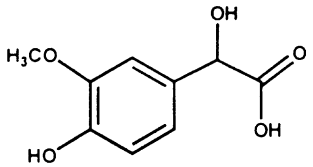
The formation of these adduct ions is confirmed by the following experiment: 2-phenylethylamine was deuterated in the amino group and the MIKE spectra of the ions $[M + 30]^+$ and $[M(d_2) + 32]^+$, where M refers to 2-phenylethylamine, $M(d_2)$ to deuterated 2-phenylethylamine and 32 is the ion $CH_2ND_2^+$, were compared (Fig. 2a and b). The peak at *m/z* 122 in spectrum (a) shifts to *m/z* 125 in spectrum (b), which is consistent with a $CH_2{=}NH$ (or $CH_2{=}ND$) elimination from the $[M +$ immonium$]^+$ adduct ion. The ion *m/z* 120 (spectrum (a)) which is absent in spectrum

Table 4
Relative abundance[a] of the fragment ions in the MIKE spectra of the $[M + CH_3]^+$ adduct ions

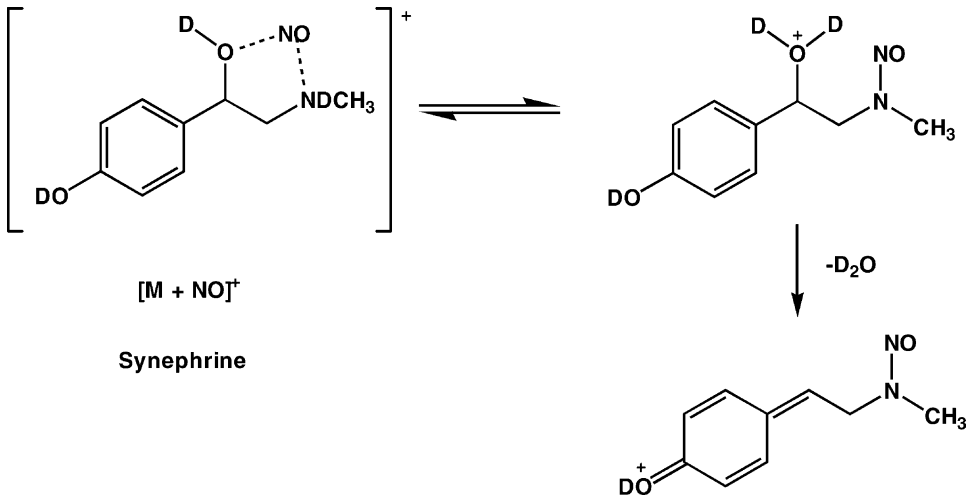
Substrate	Fragment ions				
	$[M + CH_3 - CH_3NH_2]^+$ 100%				
	$[M + CH_3 - CH_3NH_2]^+$ 100%	$[M + CH_3 - NH_3]^+$ 13%	$[M + CH_3 - CH_3^{\bullet}]^{\bullet+}$ 7%		
	$[M + CH_3 - (CH_3)_3N]^+$ 100%	$(CH_3)_3NH^+$ 15%	$[M + CH_3 - (CH_3)_2NH]^+$ 14%	$[M + CH_3 - CH_2{=}NH]^+$ 7%	$(CH_3)_2N{=}CH_2^+$ 3%
	$[M + CH_3 - H_2O]^+$ 100%	$[M + CH_3 - CH_3OH]^+$ 25%	$C_7H_7O^+$ 10%	$C_7H_7O_2^+$ 10%	

[a] Calculated as percentage relative to the base peak (100%).

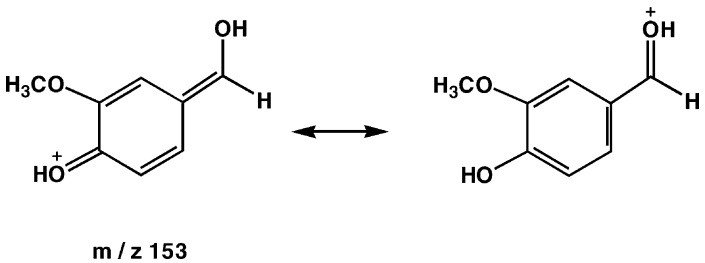
Table 5
Partial MIKE spectra[a] of the $[M + NO]^+$ adduct ions

Substrate	Fragment ions			
	$[M + NO - HNO]^+$ 100%			
	$[M + NO - H_2O]^+$ 100%	$[M + NO - CH_4]^+$ 28%	$[M + NO - HNO]^+$ 16%	
	$[M + NO - H_2O]^+$ 100%	$[M + NO - HNO]^+$ 97%	$[M + NO - 61]^+$ 31%	
	$[M + NO - HNO - HCHO]^+$ 100%	$[M + NO - H_2O]^+$ 51%	$[M + NO - CH_4]^+$ 11%	
	$[M + NO - H_2O]^+$ 100%	$[M + NO - HNO - CO_2]^+$ 93%	$[M + NO - CH_4]^+$ 31%	$[M + NO - 61]^+$ 20%

[a] The abundance of each ion was calculated as a percentage of the base peak (100%).



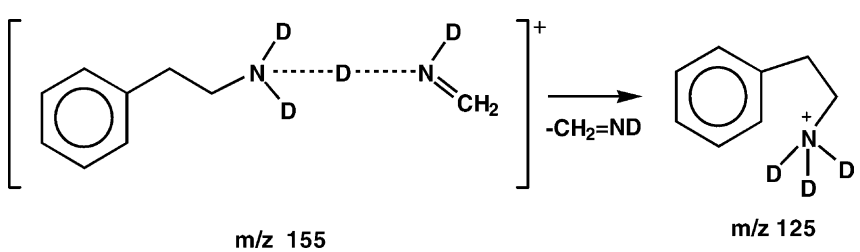
Scheme 2.



Scheme 3.

(b), is explained by HNO loss from the adduct ion $[M + NO]^+$. These observations confirm the assumption made previously that, for primary amines, the $[M + 30]^+$ ions have two different compositions: $[M + CH_2{=}NH_2]^+$ and $[M + NO]^+$.

The behavior and structure of the immonium adduct ions have been discussed previously, for the case of glycine, by O'Hair et al. [23]. They proposed that the observed loss of CH_2=NH from the adduct ion could be explained by assuming a proton bound dimer structure (illustrated in Scheme 4 for 2-(d_2)-phenylethylamine), where after fragmentation the proton stays with the neutral that has a higher proton affinity (in our case PA (CH_2=NH) =



Scheme 4.

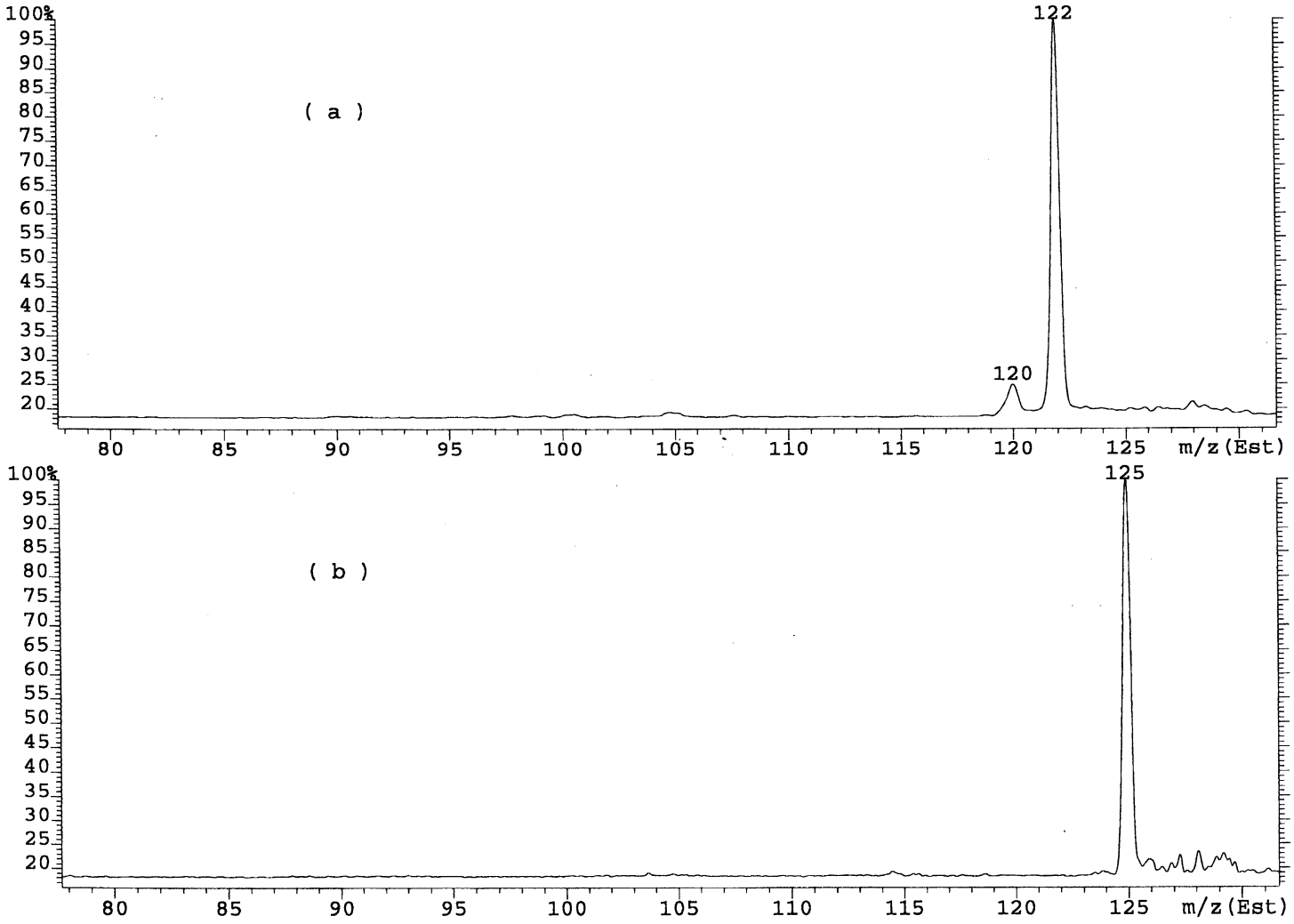
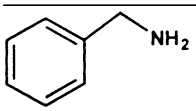
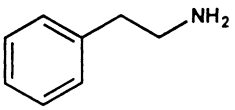
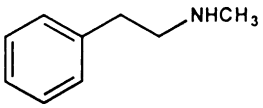
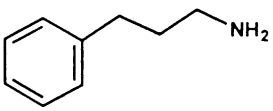
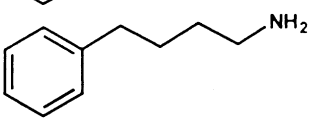


Fig. 2. (a) MIKE spectrum of ion $[M+30]^+$, where M is 2-phenylethylamine (*m/z* 151). (b) MIKE spectrum of ion $[M(d_2)+32]^+$, where M is deuterated 2-phenylethylamine and 32 is ion $CH_2{=}ND_2^+$ (*m/z* 155).

Table 6
Partial MIKE spectra[a] of the $[M + 91]^+$ adduct ions

Amine	Loss (%)					
	NH_3 (or CH_3NH_2)	M	$C_6H_5CH_3$	C_6H_6	C_2H_4	C_3H_6
	100	17	6			
 [b]	100	7	2			
	100	7	12			
	100[c]	41	13[d]	6	6	
 [e]	92[f]	42	11[g]			6

[a] The abundance of each ion was calculated as a percentage of the base peak (100%).
[b] The MIKE spectrum contains also a peak at *m/z* 105 (2%) corresponding to loss of benzylamine.
[c] These ions decompose further by loss of C_2H_4 to give *m/z* 181 (35%) and C_6H_6 to give *m/z* 131 (10%).
[d] These ions decompose further by loss of NH_3 to give *m/z* 117 (4%) and CH_2=NH to give *m/z* 105 (2%).
[e] The MIKE spectrum contains also a peak at *m/z* 108 (18%) due to protonated benzylamine (see further text).
[f] These ions decompose further by loss of C_3H_6 to give *m/z* 181 (100%) and C_6H_6 to give *m/z* 145 (9%).
[g] These ions decompose further by loss of NH_3 to give *m/z* 131 (6%).

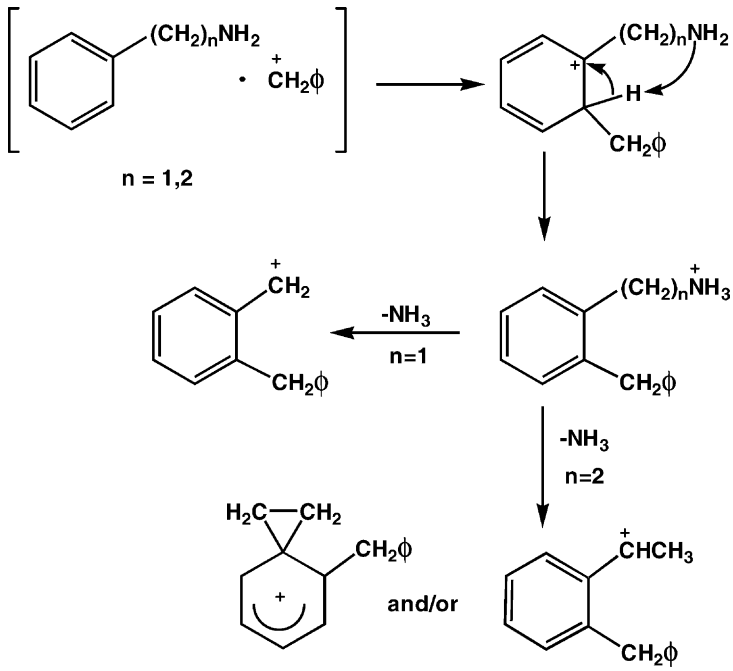
204.1 kcal mol^{-1} [24] and PA (2-phenylethylamine) = 221.3 kcal mol^{-1} [20]). Besides the $[M+CH_2=NH_2]^+$ adduct ions, the decomposition routes of the following adduct ions have also been investigated: $[M + CH_2=N(CH_3)_2]^+$ (hordenine) and $[M + CH_2=NHCH_3]^+$ (synephrine and adrenaline). The $[M + 44]^+$ adduct ions eliminate $CH_2=NCH_3$ through a mechanism analogous to that outlined in Scheme 4. Water loss, observed for adrenaline, is best rationalized by assuming the formation of a covalent bond between the methylenic carbon atom of the ion and, for example, the nitrogen atom of the molecule, followed by proton transfer to the benzylic hydroxy group and elimination of water. $CH_2=N(CH_3)_2^+$ is the only ion observed in the MIKE spectrum of the $[M + 58]^+$ adduct probably because the collision complex formed between the ion and the neutral molecule is so loosely bound, due to the presence of the methyl groups, that it separates apart before any reaction takes place.

3.2.5. $[M+C_7H_7]^+$ ions

There are three fragmentation pathways common to all $[M + 91]^+$ adduct ions: (a) loss of ammonia (or methylamine in the case of 2-phenyl-*N*-methylethylamine), (b) loss of the neutral molecule M and (c) loss of toluene (Table 6). These reaction channels will be discussed below successively.

The elimination of ammonia or methylamine points at an initial attack of the benzyl cation[2] on the aromatic ring of the amine, which in the schemes below has been assumed to be an *ortho*-position to form

[2] In ion/molecule reactions with amines the benzyl cation has been shown to be reactive, whereas the tropylium ion not [25].



Scheme 5.

a covalently C–C bonded ion. In an intramolecular acid–base reaction the amino group can then abstract the proton from the *ortho*-position, followed by loss of ammonia as shown in Scheme 5 for benzylamine and 2-phenylethylamine. The former would lead to the formation of an *ortho*-benzyl substituted benzyl cation, the latter to the formation of either a benzyl substituted phenonium ion via anchimeric assistance in the ammonia loss or an *ortho*-benzyl substituted 1-phenylethyl cation by a 1,2 H-shift during the expulsion of ammonia.

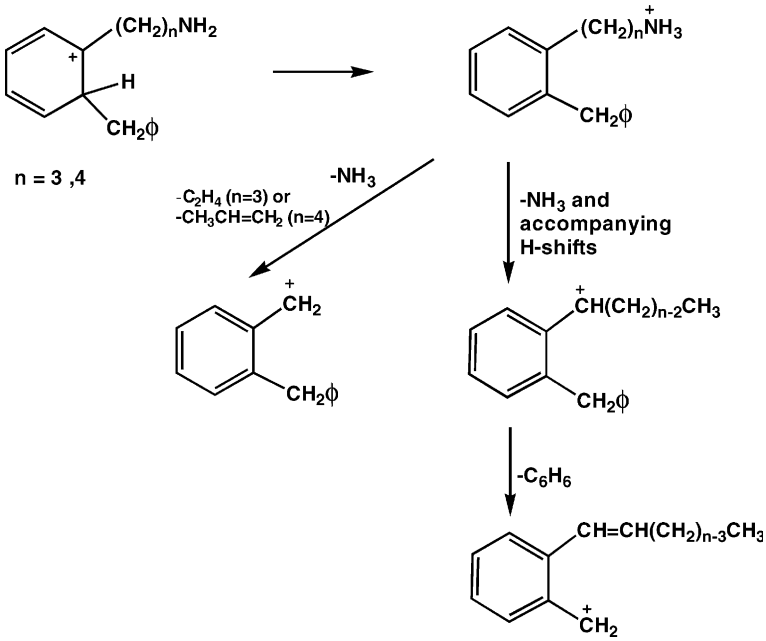
A similar intramolecular acid–base reaction, following the initial benzyl cation attack on an *ortho*-position of 3-phenylpropylamine and 4-phenylbutylamine, can occur prior to the ammonia loss. This loss can be followed by the elimination of ethene for 3-phenylpropylamine and propene for 4-phenylbutylamine, both in competition with expulsion of benzene, as mechanistically visualized in Scheme 6.

The $[M + 91]^+$ adduct ion of 3-phenylpropylamine also appears to eliminate directly benzene. This competition with the ammonia loss is most probably due to the length of the alkyl chain, which entropically disfavors the intramolecular *ortho*-proton abstraction by the amino group. This enables the entropically more favored intramolecular *ortho*-proton abstraction by the less basic phenyl group to compete, eventually leading to the expulsion of benzene as visualized in Scheme 7.

The resulting *ortho*-substituted benzyl cations may well form eventually a bond with the nitrogen atom by a nucleophilic attack of the amino group, thus leading to a fused bicyclic ion.

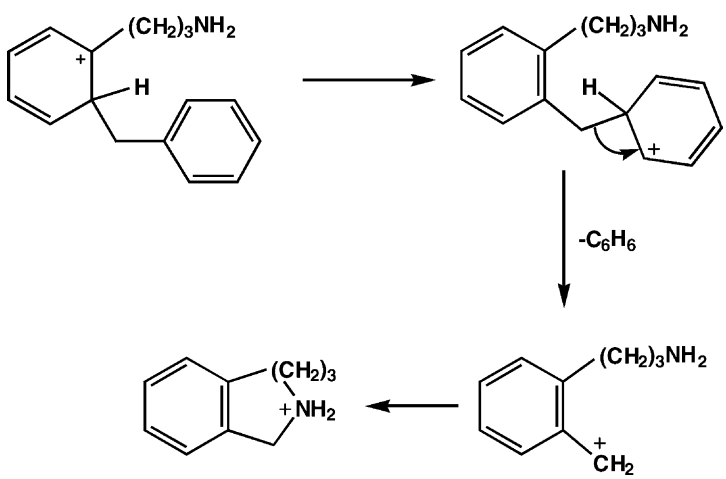
Very interesting is the observation that the $[M + 91]^+$ adduct ions of 3-phenylpropylamine and 4-phenylbutylamine also eliminate ethene and propene, respectively, to give the ions $[M + 91 - C_2H_4]^+$ and $[M + 91 - C_3H_6]^+$ (Table 6). The most plausible explanation for these eliminations is that the benzyl cation initially not only attacks the aromatic ring as discussed above, but also the amino group of the amines to form a covalently C–N bonded ion as shown for 3-phenylpropylamine in Scheme 8.

A subsequent heterolytic cleavage of the original C–N bond of the amine can then lead to a complex

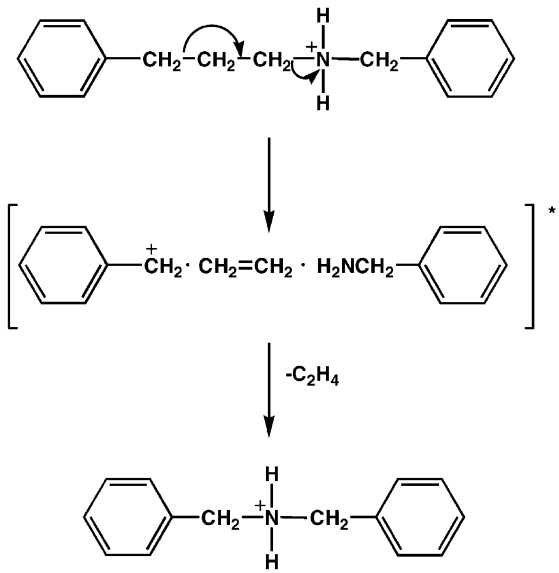


Scheme 6.

consisting of a benzyl cation, ethene (or propene in the case of 4-phenylbutylamine) and benzylamine, which eventually eliminates ethene (or propene for 4-phenylbutylamine) and collapses to nitrogen protonated dibenzylamine (Scheme 8). Support for the proposed mechanism in Scheme 8 is provided by the presence of a relatively intense peak at *m*/*z* 108, corresponding to protonated benzylamine, in the MIKE spectrum of the $[M + 91]^+$ adduct ion of 4-phenylbutylamine. In contrast with the mechanism proposed in Scheme 8 for 3-phenylpropylamine, where the covalently C–N bonded ion can break up smoothly and rapidly without hydrogen rearrangements into a complex consisting of a benzyl cation,



Scheme 7.

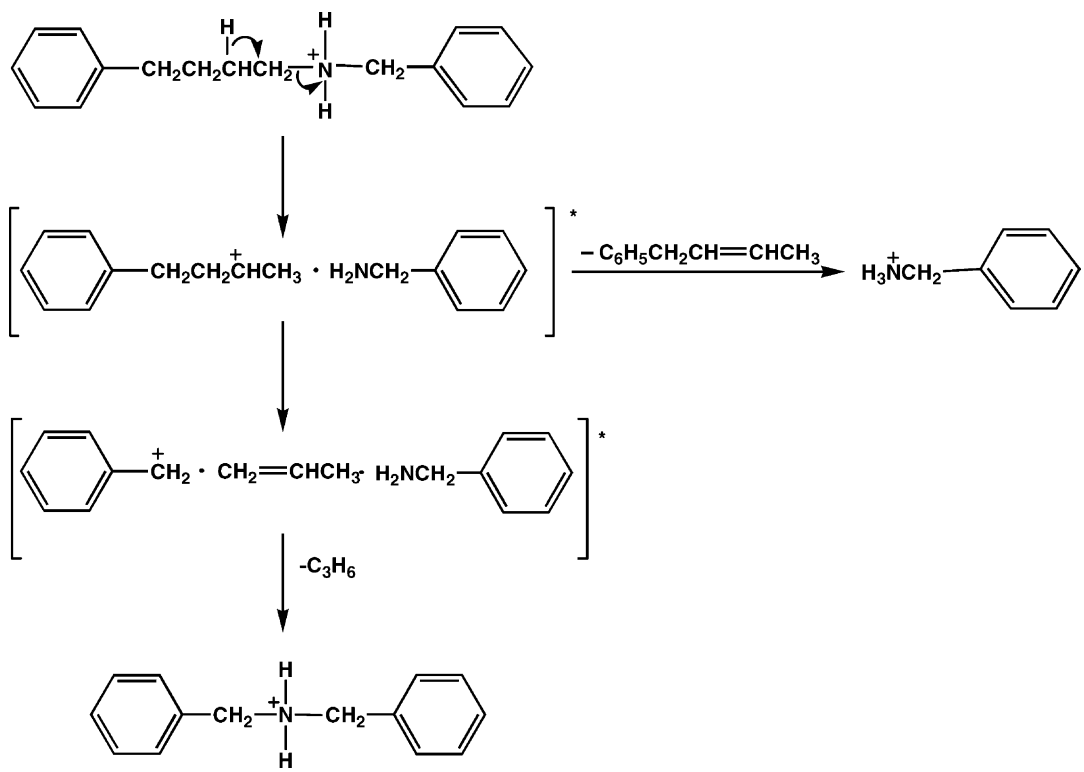


Scheme 8.

ethene and benzylamine, the corresponding ion from 4-phenylbutylamine might well break up first in a 4-phenyl-2-butyl cation and benzylamine prior to formation of a complex consisting of the benzyl cation, propene and benzylamine as pictured in Scheme 9.

The 4-phenyl-2-butyl cation can then transfer a proton to yield protonated benzylamine (see Scheme 9).

The loss of the neutral molecule M to give the $C_7H_7^+$ ions is expected to be mostly due to dissociation of the $[M+91]^+$ adduct ions back into the initial reactants. These $[M+91]^+$ adduct ions may have either the initially formed covalently bonded and unrearranged ion structure or a non-covalently bonded ion structure between M and $C_7H_7^+$ (in the latter case part of the $C_7H_7^+$ ions may have the tropylium structure known to be non-reactive [25]). However, it cannot be excluded that some of the $C_7H_7^+$ ions are generated from the protonated dibenzylamine ions, generated by fragmentation from the covalently



Scheme 9.

bonded $[M + 91]^+$ adduct ions, discussed above and presented in Schemes 8 and 9. This may also be true for benzylamine where electrophilic attack of the benzyl cation upon the nitrogen atom may lead directly to the formation of protonated dibenzylamine as a structure for the corresponding $[M + 91]^+$ adduct ion.

The loss of toluene from all $[M + 91]^+$ adduct ions most probably occurs via hydride abstraction from the benzylic carbon atom by the $C_7H_7^+$ ion in a non-covalently bonded ion structure of $[M + 91]^+$. The $[M + 91 - \text{toluene}]^+$ ions from 3-phenylpropylamine and 4-phenylbutylamine decompose further by loss of ammonia to give the ions $[M + 91 - \text{toluene} - \text{ammonia}]^+$.

4. Conclusions

Three main reaction channels are observed in the gas-phase ion/molecule reactions of organic molecules containing several functional groups, including amino, hydroxy and carboxy groups, under nitromethane chemical ionization conditions: (a) proton transfer, (b) electron transfer and (c) hydride abstraction. Also $[M + NO]^+$ is formed as product ion, albeit in a very low abundance. Fragment ions resulting from cleavage of the molecular ions of the amines, formed by charge transfer, react with the neutral molecules yielding two types of adduct ions: $[M + \text{immonium}]^+$ and $[M + C_7H_7]^+$.

For these latter adduct ions covalent and non-covalent ion structures seem to co-exist, as suggested by their unimolecular dissociations. All the $[M + NO]^+$ adduct ions eliminate HNO, which is explained by an initial electrophilic attack of the nitrosonium ion upon the aromatic ring, as shown by deuteration of 2-phenyl-*N*-methylethylamine. Elimination of water occurs, when a benzylic hydroxy group is present.

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