# **Ammonium Adduct Ion in Ammonia Chemical Ionization Mass Spectrometry**

2-Mechanism of Elimination of Neutrals from the Ammonium Adduct Ion

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The mechanism of elimination of ROH (R = H or CH<sub>3</sub>) from the ammonium adduct ion,  $[M+NH_4]^+$ , of 1-adamantanol and its methyl ether is examined by using linked-scan metastable ion spectra and by measuring the dependence of the peak intensity ratio  $[M+NH_4]^+/[M+NH_4-ROH]^+$  on ammonia pressure. For 1-adamantanol both  $S_N$ i and  $S_N$ 1 reactions are suggested in metastable ion decomposition, while only the  $S_N$ 1 mechanism is operative in the ion source. For 1-adamantanol methyl ether the  $S_N$ 1 reaction predominates both in metastable ion decomposition and in the ion source reaction.

### INTRODUCTION

The ammonium adduct ion,  $[M+NH_4]^+$ , is often observed in ammonia-mediated chemical ionization mass spectra of oxygen-containing compounds such as alcohols, ethers, aldehydes, ketones and esters. The formation of the adduct ion is favoured when the proton affinity of the substrate molecule is close to that of ammonia.<sup>1</sup> When the molecule has a monovalent functional group such as the hydroxyl or alkoxyl group, the elimination of these functional groups as  $H_2O$  or ROH sometimes takes place from the adduct ion to afford  $[M+NH_4-ROH]^+$  peaks (R=H or alkyl). The feature of this fragmentation is that the resulting fragment ion retains, at least formally, the initially added ammonium ion moiety.

From the mechanistic point of view, several pathways are possible for this fragmentation reaction<sup>2.3</sup> (see Scheme 1). One is the unimolecular decomposition of the adduct ion through intramolecular attack of ammonia to form the  $[M+NH_4-ROH]^+$  ion (S<sub>N</sub>i-like mechanism). On the other hand, there are two



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mechanistic alternatives that involve nucleophilic attack of one extra ammonia molecule, i.e. attack of ammonia occurs *after* the decomposition of the adduct ion to a carbocation intermediate ( $S_N$ 1-like mechanism), or attack of ammonia and elimination of a neutral (and elimination of initially added ammonia) takes place *simultaneously* ( $S_N$ 2-like mechanism).

In recent years there has been a considerable controversy on these  $S_Ni-S_N1-S_N2$  mechanistic possibilities for this fragmentation reaction.<sup>4-7</sup> The latest report<sup>8</sup> has emphasized the general applicability of the  $S_N2$  reaction. The fragmentation mechanism, however, seems to depend on the structure of the substrate molecule and also on the experimental conditions. We now wish to present an unequivocal result for the mechanism of this fragmentation in one particular type of compound.

## EXPERIMENTAL

Normal and linked-scan mass spectra were measured on a Hitachi M-80A mass spectrometer on-line to an M-003 data system under the following conditions: accelerating voltage, 3 kV; electron energy, 100 eV; emission current,  $100 \mu \text{A}$ ; source temperature,. 120 °C. Collisional activation in the 1st field-free region was performed by using He as the collision gas, leading to a reduction of main beam intensity of 30%.

Pressure dependence of the peak intensity ratio was measured by a Shimadzu LKB 9000A mass spectrometer/GCMS-PAC-90 computer system. The source pressure was checked with an MKS Baratron manometer Type 221A. The spectra were recorded at a source temperature of 250 °C and an accelerating voltage of 3.5 kV. The total emission current was  $120 \ \mu\text{A}$  and the electron energy 150 eV.

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Liquid samples were introduced through a heated inlet system at 150 °C, while solid samples were introduced directly from a solid insertion probe. Ammonia reagent gas (99.99% purity) was obtained from Takachiho Trading Co., Ltd.

The sample of 1-adamantanol (1) was purchased from Tokyo Kasei Kogyo Co., Ltd, Japan. The alcohol was methylated with methyl iodide and sodium hydride in tetrahydrofuran under the usual conditions to afford 1-adamantanol methyl ether (2).

### **RESULTS AND DISCUSSION**

The compounds selected for the present study are 1-adamantanol (1) and its methyl ether (2). The well-known bridgehead nature of these 1-substituted adamantane derivatives clearly excludes the back-side nucleophilic attack in substitution reactions, and this precludes the  $S_N 2$  mechanism for the fragmentation.



For both compounds 1 and 2, the  $[M+NH_4-ROH]^+$  peak (R = H and CH<sub>3</sub>, respectively) appears as the base peak in the normal ammonia chemical ionization mass spectra (Fig. 1). In order to distinguish between the S<sub>N</sub>i and S<sub>N</sub>1 mechanisms, it is necessary to examine whether or not an extra ammonia molecule is required for the formation of the  $[M+NH_4-ROH]^+$  ion. The linked-scan spectrum of metastable ions at constant magnetic (B) and electric (E) field ratio (B/E) is certainly promising for this purpose.



Figure 1. Ammonia chemical ionization mass spectra of 1-adamantanol (1) and 1-adamantanol methyl ether (2).

468 ORGANIC MASS SPECTROMETRY, VOL. 20, NO. 7, 1985

Table 1. Linked-scan spectra of  $[M+NH_4]^+$  ions from compounds 1 (m/z 170) and 2 (m/z 184)<sup>a</sup>

Compound	Neutrals lost	m/z	B/E const. linked-scan (%)	CAD–B/E const. linked-scan (%)
1	NH <sub>3</sub>	153	10	7
	H₂Ō	152	50	28
	$(NH_3 + H_2O)$	135	40	65
2	NH3	167	60	35
	CH <sub>3</sub> OH	152	2	2
	(NH <sub>3</sub> +ČH <sub>3</sub> OH)	135	38	63
<sup>a</sup> The peak	heights are norm	alized to	100% of tota	al ion current.

When the  $[M+NH_4]^+$  ion  $(m/z \ 170)$  of compound 1 was selected as a precursor ion, a very strong  $[M+NH_4-H_2O]^+$  peak appeared at  $m/z \ 152$  in the B/Econstant linked-scan spectrum (Table 1). The result clearly shows that the  $[M+NH_4-H_2O]^+$  ion is formed, though not exclusively, by the unimolecular decomposition of the  $[M+NH_4]^+$  ion, and that no other extra ammonia molecule is necessary for this fragmentation to occur. Therefore, the  $S_N$  i mechanism is suggested for compound 1 at least for the metastable ion decomposition.

A contrasting result was obtained from the linkedscan spectrum of compound **2**. In this case, the intensity of m/z 152, which corresponds to  $[M+NH_4-CH_3OH]^+$ , was very low and almost negligible. The situation did not change very much when the monitored  $[M+NH_4]^+$  ion was collisionally activated with helium, and the peak intensity of m/z 152 was again very low (see Table 1). These results show that the m/z 152 of compound **2** was not formed unimolecularly from the  $[M+NH_4]^+$  precursor.

As mentioned above, however, the m/z 152 ion is evidently formed in the ion source, because a strong peak is observed at m/z 152 in the normal spectrum of **2** (Fig. 1). A plausible explanation for the genesis of this ion is a nucleophilic capture of a bare carbocation of m/z 135 (adamantyl cation or its equivalent) by an ammonia molecule. The process should be termed  $S_N 1$ above. Actually, the linked-scan spectrum indicated that the  $[M+NH_4]^+$  ion from **2** decomposed effectively to afford the m/z 135 ion (see Table 1).

The search for precursor ions by the  $B^2/E$  constant linked-scan spectrum led to a consistent result. When the  $[M+NH_4-H_2O]^+$  ion at m/z 152 from 1 was selected, a sole precursor ion at m/z 170,  $[M+NH_4]^+$ , was revealed by the spectrum. On the other hand, in the case of 2, the intensity of the  $[M+NH_4]^+$  ion at m/z 184 as a precursor was very low, which suggested that the m/z 152 ion was not formed directly from the  $[M+NH_4]^+$  ion.

Keough and DeStefano have pointed out the pressure dependence of the peak intensity ratio  $[M+NH_4]^+/[M+NH_4-ROH]^+$  in the ordinary spectrum as a good indication of the mechanism in the ion source.<sup>4</sup> They suggested that the ratio should remain constant for the S<sub>N</sub>1-like mechanism as ammonia pressure increased. As was shown in Fig. 2, this can be substantiated for compound **2**.

These authors have also demonstrated<sup>4</sup> that the peak intensity ratio for benzyl alcohol increased as the



**Figure 2.** Variation of the relative intensity ratio  $l([M+NH_4]^+)/l([M+NH_4-ROH]^+)$  from 1-adamantanol methyl ether (2) and benzyl alcohol as a function of ammonia pressure.

ammonia pressure increased, and suggested the S<sub>N</sub>i reaction for this compound. We confirmed the reported pressure dependence, at least in the lowpressure region (see Fig. 2), and revealed further the  $S_N$  i character of the fragmentation by using the B/Econstant linked-scan spectrum. Thus, the ion at m/z 126,  $[M+NH_4]^+$ , from benzyl alcohol afforded a strong peak at m/z 108,  $[M+NH_4-H_2O]^+$ , in the linked-scan metastable ion spectrum. On the contrary, the similar measurement for the ion at m/z 140, [M+  $NH_4$ ]<sup>+</sup>, from benzyl methyl ether exhibited a strong peak at m/z 91 (benzyl cation) but did not show any peak at m/z 108,  $[M+NH_4-CH_3OH]^+$ , in the metastable ion spectrum, despite the fact that the m/z 108 peak appeared in moderate intensity in the normal spectrum. The result again suggests the alteration of the mechanism from  $S_N i$  to  $S_N 1$  as the substrate changes from the alcohol to its methyl ether. The situation appears to be parallel to the case of adamantanol (1) and its methyl ether (2).

It should be pointed out that even in the case of compound 1, the  $S_N$  i mechanism is not the only one available for  $[M+NH_4-H_2O]^+$  ion formation. In the B/E constant linked-scan spectrum of 1, the m/z 135 peak corresponding to the adamantyl cation or its equivalent is very strong, and there must be a very good chance for this ion to be captured by an extra ammonia molecule in the ion source ( $S_N$ 1 process). This possibility is even enhanced when the  $[M+NH_4]^+$ precursor ion is collisionally activated. The energized  $[M+NH_4]^+$  ion predominantly affords the m/z 135 ion rather than the  $[M+NH_4-H_2O]^+$  ion. Since the internal energy of decomposing precursor ions for the ion source reaction is usually higher than that for metastable ion decomposition, the above result suggests that a large proportion of this fragmentation of 1 in the ion source proceeds through the S<sub>N</sub>1 mechanism.

The present experimental evidence shows that the mechanism of the fragmentation of the ammonium adduct is susceptible to the structure of the substrate, especially to the nature of the leaving neutrals, as well as the internal energy of the decomposing ion. It also reflects a very delicate balance between bond cleavage and bond formation in the transition state of the fragmentation.

During the fragmentation of the ammonium adduct ion, the C-O and N-H bonds must both be weakened, while the O—H bond is strengthened as the reaction proceeds (see structure below). It is generally accepted that the hydroxyl group (R = H) is eliminated more easily than the alkoxyl group (R =alkyl) in chemical ionization mass spectrometry.<sup>3,9</sup> If R = H, therefore, one can assume that the C—O bond will be cleaved to a considerable extent at the earlier

stage of the reaction, and a positive charge may well be developed at the central carbon atom. At this stage, the initially added ammonium ion moiety is not very far from the central carbon atom and can coordinate this carbon atom intramolecularly, which finally gives rise to the  $[M+NH_4-H_2O]^+$  ion.

On the other hand, if  $R = CH_3$ , the C—O bond cleavage is expected to take place much more slowly. Consequently, before the positive charge at the central carbon atom becomes large enough to be coordinated by any nucleophiles, the leaving ammonia molecule will have receded further and will not be able to attack the carbon atom. The resultant bare carbocation must then be captured and stabilzed by another ammonia molecule in the ion source.

As is evident from the above argument, the  $S_Ni$  reaction involves a new bond formation between the central carbon and the ammonia nitrogen atoms in the transition state when compared with the  $S_N1$  reaction, and accordingly, the reaction critical energy will be lower and the frequency factor will also be lower than those for the  $S_N1$  reaction. Both mechanisms compete effectively in the metastable ion decomposition of 1, but the more energized precursor ions in collisionally activated dissociation (CAD) and the ion source reactions will prefer the kinetically favourable  $S_N1$  reaction as is usually expected from the above reaction characteristics.

Finally, the structure of the product ion  $([M+NH_4 ROH^{+}$  at m/z 152 from both 1 and 2 in this fragmentation reaction was confirmed as the protonated 1adamantylamine (mol. wt 151) by comparing the CAD spectra of the respective species. Thus, the ions at m/z 152 from either 1, 2 or 1-adamantylamine all exhibited weak but significant peaks at m/z 93 and 79 together with the base peak at m/z 135 in the CAD spectra. The whole spectral pattern including other minor peaks at m/z 94, 92, 91, 78, 77, 67 and 65 was essentially the same for all three spectra. It should be noted, however, that a minor change in the CAD spectra was observed when the ion source pressure was low; a peak at m/z 95 was slightly enhanced for 1, while a peak at m/z 94 became abundant for 1-adamantylamine. These phenomena may be associated with the intervention of the electron impact mode of fragmentation under these low-pressure conditions.

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