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Evidence of charge-remote fragmentation in protonated [60]fulleropyrrolidine multi-adducts☆

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ABSTRACT

[60]fulleropyrrolidine derivatives (Prato adducts of C_{60}) with up to three ligands were protonated by electrospray ionization (ESI) and the collision-induced dissociation (CID) behaviour of these ions was studied with a quadrupole ion trap mass spectrometer. The systems under investigation showed distinctly different fragmentation behaviour for the neutral and the protonated ligands regarding both extent of fragmentation and pattern. This provided a means to distinguish reactions at the site of the charge from those occurring remote from it. In fact, evidence of charge-remote fragmentation (CRF) was obtained, with the neutral, charge-remote ligands showing efficient fragmentation and the protonated ligand largely resisting decomposition.

1. Introduction

The term "charge-remote fragmentation" (CRF) refers to gas-phase dissociations of ions, which are characterized by the spatial separation of the location of the charge and the place where the actual fragmentation reaction occurs. The charge is thus located on a particular site of the ion, often firmly fixed with little or no mobility, while the fragmentation occurs on a different site of the ion. The fragmentation as such is therefore not induced by the charge and could in principle also occur in an energised neutral molecule resembling the fragmenting moiety of the ion. Historically, CRF was discovered employing the then newly developed soft ionization method FAB (fast atom bombardment) in conjunction with high-energy collision-induced dissociations (CID). Over the last three decades, CRF has continued to be of importance to gas-phase ion chemistry, occurring with numerous different molecular systems, [1,2] enhancing insight into the mechanisms of CRF [1,2] and extending applicability from the initially used sector field instrumentation to modern mass spectrometry. [3–9] Recent selected examples include the use of matrix-assisted laser desorption/ionization (MALDI) in conjunction with post-source decay (PSD) and/or high energy CID, [3–6] as well as the ion formation by electrospray ionization (ESI) employing derivatisation and low energy CID [7,8] and also the use of electron capture (ECD) and electron-transfer dissociations (ETD). [9]

The present study reveals that multi-ligated fullerenes can undergo CRF in that one ligand may carry the charge (proton) while a neutral ligand may decompose. This kind of CRF has been proposed in an earlier investigation covering the CID behaviour of protonated fulleropyrrolidine derivatives, commonly known as "Prato adducts". However, since the charge-carrying ligand showed exactly the same fragmentation pattern as the neutral, proof of the assumed CRF mechanism could not be provided [10]. These fullerene derivatives can be prepared by straightforward synthetic approaches [11,12] and have found a wide range of applications in different technological fields, such as materials science and medicinal chemistry. [13–15] Earlier mass spectrometry-based studies have concentrated on the characterization of the retro-cycloaddition reaction evaluating the conditions leading to the complete loss of the ligand. [16–19] In an earlier MALDI investigation, we showed that the released ylide ligand can efficiently re-attach to an intact adduct [20], thereby potentially falsifying efforts aimed at the elucidation of the true amount of ligand attainment in the starting material [21]. Following this earlier investigation, we studied several other fulleropyrrolidines and with the Prato adduct discussed in this note we discovered a system in

☆ Dedicated to the memory of the great mass spectrometrist, Prof. Nico M.M. Nibbering.

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which neutral and charged ligands decompose differently, allowing us to make a clear decision upon the occurrence of CRF.

2. Experimental section

2.1. Materials and reagents

The fulleropyrrolidine adducts were prepared as described previously [20]. Unreacted C_{60} was removed from the raw product which was then used without further purification, as the multiligated adducts were the target of this study. A stock solution of the raw product in toluene (1 g/L) was prepared and further diluted with dichloromethane and methanol in a 1:1 ratio resulting in a solution with a monoadduct concentration of roughly 5×10^{-5} mol/L. To every 1 mL of solution, 10 μL of concentrated acetic acid was added in order to promote protonation.

2.2. Mass spectrometry

The sample solutions were infused *via* a syringe pump (Cole Parmer, Illinois) through a pneumatically assisted nebuliser (N_2) into the ESI-source chamber. MS^n experiments were carried out with an ESI- quadrupole ion trap instrument (esquire6000, Bruker). The instrument has been frequently employed in our research into new synthetic carbon allotropes with the most recent studies covering multiply charged fluorofullerene anions [22] and dimerization of fullerene/crown ether-conjugates in ESI [23,24]. The instrumental settings were as follows: sample flow rate 4.0 μL/min, nebuliser nitrogen pressure 689 hPa, capillary entrance voltage −4000 kV, spray shield voltage −3500 kV, nitrogen dry gas temperature 573 K, dry gas flow rate 5.0 L/min, the helium buffer/collision gas pressure was set to 4.0×10^{-6} hPa (the actual pressure in the analyser is approximately 100 times higher [25]). Generally, the ion transfer settings vary due to spectra tuning.

3. Results and discussion

The present study was inspired by an investigation by Ramos et al. [10] into the ESI–MS/MS behaviour of different fullerene derivatives including fulleropyrrolidine **1** shown in Fig. 1. CID of the protonated mono- and bis-adduct of compound **1** showed basically the same fragmentation behaviour. Protonation in both adducts takes place at the nitrogen atom of the pyrrolidine ring. The protonated mono-adduct showed two fragment ions: $C_{60}H^+$ and the loss of 43 Da. Accurate mass measurements established that the loss of 43 Da corresponds to C_2H_5N, for which $CH_2=N-CH_3$ was assumed as a reasonable structure [10]. The bis-adduct showed also two fragment ions: the loss of one intact ligand and the loss of $CH_2=N-CH_3$. The bis-adduct thus showed the same fragmentation pattern, however, dissociated to a much higher extent than the mono-adduct. The authors attributed this behaviour to an assumed CRF of the bis-adduct involving dissociation of the neutral ligand rather than the protonated as in the mono-adduct. The dissociations of the mono-adduct would be less efficient as they involved the protonated ligand. Unfortunately, no further evidence was provided to support this hypothesis. To illustrate the scenario we employ compound **2** (Fig. 1) as a substitute of compound **1**. Fig. 2 displays the (+)-ESI MS of compound **2** featuring signals for the protonated mono-, bis- and tris-adduct, together with the corresponding CID mass spectra. For the complete dissociation of the protonated mono-adduct, the excitation amplitude had to be adjusted to approximately twice the value needed for the complete dissociation of the bis- and tris-adduct. Moreover, the product ion abundances were orders of magnitude lower for the mono-adduct and in fact remained at noise level (Fig. 1b). This is attributed to the loss of either the charge itself (H^+) or a protonated fragment, which is too small to be detected by our instrument. Thus, the intensity of the precursor ion decreases despite the lack of observable product ions. This is referred to in the following as an "inefficient" dissociation. Similar to the fragmentation reported for compound 1, CID of compound 2 also shows the loss of the intact ligand, resulting in $C_{60}H^+$ (m/z 721). The neutral loss of $CH_2=N-CH_3$ (43 Da) yields the second product ion at m/z 825. Another minor signal appeared at m/z 776. Similarly, the bis- and tris-adducts showed losses of ligand and $CH_2=N-CH_3$ units, although the fragment ions are observed in much higher intensity (Figure 1c, d). This is attributed to the facile dissociation of the second and third ligand, which do not carry the charge. The CID mass spectrum of the tris-adduct provides another hint for the occurrence of CRF (Figure 1d), due to the fact that losses from two ligands are observed. In addition to the product ions at m/z 1015 and m/z 1119, which correspond to the loss of one ligand and one $CH_2=N-CH_3$ molecule, respectively, two other fragment ions are observed. The product ion at m/z 972 results from the combined loss of one ligand and one $CH_2=N-CH_3$ molecule, while the ion at m/z 1076 stems from the loss of two $CH_2=N-CH_3$ molecules. These latter dissociations can only occur if two ligands are involved in the fragmentation. There is, however, no evidence for the loss of two intact ligands, which would yield the product ion $[C_{60}L+H]^+$ (m/z 868). This dissociation is probably energetically not accessible under the applied conditions. Obviously, the fragmentation of the tris-adduct involves both available neutral ligands, while that of the bis-adduct can involve only one neutral ligand, and that of the mono-adduct, at much reduced efficiency, the protonated ligand. MS^n experiments (n = 3 and 4) confirm that the loss of 43 Da is abundant when there is still an intact neutral ligand in the ion. In MS^n experiments involving fragment ions without intact neutral ligand, the loss of 43 Da can only occur from the protonated ligand and is in fact observed as a low abundant process similar to the MS^2 experiment of the protonated mono-adduct. Even though these findings provide circumstantial evidence of CRF, more compelling evidence would result if the neutral and protonated ligand showed a distinctly different decomposition pattern. Compound **3** (Fig. 1) represents such a system.

In the top trace of Fig. 3, the (+)-ESI MS of the synthetic raw product of compound **3** is depicted. The protonated mono- (m/z 976), bis- (m/z 1232) and tris-adducts (m/z 1487) of compound **3** are labelled with the letters **a**, **b** and **c**, respectively. The corresponding MS^2 (CID) spectra for the ions **a**, **b** and **c** reveal clear distinctions in the dissociation behaviour of the protonated mono-adduct (**a**), on the one side, and the bis- (**b**) and tris-adduct (**c**), on the other. The protonated mono-adduct (**a**) of compound **3** features the loss of a neutral entity with 100 Da. A likely neutral loss could be seen in the rupture of the long alkyl chain releasing an intact C_7H_{16} heptane moiety (cp. Fig. 4). Obvious is the high noise level in the CID mass spectrum, indicating that this reaction from the protonated ligand is again inefficient. In contrast, the bis- and tris-adduct of compound **3** show efficient losses of the entire ligand and of a neutral entity with 141 Da. This latter species is formed by the same dissociation that would lead to the loss of 43 Da in compounds **1** and **2** (Fig. 4). Also here the observation is made, that the bis-adduct shows dissociations from only one ligand, while the decay of the tris-adduct would involve two ligands, this time even showing the loss of two intact ligands. Clearly, the bis- and tris-adduct do not show dissociations from the protonated ligand, but decompositions of the neutral ligand(s).

The ESI mass spectrum of the raw product of compound **3** reveals a second, even more pronounced ion series labelled as **a'**, **b'** and **c'** (Fig. 3). These ions cannot result from either neutral or ion fragmentation of compound **3** molecules, but are probably caused by by-products of the synthesis. Though they were not isolated and characterised, we include the corresponding ions labelled **a'**, **b'** and