Gas-Phase Observation of the Heterolytic Dissociation of Negative Ions into Counter Ions: Dissociation of [Cu phthalocyanine (SO₃)₄Na]³⁻

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Ion pair formation proceeding in solution at room-temperature, where it is driven by energies of solvation, has been observed in the gas-phase in the collision-induced dissociation of [Cu phthalocyanine (SO₃)₄Na]³⁻ and [Cu phthalocyanine (SO₃)₄Na₂]²⁻ at low energies. The gas-phase observation of these charge separations into positive and negative ions, seemingly counter-intuitive, is favored sufficiently by thermodynamics to proceed at low collision energies. The combination of a high stability of the negative product anion against electron detachment and a low recombination energy of the departing positive counter ion appears to be the key requirement for such dissociations to proceed at low energies in the gas-phase. (J Am Soc Mass Spectrom 2008, 19, 375–379) © 2008 American Society for Mass Spectrometry

Solution chemistry is often initiated or enhanced by the spontaneous dissociation of molecules (and ions) into counter ions. Such dissociations are thermodynamically driven by the preferential solvation of the counter ions, as is the case, for example, in the spontaneous dissociation of NaCl in aqueous solution into the counter ions Na⁺ and Cl⁻. In contrast, the analogous dissociations of isolated molecules into counter ions in the gas phase, as generalized in reaction (1), are thermodynamically very unfavorable. They do

however become more favorable as the ionization energy of A, IE(A), decreases and the electron affinity of B, EA(B), increases.

Analogous heterolytic dissociations of anions into positive and negative counter ions, reaction (2) for a charge state of -1, are not known or expected to occur

spontaneously in the gas-phase at room-temperature. Such dissociations, for which the enthalpy change $\Delta H = IE(A) + D(A-B^-) - EA(B^-)$ in the absence of solvent, are *intrinsically* more favorable when IE(A) is low and EA(B⁻) is high.

Elevated energies sufficient to cause dissociation are readily applied to ions of type AB⁻ in the gas phase, for

example by collisions with neutral molecules when the ions are accelerated in a mass spectrometer. Dissociations induced by collisions in the gas phase [1] invariably lead to bond cleavage, reaction (3a), or electron detachment, reaction (3b), or, in the case of multiply charged anions of the type ABⁿ⁻, also to charge separation into two negative ions, reaction (4). This charge separation is driven by Coulombic repulsion, but must overcome an electrostatic kinetic barrier.

We report here what we believe to be the first recorded observation of collision-induced charge separation of a multiply-charged anion into positive and negative counter ions in the gas phase, viz., a *heterolytic* cleavage of type 5.

We have found, quite serendipitously, a negative ion for which this gas-phase dissociation is favored by a low IE(A) and a high EA(Bⁿ⁻). This ion, shown in Scheme 1, is born in a solution of Cu(II) phthalocyanine-tetrasulfonic acid tetrasodium salt (60 μM) in CH₃CN/H₂O (1:1) at room temperature and appears as the core ion [Cu phthalocyanine (SO₃)₄Na]³⁻ when the solution is electrosprayed [2].

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Scheme 1

Experimental

Electrospray Mass Spectrometry

Electrospray ionization mass spectrometry data were acquired using an API 2000 (MDS-SCIEX, Concord, ON, Canada) triple quadrupole mass spectrometer equipped with a “turbo ion spray” ion source. The mass spectrometer was operated in the negative ion mode at a potential of 4500 V at the ionization tip, a ring-electrode potential of 350 V and a range of declustering potentials applied between the orifice and the skimmer. N₂ was used as a curtain gas at a setting of 10 psi, and air was used as a nebulizer gas at 10 L min⁻¹. Solutions were introduced by direct infusion into the ion source at a flow rate of 4 μL min⁻¹.

MS/MS was carried out in product ion and multiple reaction monitoring (MRM) modes with N₂ as collision gas with a pressure estimated to be 3 mTorr. The collision offset voltage [the potential difference between the quadrupole prefilter (q₀) and the collision cell quadrupole (q₂)], which gives the laboratory frame collision energy, spanned from 0 to 130 V at 1 V intervals. Product ion spectra were obtained by scanning Q₃ over the range of 10 to 1000 *m/z*. The inter-quadrupole lens potentials and the float potential of the resolving quadrupole Q₃ were linked to the q₂ potential, to maintain proper transmission through Q₃.

Preparation of Sample

Copper (II) phthalocyanine-tetrasulfonic acid tetrasodium salt was obtained from Sigma Aldrich, St. Louis, MO (Dye content ~50%). HPLC grade acetonitrile and Millipore (Millipore, Billerica, MA) (18.2 mΩ) water were used to prepare the solvent mixtures. The sample was dissolved in a 1:1 water/acetonitrile solution at a final concentration of between 20 and 60 μM.

Results and Discussion

The negative ion spectrum of the electrosprayed copper (II) phthalocyanine solution (Figure 1) is dominated by the presence of [Cu phthalocyanine (SO₃)₄]⁴⁻ for which [Cu phthalocyanine (SO₃)₄Na]³⁻, shown in Scheme 1, is the likely precursor in solution.

When exposed to collisions with N₂ molecules, the [Cu phthalocyanine (SO₃)₄Na]³⁻ ion is observed to dissociate at low collision energies solely by heterolytic cleavage to yield the quadruply-charged species [Cu phthalocyanine (SO₃)₄]⁴⁻, and presumably the positive counter ion, Na⁺, as shown in the experimental collision-induced dissociation (CID) profile in Figure 2 and in reaction (6).

We believe this to be the first reported observation of the dissociation of a negatively-charged anion into positive and negative counter-ions in the gas phase.

At slightly elevated collision energies, the loss of Na⁺ from the parent ion becomes a minor channel, and the [Cu phthalocyanine (SO₃)₄Na]³⁻ ion is observed to dissociate primarily by electrostatically-driven charge dissociation, reactions (7a) to (7c), or by loss of a neutral, reaction (7d).

The apparent heterolytic dissociation into the counter ions Na⁺ and [CuPc(SO₃)₄]⁴⁻, reaction (6), was a surprise to us since the products must overcome Coulombic attraction as they separate. However, this channel is likely favored at low collision energies since it is a barrierless process. In contrast, charge separation reactions must overcome an electrostatic kinetic barrier. This phenomenon is illustrated qualitatively in Figure 3.

In light of the novelty of the observation of gas-phase dissociation of an anion into positively- and negatively-charged counterions, we have made every attempt to eliminate the possibility of an alternative source for the quadruply-charged product ion at *m/z* 222.8. The identity and charge state of the *m/z* 222.8 product ion has been confirmed based on the observed isotopic pattern. To rule out the possibility that any of this quadruply-charged ion is “leaking through” the first quadrupole mass filter, a CID “blank” was performed in which the collision gas was switched off and the “fragmentation

Figure 1. Negative electrospray ionization mass spectrum of 60 μM Cu (II) phthalocyanine-tetrasulfonic acid tetrasodium salt in 1:1 acetonitrile and water solution, on the MDS SCIEX API 2000 triple quadrupole, at a declustering potential DP = 50 V. The unsodiated $[\text{CuPc}(\text{SO}_3)_4]^{4-}$ ion is observed at m/z 222.8, while singly- and doubly-sodiated $[\text{CuPc}(\text{SO}_3)_4\text{Na}_{1,2}]^{3-,2-}$ ions are observed at m/z 304.8 and 468.6, respectively. The large peak at 270.6 is assigned to the loss of SO_3^- from the quadruply-charged ion at m/z 222.8.

products" of $[\text{CuPc}(\text{SO}_3)_4\text{Na}]^{3-}$ were monitored with the second quadrupole mass filter. None of the m/z 222.8 quadruply-charged ion was observed, nor was any ion other than the parent at m/z 304.8. This experiment indicates that the m/z 222.8 ion must be the dissociation product of an ion with m/z near 305. A comparison of the "blank" experiment with a sample CID at a collision energy of 10 V is given in Figure 4.

An alternative route was considered for the formation of the $m/z = 222.8$ ion from a quadruply-charged impurity ion with m/z close to the selected triply-charged precursor ion at $m/z = 304.8$. To address this concern, a high-resolution Q/q/TOF instrument was used to investigate the possible presence of a quadruply-charged impurity ion in the vicinity of m/z 305, but no such impurity was found. Furthermore, we have performed additional CID experiments in which the m/z 304.8 $[\text{CuPc}(\text{SO}_3)_3\text{Na}]^{3-}$ ion was generated indirectly via dissociation of its solvent clusters in the collision cell. In so doing, we eliminated the possibility that an impurity ion in the vicinity of m/z 305 was the source of the m/z 222.8 product ion. In these experiments, water and acetonitrile clusters of the m/z 304.8 ($[\text{CuPc}(\text{SO}_3)_3\text{Na}]^{3-}$) ion were selected by the first quadrupole and CID performed in the collision cell yielded the triply-charged $[\text{CuPc}(\text{SO}_3)_3\text{Na}]^{3-}$ ion, which dissociated further as expected to yield product ions according to reactions (6) and (7) (see Figure 5).

For the CID of the water and acetonitrile clusters, we observed that the onset voltages for the appearance of the product ions are shifted higher by ~ 8 to 10 V compared with the CID of the unsolvated

$[\text{CuPc}(\text{SO}_3)_3\text{Na}]^{3-}$ ion. It is worth noting that a precursor ion scan showed that at low collision energies the m/z 304.8 ($[\text{CuPc}(\text{SO}_3)_3\text{Na}]^{3-}$) ion and its water and acetonitrile clusters are all sources of the quadruply-charged $[\text{CuPc}(\text{SO}_3)_4]^{4-}$ ion at m/z 222.8. In our estimation, these experiments conclusively demonstrate that the triply-charged $[\text{CuPc}(\text{SO}_3)_4\text{Na}]^{3-}$ ion at m/z 304.8 is

Figure 2. CID profile for the appearance of the dissociation products of $[\text{CuPc}(\text{SO}_3)_4\text{Na}]^{3-}$ (m/z 304.8, not shown), generated by negative electrospray ionization from a 20 μM solution of Cu(II) phthalocyanine-tetrasulfonic acid tetrasodium salt in 1:1 acetonitrile and water. Product ions with low intensities have not been included in the profile.

Figure 3. Illustration of the collision-energy dependence of the fragmentation of [Cu phthalocyanine (SO₃)₄Na]³⁻. The charge separation of the triply-charged parent ion into singly- and doubly-charged fragments (Channel A) is thermodynamically favored, however at low collision energies this process is not observed due to the presence of an electrostatic kinetic barrier. The barrierless dissociation of the triply-charged parent ion into positive (1+) and negative (4-) counter-ions (Channel B) is more endothermic, however this channel is dominant at low collision energies.

a source of the quadruply-charged product ion at m/z 222.8.

In addition, our observation of an analogous dissociation with [CuPc(SO₃)₄Cs]³⁻ (m/z 341.5) would require the unlikely presence of two Cu-containing impurity ions with different compositions, having m/z = 304.8 and 341.5, respectively.

Exploratory CID experiments with selected [CuPc(SO₃)₄Na₂]²⁻ also revealed the occurrence of the heterolytic dissociation reaction (8) (followed by the dissociation reaction (7)).

Of interest now is the influence of other alkali-metals and the central metal on dissociations of this type and these will be investigated soon.

We were able to find only one previous report of the observation of a gain in charge during CID. Sobott et al. have reported the gain of positive charge during CID of multiply positively-charged noncovalent protein com-

Figure 4. (a) CID "blank": The [CuPc(SO₃)₄Na]³⁻ ion is selected by the first quadrupole mass filter, and the "fragmentation products" are monitored by the second quadrupole mass filter, with the collision gas turned "off". (b) Sample CID of [CuPc(SO₃)₄Na]³⁻ at a collision energy of 10 V. The largest product observed is the quadruply-charged ion at m/z 222.8, resulting from the dissociation of the parent ion into counter-ions. Also present are the doubly-charged product ions at m/z 417.2, 425.2, and 433.2, resulting from the charge separation of the parent ion.

Figure 5. 10 V CID spectrum of $m/z = 310.8$ ($[\text{CuPc}(\text{SO}_3)_4\text{Na}(\text{H}_2\text{O})]^{3-}$), a precursor of $m/z = 304.8$ ($[\text{CuPc}(\text{SO}_3)_4\text{Na}]^{3-}$), generated by negative electrospray ionization from a 50 μM solution of Cu(II) phthalocyanine-tetrasulfonic acid tetrasodium salt in 1:1 acetonitrile and water. The loss of neutral H_2O is followed by additional losses of Na^+ and SO_3^- from the $[\text{CuPc}(\text{SO}_3)_4\text{Na}]^{3-}$ product ion.

plexes which they attribute to the loss of an attached negative counter ion such as the acetate anion [3]. Also, it is interesting to note that an analogous process for the dissociation of a positive ion, reaction (9), has been suggested as a possible source for the production of doubly-charged ions in the electron-impact ionization of bis-benzyl tetrahydroisoquinolines [4], 1,3,5-trichlorobenzene [5], and 6,6-diphenyl-2,4-pentadienyliden-1 [5].

Conclusions

The $[\text{Cu phthalocyanine}(\text{SO}_3)_4\text{Na}]^{3-}$ ion has been produced by electrospray ionization and found to dissociate in the gas phase primarily by homolytic cleavage leading to charge separation and the loss of SO_3^- and SO_2^- . The predominant dissociation pathway observed

corresponds to charge separation via homolytic cleavage to form SO_3^- . The other major channel leads to charge separation and SO_2^- formation, perhaps via loss of SO_2 that was also observed, but accompanied by intramolecular electron transfer. An unexpected heterolytic cleavage into counter ions, including Na^+ , also was observed at relatively low collision energies for both $[\text{Cu phthalocyanine}(\text{SO}_3)_4\text{Na}]^{3-}$ and $[\text{Cu phthalocyanine}(\text{SO}_3)_4\text{Na}_2]^{2-}$. The combination of a low recombination energy of the product cation and a high stability of the more negative product anion against electron detachment appears to be the key requirement for such dissociations to proceed at low energies in the gas phase. Furthermore, at low energies this type of reaction is kinetically favored over charge separation reactions, owing to the absence of a barrier. These same dissociations become spontaneous in solution at room temperature through the higher energy of solvation of the product counter ions compared with that of the dissociating anion.

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