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Reactions of doubly deprotonated 2,6-naphthalenedicarboxylic acid with alcohols: Proton transfer versus solvation☆

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ABSTRACT

Electrospray ionization of 2,6-naphthalenedicarboxylic acid readily affords its doubly deprotonated dicarboxylate dianion (**1^{2-}**). This species clusters with background water and added alcohols in an ion trap at ~10^{-3} Torr. Sequential solvation is observed to afford mono and dicoordinated ions. Surprisingly, the latter cluster (**1^{2-}• 2TFE**) is protonated by 2,2,2-trifluoroethanol (TFE) whereas **1^{2-}** and **1^{2-}• TFE** are not even though ΔH°_{acid}(TFE) = 361.7 ± 2.5 kcal mol^{-1} (as given in the NIST website at http://webbook.nist.gov) and the B3LYP/6-31+G(d,p) proton affinities are 384.7 (**1^{2-}**), 377.6 (**1^{2-}• TFE**), and 362.7 (**1^{2-}• 2TFE**) kcal mol^{-1}. That is, only the weakest base in this series, and the dianion with an equal number of solvent molecules and charged sites, undergoes proton transfer. In a FTMS instrument at lower pressures (~10^{-8} Torr) inefficient proton abstraction is observed with the monosolvated dianion. This difference, and the observed reactivities of **1^{2-}**, **1^{2-}• TFE** and **1^{2-}• 2TFE** are rationalized with the aid of computed potential energy surfaces. The chemical structures of these cluster ions were also probed via collision-induced dissociations, infrared photodissociation from 2700 to 3200 cm^{-1}, and extensive calculations. All of the TFE species are found to be solvated dianions, but incipient proton transfer to afford electrostatically defying anion-anion clusters is noted in two cases. In proton transfer reactions, formation of the conjugate acid as a solvated ion lowers the energy of the system and reduces the Coulomb repulsion barrier facilitating the overall process.

1. Introduction

Solvents play a critical role in influencing structure and reactivity in both chemistry and biology [1]. They serve as a medium, function as passive participants in chemical transformations, but often play a more active role. For example, solvents can be involved in proton transfer reactions, serve as nucleophiles or ligands to metal centers, solvate reactants, products, reactive intermediates and transition structures, and influence aggregation states of salts and organometallic reagents [2].

In the gas phase solvent effects can be eliminated, and this has led to surprising findings and new chemical insights. A landmark example is the reversal of the acidity ordering of alcohols upon alkyl substitution at the hydroxyl bearing carbon (i.e., $CH_3OH < CH_3CH_2OH < (CH_3)_2CHOH < (CH_3)_3COH$, where *tert*-butyl alcohol is the strongest gas-phase acid in this series but the weakest one in solution) [3]. Mass spectrometry based methods also can be used to gain an understanding of ion microsolvation, thereby providing a means to explore nucleation processes, reaction intermediates and the transition from an isolated species to its bulk phase behavior [4]. Small cluster ions are consequently of general interest and have been extensively investigated [5].

High pressure mass spectrometers and flowing afterglow devices can be used to synthesize clusters via association processes, but this method generally is not effective in low pressure environments. In 1973 Riveros et al. addressed this problem by reporting that $COCl^-$, generated by electron ionization of phosgene, transfers

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☆ Dedicated to our friend Prof. Jose Riveros in celebration of his being named Emeritus Professor and in recognition of his important contributions to gas-phase ion chemistry.

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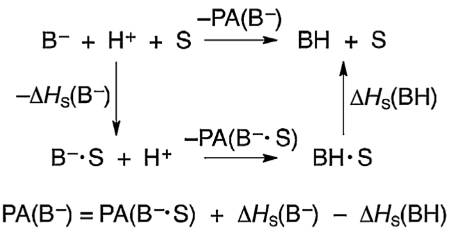

Scheme 1. Thermodynamic cycle relating the proton affinities (PA) of anions B^- and $B^- \bullet S$ with the solvation energies (ΔH_S) of B^- and BH.

Cl^- to a wide variety of organic compounds under high vacuum conditions [6]. Anionic nucleophiles subsequently were found to react with alkyl formates predominantly via an α-elimination pathway leading to mono solvated anions (Eq. (1)).

$$B^- + HCO_2R \rightarrow B - H \cdot OR^- + CO \quad (1)$$

This latter transformation and several variants of it have come to be known as the Riveros reaction [7]. It enables a wide range of cluster ions to be prepared and subsequently studied. These adducts are invariably less basic than their naked ion counterparts, and are also typically less reactive and can undergo different reactions [8]. This is because solvation is a stabilizing phenomenon, and the interaction of an ion with a neutral species via a single hydrogen bond such as in $BH \bullet {}^-OR$ or $B^- \bullet HOR$ is worth ~15–25 kcal mol^{-1} whereas the analogous non-charged adduct $HB \bullet HOR$ has a weak association energy of ~2–5 kcal mol^{-1} [9]. As a result, monosolvated anions usually have proton affinities that are ~15–20 kcal mol^{-1} smaller than their free analogs (Scheme 1).

The advent of electrospray ionization (ESI) has enabled multiply charged ions to be routinely produced and provides another versatile approach for preparing solvated ions. This has enabled IR [10] and photoelectron spectroscopy [11] to be used to interrogate their structures, while unimolecular dissociations can be used to probe the competition between solvent evaporation and dissociative proton transfer [12], and electron capture experiments enabled an absolute electrochemical scale to be determined [13]. A new class of electrostatically defying cation–cation [14] and anion–anion [15] gas-phase clusters also has been proposed, and these species have strong parallels in a variety of biological systems including oligomers of HIV capsid proteins, the human rhinovirus capsid envelope, the HY-HEL5 Fab-lysozyme complex and many protein structures [16]. These studies raise questions such as can one generate like-ion complexes via proton transfer reactions and what happens to the Coulomb barrier in multiply charged ions upon solvation [17]? To address these issues, here we explore how doubly deprotonated 2,6-naphthalenedicarboxylic acid reacts with various alcohols via sequential solvation. The resulting structures were probed experimentally and computationally, and potential energy surfaces were calculated to explore the Coulombic barriers.

2. Experimental section

Commercial reagents were used as supplied. Gas phase ion-molecule reactions were carried out using a Finnigan LTQ FT hybrid linear ion trap (Finnigan, Bremen, Germany) fitted with an electrospray ionization source and modified as described previously to allow the introduction of gaseous neutral reagents into the ion trap [18]. Accurate mass measurements using the FT-ICR allowed unambiguous assignment of the observed ions. Doubly deprotonated 2,6-naphthalenedicarboxylic acid was generated by ESI from a ca 10^{-4} M solution mixture of 2,6-naphthalenedicarboxylic acid and trimethylamine in 1:1 H_2O/CH_3OH. This solution was injected into the ESI at a flow rate of 5 μL min^{-1}. The instrument was tuned to optimize the signals of the desired ions. For instance, sheath gas flow rate, source voltage and temperature were adjusted to ca. 20 (arbitrary units), 3.0 kV and 250 °C, respectively. Low-energy collision-induced dissociation (CID) studies using helium as the collision gas were performed within the LTQ using the standard procedure of mass selection of the precursor ions and subjection of these ions to collisional activation. The activation time for these experiments was 30 ms with the normalized collisional energy varied to ensure that ca 20% of the precursor ion remained. For ion-molecule reactions, the 2,2,2-trifluoroethanol (TFE) was injected at flow rates of 3–10 μL h^{-1} directly into a heated stainless steel line that supplies helium to the linear ion trap. Since the flow of helium is controlled, the composition of the reagent/helium mixture can be calculated using the known molar flow rates of helium and neutral reagent. The helium pressure regulator that controls the flow of gas into the ion trap under normal operating conditions is bypassed, and instead, the helium pressure is controlled manually by matching the pressure in the vacuum chamber surrounding the ion trap, measured using the ion gauge, to that under normal operating conditions (ca. 7–8 × 10^{-6} Torr). This will then indicate a pressure of ca. 2 × 10^{-3} Torr inside the linear ion trap. For kinetics experiments, data points were collected over a time range from 0.03 to 5 s, under pseudo-first order reaction conditions with TFE being the excess component. It is interesting to highlight here that a previous study has demonstrated that ions stored in the linear ion trap are essentially quasi-thermalized to room temperature [19]. The data demonstrated complex kinetics, and rate constants were extracted by fitting to a multi-step reaction mechanism. Second-order rate constants are compared to average dipole orientation (ADO) theory ion-molecule collision rates. ADO calculations were performed using the program COLRATE [20].

A 3 T FT instrument equipped with a modified IonSpec ESI cart that has additional sample inlets and pulsed valves as well as a 1″ CaF_2 window to enable infrared multiphoton dissociation (IRMPD) studies was used [21]. An Omega data system was employed to control the mass spectrometer and was interfaced to a PC that operated a Laser Vision optical parametric oscillator (OPO)/optical parametric amplifier (OPA) laser. Doubly deprotonated 2,6-naphthalenedicarboxylic acid was generated by ESI from slightly basic ~10^{-4} M 1:1 H_2O/CH_3OH solutions and allowed to react with TFE added through a slow leak or pulsed valve. The resulting species of interest were mass isolated using frequency sweeps and/or select chirp excitations [22]. Reactions were followed as a function of time and double resonance experiments were carried out to establish the first formed products and their distributions. An action IRMPD spectrum of 2,6-naphthalenedicarboxylate • TFE was obtained by irradiating the cluster at 10 Hz for 10 s from 2700 to 3200 cm^{-1} in 10 cm^{-1} step sizes. Fragmentation yields were background corrected for a small amount of thermal fragmentation (7%) and linearly adjusted for the differences in the wavelength energies.

Density functional theory calculations were carried out using Gaussian 09 at the Minnesota Supercomputer Institute for Advanced Computational Research [23]. Geometry optimizations and vibrational frequencies were computed for stationary points using B3LYP and the 6-31+G(d,p) basis set [24]. Unscaled vibrational frequencies were used to provide proton affinities at 298 K, all other energetic quantities correspond to ΔE and do not include thermal or zero-point energy corrections. Inclusion of these terms, however, typically had a small effect (≤0.2 kcal mol^{-1}). Partial optimizations in which a single O••H distance was fixed and the rest of the structure was left unconstrained were carried out to explore potential energy surfaces.