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Stability and Ring-Shift Tautomerization of Cyclic Anhydrides of Benzenehexasulfonic Acid

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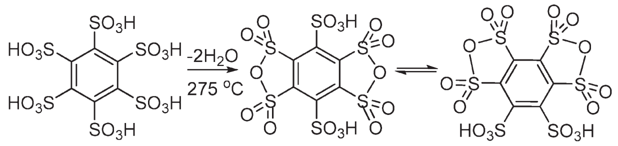

Upon heating in a dry atmosphere, benzenehexasulfonic acid forms three cyclic anhydrides. Mono- and dianhydride do not hydrolyze readily due their flatter structures compared to the hydrolysis products. The trianhydride appears more to be reactive toward hydrolysis. In solutions, the mono- and dianhydride undergo ring-shift tautomerization, which is in the latter case shifted toward the para isomer.

Benzenehexasulfonic acid (BHSA) was synthesized for the first time in the 1970s by Dokunikhin et al. via treatment of 1,4-dinitrotetrachlorobenzene with sulfite in the presence of Cu^{2+}.[1,2] X-ray crystallographic structures have been determined for $Na_6BHSA \cdot 8H_2O$[3,4] as well as for $BHSA \cdot 12H_2O$ and $BHSA \cdot 14H_2O$.[5] In all cases, the steric repulsions between sulfonates on the same phenyl ring are so significant that they distort the aromatic ring into a chair conformation. Interest in BHSA was sparked recently by the discovery of fast protonic conductivity in its crystals at low humidities which models the behavior of a new generation of polymer electrolyte fuel cell membranes.[5] During these studies, we found to our surprise that, upon heating in a dry atmosphere, BHSA forms cyclic anhydrides rather than undergoing desulfonation known from previous studies in the presence of water.[1,2] Another surprise was the stability of the anhydrides toward hydrolysis. No less striking was the discovery of a ring shift in the anhydrides at room temperature.

The TGA scan of the $BHSA \cdot 12H_2O$ crystals shows several mass loss steps from 20 to 600 °C as shown in Figure 1. In order to prepare samples for more detailed structural and chemical characterization, we performed scan-stop TGA by holding the temperature at various points along the TGA curve until constant mass was attained (typically 5 min). After cooling, the samples were quickly transferred to dry vials to minimize water absorption. The results of this study are summarized in the Supporting Information, Table S1.

The mass loss between 85 and 140 °C corresponds to a loss of eight water molecules. This step does not involve chemical changes in the BHSA molecule as the ^{13}C NMR and ESI-MS spectra of samples heated to 140 °C and dissolved in D_2O (or DMSO-d_6) do not differ from untreated samples. Moreover, elemental analysis agrees with the assignment of this sample as $BHSA \cdot 4H_2O$.

Between 140 and 180 °C, two additional water molecules are lost. This mass loss coincides with a change in the chemical shift of the sole singlet peak in the room temperature ^{13}C NMR spectra from 148.8 ppm to 142.7 ppm in D_2O (Figure 1, right axis). The m/z value of the highest peak in the ESI-MS spectrum also changes from 557 to 521 Da as shown in Figure 2. In going from 180 to 210 °C and then to 275 °C, two water molecules are lost in each step without further change in the ^{13}C NMR or ESI-MS spectra.

The sudden change in ESI-MS spectra (of aqueous solutions at 25 °C) of samples heated above 140 °C (and up to 300 °C) without change in the C/S ratio (1.01 ± 0.01 from elemental analysis) can be explained by the formation of a cyclic dianhydride (DA) as illustrated in Scheme 1. The calculated isotope patterns of molecular ions $(DA\text{-}H)^-$ and $(DA\text{-}2H)^{2-}$ agree well with the experimental ESI-MS data (see Figure 2).

In order to study the reactivity of the dianhydride, it was dissolved in water at room temperature, and aliquots of this solution were taken periodically for ESI-MS analysis. After 2 weeks at room temperature, the peak corresponding to the dianhydride (DA) disappeared while a peak corresponding to a monoanhydride (MA) emerged (see Figure 2). Further hydrolysis to BHSA occurs at room temperature in the time scale of several weeks and within hours upon boiling. XRD of $DA \cdot 5.5H_2O$ (Supporting Information, Figure S8) shows that only the para isomer is present in the crystals. Gas-phase calculations also confirm that the *p*-DA is more stable than *o*-DA both in its protonated form and as a dianion (Supporting Information, Table S3).

Although the chemistry outlined in Scheme 1 agrees with the experimental data discussed so far, it is counterintuitive to the chemical behavior expected for sulfonic acids and their anhydrides. First, BHSA is known to undergo desulfonation in aqueous solutions at 180 °C yielding quantitatively 1,2,4,5-benzenetetrasulfonic acid,[1,2] and our previous data show that the desulfonation starts in solid BHSA at temperatures as low as 100 °C and relative humidity of 4%.[5]

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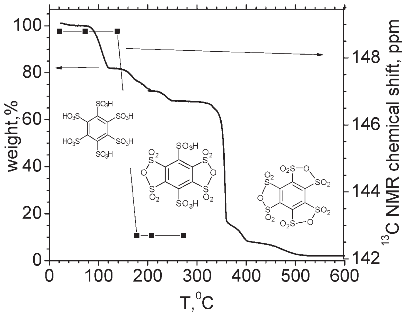


FIGURE 1. TGA (left scale) of BHSA·12H_2O (solid line) under a flow of dry N_2 with a heating rate of 5 °C/min. Also shown (right scale) are ^{13}C NMR chemical shifts vs TMS at 25 °C of samples preheated at the temperatures shown and dissolved in D_2O.

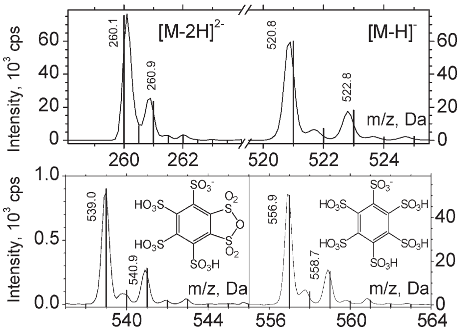
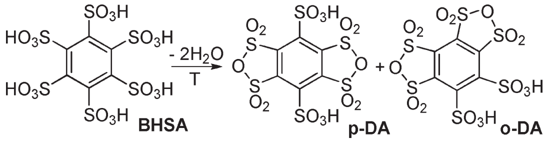


FIGURE 2. Negative-ion mode ESI-mass spectra of freshly made 50 μM MeOH/H_2O 1:1 v/v solutions of BHSA previously heated to 275 °C (upper panel), same sample aged for 2 weeks in pure water (lower left panel), and of BHSA × 12H_2O (lower right panel). Also shown as vertical bars are calculated 1 Da-resolution mass spectra of the assigned ions descrined in the upper right corners.

SCHEME 1. **Formation of DA**



On the other hand, desulfonation requires the presence of water,[6] and formation of aliphatic sulfonic acid anhydrides upon heating in a dry atmosphere is well-documented.[7] Second, sulfonic anhydrides are known to undergo protolysis extremely easily.[8,9] For example, 1,2-benzenedisulfonic acid anhydride has a half-life of 37s in methanol at −29 °C.[10] Thus, it seems surprising that DA and MA remain stable in aqueous solution for days. A sterically crowded 3,4,5,6-tetramethylbenzene-1,2-disulfonic acid anhydride has been reported to form much easier from the corresponding 1,2-disulfonic acid and to be less reactive in hydrolysis than its less substituted homologues.[11] We can speculate that out-of-plane distortions

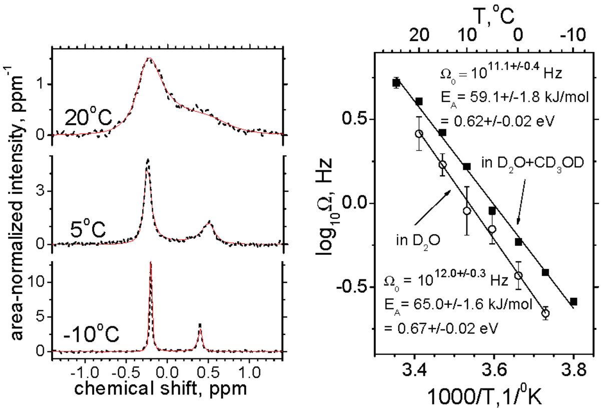


FIGURE 3. (Left) ^{13}C NMR spectra of BHSA dianhydride in D_2O/CD_3OD (1:1 v/v) at −10, +5, and +20 °C: dotted lines, experimental data; solid red lines, fit from eq 1. Zero chemical shift corresponds to the center of mass of the peaks (ca. 142.7 ppm vs TMS). (Right) Arrhenius plots for the tautomerization rate, Ω, of BHSA dianhydride in D_2O (lower line) and in D_2O/CD_3OD (1:1 v/v) (upper line).

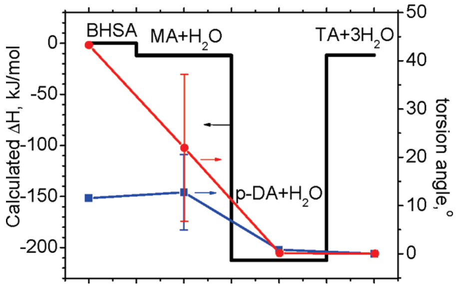


FIGURE 4. Calculated ΔH changes upon different stages of dehydration of BHSA (black ladder line) and the calculated S−C−C−S (red circles) and C−C−C−C torsion angles (blue squares) in BHSA and its anhydrides. The structural data shown are the averages (and standard deviations) of the calculated values for fully deprotonated molecules grouped according to the highest possible symmetry of the isolated molecules.

of the aromatic ring present in benzenehexasulfonic acid are relieved when DA is formed ($\Delta H_{\mathrm{calc}} = -212$ kJ/mol, Figure 4). The higher stabilization energy of *p*-DA compared to that of the monoanhydride (MA) (−11 kJ/mol) can also explain why the latter cannot be isolated during heating of BHSA.

After establishing the nature of the compound formed upon heating BHSA between 140 and 300 °C as *p*-DA, we need to explain its seemingly conflicting solution-phase ^{13}C NMR spectrum. The ^{13}C NMR spectrum of DA in D_2O at 25 °C yields only one line, whereas two lines are expected for *p*-DA and three for *o*-DA. More detailed temperature-dependent NMR studies revealed that, at lower temperatures, the peak splits into two peaks with the area ratio of 2:1 (Figure 3). The line shapes at different temperatures for the dianhydride solutions in D_2O and in D_2O/CD_3OD (1:1 v/v) fit well to the equation for chemical exchange with the frequency Ω and the population ratio of 2:1[12]

$$I(\omega) = \frac{6K\Omega\delta^2}{[2\delta^2 + (\omega-\omega_0)\delta - (\omega-\omega_0)^2]^2 + 9\Omega^2(\omega-\omega_0)^2} \tag{1}$$

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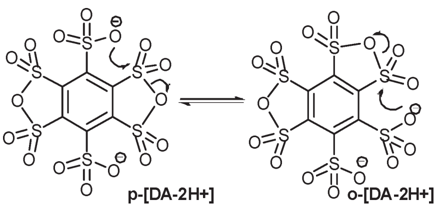
SCHEME 2. Ring Shift Tautomerization of DA



where K is a normalization factor, ω is the NMR frequency, ω_o is the position of the center of mass of the peak(s), and 3δ is the NMR frequency difference between the two nonequivalent types of ^{13}C atoms undergoing scrambling.

We considered several possible mechanisms in an attempt to determine the structural changes responsible for the data shown in Figure 3. The only explanation fully consistent with all experimental findings is that the dianhydride undergoes an intramolecular ring-shift tautomerization as shown in Scheme 2. In support of this mechanism, we offer several arguments: (i) A ^{13}C in a 5-membered cyclic anhydride and a ^{13}C connected to a sulfonic group differ in the third neighbor, which can easily account[13,14] for the 0.6−0.9 ppm chemical shift difference (3δ) seen in our experiments. (ii)There is a difference between ^{13}C atoms in the para and ortho isomers of DA in the fourth neighbor, and thus, they are expected to have a smaller chemical shift difference,[13,14] which is likely not resolved in our experiments. (iii) The activation energy of the isotope scrambling (62 ± 3 kJ/mol) falls within the range for known activation energies of S_N2 at S atoms in RSO_2X, i.e., 50−90 kJ/mol.[15−19] (iv) The Arrhenius pre-exponential factor for the chemical exchange ($(0.12-1) \times 10^{12}$ Hz) is on the order of bond vibration frequencies. It is orders of magnitude higher than those of intermolecular S_N2 reactions at S atoms,[15−19] and it agrees with the simple intramolecular mechanism shown in Scheme 2. An alternative explanation involving a synchronized shift of two rings is incompatible with the high pre-exponential factor.

The first two arguments explain why there are only two peaks in the low-temperature ^{13}C NMR spectra of the BHSA dianhydride with 2:1 peak area ratio and why *p*-DA and *o*-DA are not distinguishable. The last two arguments support the feasibility of the previously unknown tautomerization shown in Scheme 2.

Scheme 2 suggests that *p*-DA and *o*-DA should be present in equilibrium in a solution. However, we have not been able to detect peaks attributable to *o*-DA using variable-temperature (−40 to +23 °C) Raman spectroscopy (Supporting Information, Figures S4 and S5). This suggests that the ring-shift reaction scrambles all aromatic C atoms through a *transient* ($[o\text{-DA}]/[p\text{-DA}] < 0.02$) formation of *o*-DA, which can, in principle, be detected by a chemical trap.

The monoanhydride (MA) shows one peak in its ^{13}C NMR spectrum (Supporting Information, Figures S6 and S9) which broadens without splitting down to −65 °C, indicating that the ring shift is even faster in this molecule. This is likely because the ring shift in MA does not require the formation of a high energy isomer and because the activation barrier may be lower in this nonflat molecule.

Finally, we note that the final ~65% mass loss that occurs above 300 °C (Figure 1) may be caused by direct sublimation of anhydrous DA or by further loss of water and formation of volatile trianhydride (TA). Both DA and TA were detected as protonated molecular ions using APCI-MS (Supporting Information, Figure S7) above 250 °C, but only DA was isolated as the sublimation product at 300 °C (Supporting Information, Figure S2).

Calculations show that the TA molecule is flat, like DA, and that its hydrolysis into DA has a −200 kJ/mol enthalpy (Figure 4). The coexistence of TAH^+ and DAH^+ during APCI imples that TA has a typical reactivity expected from sulfonic acid anhydrides in reactions with water. (Note that the 541 Da peak corresponding to MAH^+ is absent in the mass spectrum, proving that the DA does not hydrolyze under these conditions.) This further supports the notion that the reduced reactivity of DA and MA to hydrolysis is due to the formation of sterically distorted products (i.e., with a more product-like transition state), as illustrated by comparison of torsion angles in Figure 4.

To summarize, we found that upon heating to 140−300 °C in a dry atmosphere benzenehexasulfonic acid forms a cyclic *p*-dianhydride and a volatile trianhydride at higher temperatures. The monoanhydride can be obtained by partial hydrolysis of the *p*-dianhydride. The mono- and *p*-dianhydrides show remarkable stability toward hydrolysis due to increased steric distortions in the reaction products. Yet, the most unexpected result of this work is a discovery of a ring-shift tautomerization in the cyclic anhydrides with a vicinal sulfonic group. It is worth noting that while the TGA of benzenehexacarboxylic (mellitic) acid shares many similarities with the TGA of BHSA, particularly regarding the type of anhydrides formed,[20] the analogous ring shifts are unknown for carboxylic acid anhydrides at room temperature,[21] although their reactivity at higher temperatures supports such behavior.[20] The ring shift reported in this work has a potential use for molecular logic devices.[22]

Experimental Section

Benzenehexasulfonic Acid 1,2;4,5-Dianhydride (DA). BHSA· $12H_2O$ (0.30 g, 0.39 mmol) was heated in the tube furnace at rate 5 °C/min in a dry N_2 to 275 °C and held until constant mass (10 min). The product was obtained as a white powder (0.20 g, 98%). δ_C (500 MHz; MeOD/D_2O; −10 °C): 143.1, 142.5 or see Figure 3. δ_C (500 MHz; MeOD/D_2O; 25 °C): see the Supporting Information, Figure S10. ESI-MS: see Figure 2. HRMS: $[M - H]^-$ found *m/z* 520.7574, $C_6HO_{16}S_6^-$requires 520.7589. IR: seethe Supporting Information, Figure S2, upper panel. Anal. Calcd for $C_6H_2O_{16}S_6$: C, 13.8; H, 0.4; O, 49.0; S, 36.8. Found: C, 13.7; H, 0.6; O, 49.2; S, 36.5.

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Benzenehexasulfonic Acid 1,2;4,5-Dianhydride Dihydrate ($DA\cdot 2H_2O$). Anhydrous DA (0.23 g, 0.44 mmol) was dissolved in MeOH/H_2O (1:1 v/v). The solution was placed into a desiccator with saturated solution of KOH (9.9% humidity). The product was obtained as a white powder (0.20 g, 93%). δ_C (500 MHz; MeOD/D_2O; −10 °C): 143.1, 142.5 or see Figure 3. ESI-MS: see Figure 2. IR: see the Supporting Information, Figure S2, lower panel. Anal. Calcd for $C_6H_4O_{18}S_6$: C, 12.9; H, 1.1; O, S, 34.5. Found: C, 12.8; H, 1.2; S, 34.7.

Benzenehexasulfonic Acid 1,2;4,5-Dianhydride Pentasesquihydrate ($DA\cdot 5.5H_2O$). $DA\cdot 2H_2O$ (0.10 g) was dissolved in MeOH/H_2O (1:1 v/v) (0.5 mL), and the solution was allowed to evaporate at room temperature overnight in a desiccator with a saturated solution of $MgCl_2$ (33% humidity). White crystals appeared and were characterized by XRD (Supporting Information, Figure S8).

Benzenehexasulfonic Acid Monoanhydride (MA). $DA\cdot 2H_2O$ (0.21 g, 0.38 mmol) in DMSO (0.9 g) solution was heated to 60 °C for 2 h. The solution was filtered, and the filter was additionally washed with MeOH (aq). The obtained solution was dried in vacuo at 40 °C for 48 h. The solid was dissolved in MeOH (aq). The MeOH solution was slowly poured into dry Et_2O. The product was obtained as a white precipitate (0.15 g, 71%). The ESI-MS is shown in Figure 2; δ_H shows an absence of peaks in the aromatic region. ^{13}C NMR: Supporting Information, Figures S6 and S9. HRMS: $[M - H]^-$ found *m*/*z* 538.7702, $C_6H_3O_{17}S_6^-$ requires 538.7695.

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Supporting Information Available: Detailed experimental procedures, synthesis of BHSA, FTIR, Raman, ^{13}C NMR spectra, and calculation details. This material is available free of charge via the Internet at http://pubs.acs.org.