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Conformations of 2-Carboxy-1,4-butanedioic Acid as a Function of Ionization State in Dimethyl Sulfoxide

Gautham Nair and John D. Roberts*

Gates and Crellin Laboratories of Chemistry, California Institute of Technology,
Pasadena, CA 91125

robertsj@caltech.edu

Supporting Information:

2-Carboxy-1,4-butanedioic acid was prepared by saponification of its triethyl ester in 10% aqueous sodium hydroxide. The resulting ethanol was evaporated, the mixture filtered, and the filtrate acidified by shaking with a cation-exchange resin. The product was isolated by low-temperature evaporation of the water under reduced pressure in a rotary evaporator to minimize decarboxylation. The purity and dryness of the residue were verified by NMR.

The concentrations used for all of the NMR samples was approximately 0.05 M in DMSO- d_6 . The monoanion and dianion were prepared by dissolving the triacid and the appropriate number of equivalents of tetrabutylammonium cyanide in methanol and removing the solvent and hydrogen cyanide under reduced pressure.¹ The residue was dried in vacuo under a liquid-nitrogen-cooled cold-finger to trap residual solvent or water. Because the third ionization was impossible to achieve with cyanide as a base by the same procedure, the trianion was prepared by adding an excess of a 40% w/w aqueous tetrabutylammonium hydroxide solution and drying overnight in vacuo.

Because the monoanion and dianion preparations were not exactly stoichiometric, the samples were prepared several times. The observed J_{obs} for each species and the average values are summarized in Table 1 along with estimated uncertainties. The reported values were consistent with those obtained from spectra of solutions in which 0.5 or 1.5 equivalents of tetrabutylammonium cyanide were added and J_{obs} was taken to be the weighted average of J_{obs} for the two relevant species. The coupling for the trianion is substantially less certain, because of likely incomplete

neutralization, but still allows for useful qualitative conclusions.

The ionization constants of acids in DMSO can be determined by observing the changes in chemical shift that occur when a test acid of known pK_a in DMSO is added to a solution of the conjugate base of the compound being studied.² The ideal test acid has a pK_a close to the acid ionization being studied and very different chemical shifts between its acid and base forms. Then, if proton exchange is fast enough between all acids and bases in solution, the position of the test acid chemical shift and the compound's chemical shift will be weighted averages of the corresponding concentrations of acidic and basic species. In general, the test acid's observed chemical shift can be used to find $[H^+]$ (strictly speaking, $[D^+]$) given $pK_{a(\text{test})}$ and this value is then used with the compound's observed chemical shift to obtain pK_a .

The integrals of the NMR proton resonances for the monoanion and dianion preparations were not exactly the expected 1:1 or 1:2 equivalences, respectively. This problem of inexact stoichiometric formation of the mono and dianions was solved by adding test acids to these solutions in small amounts, generating multiple pairs of observed δ_{test} , δ_{triacid} . Thus, for pK_1 , two pairs of these values were obtained by adding propanedioic acid ($pK_a = 7.2$)⁴ to the monoanion preparation twice to achieve equivalence and using the resulting equations to simultaneously solve for pK_1 and the monoanion chemical shift. The values so obtained, along with six pairs of observed δ_{test} , δ_{triacid} resulting from the addition of succinimide ($pK_a = 14.65$)³ to the dianion were used in a least-squares fit to obtain pK_2 and the dianion chemical shift. The calculated chemical shifts for the monoanion and dianion are close to the chemical shifts observed in the many attempted preparations.

Unfortunately, K_3 and the trianion chemical shifts could not be dealt with in the same manner. Complications arose with many of the test acids, including peak broadening, unexpected changes of chemical shifts, and even disappearance of peaks. The difficulties were probably due to the excess hydroxide in solution, the high basicity of the trianion, deuterium exchange with the solvent, slow acid-base equilibria, and possible formation of clusters of ions in the solution. For these reasons, pK_3 could only be estimated as having a lower limit of about 20 and the listed

chemical shifts of the trianion are not very accurate.

References

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