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# Ionization Equilibria in Dicarboxylic Acids Undergoing Conformational Transitions

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Succinic acid and substituted succinic acids undergo conformational transitions during ionization, and these are expected to affect their ionization equilibrium. An analysis of this effect is presented. $^1$H NMR data on the dependence of the conformational equilibrium of succinic acid and *meso*-2,3-dimethylsuccinic acid on their degree of ionization are interpreted in terms of the ratio of the second ionization constants of the gauche and trans isomer, $K_{2g}/K_{2t}$, and the equilibrium constant $K_c$ for the gauche–trans transition of the un-ionized acid. The $K_{2g}/K_{2t}$ ratios obtained for the two above acids are compared with the ratio of the second ionization constants of *cis*- and *trans*-cyclohexane-1,2-dicarboxylic acids used as model compounds in which the carboxyls are gauche and trans to each other.

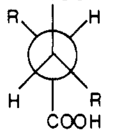
Ostwald[1] was first to point out that the ratio of the two ionization constants of a dicarboxylic acid is related to the electrostatic interaction between the hydrogen ion to be removed in the second dissociation step and the carboxylate charge on the singly ionized species. Bjerrum's quantitative theory[2] leading to

$$K_2/K_1 = (1/4)\exp(-e^2/DkTr) \qquad (1)$$

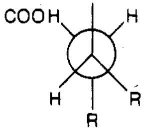
where $e$ is the electronic charge, $D$ the dielectric constant of water, and $r$ the equilibrium distance between the carboxylate charge and the hydrogen to be removed from the singly ionized acid, seemed to yield reasonable $r$ values for succinic acid and its higher homologues, but much too low $r$ values for malonic and maleic acid. Bjerrum's treatment was eventually amended by Westheimer and Kirkwood,[3] who modeled the dicarboxylic acid as an ellipsoid with a dielectric constant of 2 immersed in water with a dielectric constant of 80, so as to take account of the fact that part of the electrical lines of force between the hydrogen ion and the carboxylate pass through the organic molecule. The dimensions of the ellipsoid were estimated by assuming the acid to be in the all-trans conformation.

Another problem arose because of the unusually low $K_2/K_1$ values for maleic acid ($\Delta pK = 4.42$) and diethylmalonic acid ($\Delta pK = 5.08$).[4] McDaniel and Brown[5] suggested that these high $\Delta pK$ values are due to intramolecular hydrogen bonding in the singly ionized species: this would provide an added driving force for the first ionization and oppose the second ionization in which the hydrogen bond is broken. Later, Westheimer and Benfey[6] pointed out that the magnitude of such an effect may be assessed by comparing $K_1$ of a dicarboxylic acid with the dissociation constant $K_e$ of its monoester, and this approach was used by Levy and Magoulas[7] to quantify the effect of intramolecular hydrogen bonding on $K_2/K_1$ for dicarboxylic acids in water and in urea solution.

The extensive studies of Eberson[8] on the ionization equilibria of 2,3-disubstituted succinic acids provided dramatic proof of the importance of the conformational equilibrium in determining $K_2/K_1$. In the meso acids conformation I is favored, which places the carboxyls trans to each other. By contrast, in the racemic acids with large R substituents steric hindrance is minimized in the II conformer, placing the carboxyls gauche to each other. It is then not difficult to understand that $K_2/K_1$ is much smaller in the racemic acid: in the extreme case, with R = *tert*-butyl, $K_2/K_1 = 1.4 \times 10^{-2}$ for the meso and $K_2/K_1 = 2.9 \times 10^{-10}$ for the racemic acids in 50% aqueous methanol. Glasoe and Eberson[9] studied the racemic acid in aqueous solution and found $pK_1 = 2.20$ and $pK_2 = 10.25$, while the monoester had $pK_e = 5.57$. The large difference between $pK_e$ and $pK_1$ shows that intramolecular hydrogen bonding in the singly ionized species makes a major contribution to $pK_2 - pK_1$.

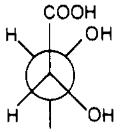


I

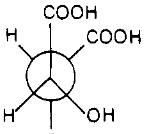


II

The acids investigated by Eberson represent extreme cases; in general one might expect the conformation to change with the degree of ionization of a dicarboxylic acid. This was established by Nunes et al.[10] for succinic acid by NMR spectroscopy. The results indicated that 82% of the un-ionized acid is in the gauche conformation; there appears to be little change in the conformational equilibrium when one carboxyl dissociates, but the gauche fraction decreases on further ionization to $P_g = 0.38$ in the fully ionized acid. A plot of $P_g$ against the fraction $\alpha_2$ of the acid in the doubly ionized state[11] is shown in Figure 1. For malic acid, Mariano and Gil[12] found a smaller conformational change on ionization—the carboxyls were 42% trans in the un-ionized species and 60% trans at full ionization. For tartaric acid Ascenso and Gil[13] found little dependence of the conformation on pH but a striking difference between stereoisomers. The racemic acid assumed conformation III with the carboxyls trans to one another, whereas *meso*-tartaric acid was in the conformation IV.



III



IV

An analysis of the ionization equilibria of a dicarboxylic acid that undergoes a conformational transition during ionization does not seem to have been presented previously. In that case we may formally treat the solution as containing a mixture of gauche and trans acids with second ionization constants $K_{2g}$ and $K_{2t}$, respectively. We shall assume that the conformational equilibrium is uneffected by the first ionization and that the gauche ⇄ trans equilibrium of the singly ionized species is determined by an

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[1] Ostwald, W. *Z. Phys. Chem.* **1892**, *9*, 658.

[2] Bjerrum, N. *Z. Phys. Chem.* **1926**, *106*, 219.

[3] Westheimer, F. H.; Kirkwood, J. G. *J. Chem. Phys.* **1938**, *6*, 513.

[4] Christensen, J. J.; Izatt, R. M.; Hansen, L. D. *J. Am. Chem. Soc.* **1967**, *89*, 213.

[5] McDaniel, D. H.; Brown, H. C. *Science (Washington, D.C.)* **1953**, *118*, 370.

[6] Westheimer, F. H.; Benfey, O. T. *J. Am. Chem. Soc.* **1956**, *78*, 5309.

[7] Levy, M.; Magoulas, J. P. *J. Am. Chem. Soc.* **1962**, *84*, 1345.

[8] Eberson, L. *Acta Chem. Scand.* **1959**, *13*, 211.

[9] Glasoe, P. K.; Eberson, L. *J. Phys. Chem.* **1964**, *68*, 1560.

[10] Nunes, M. T.; Gil, V. M. S.; Ascenso, J. *Tetrahedron* **1981**, *37*, 611.

[11] The $\alpha_2$ values were calculated with $pK_1 = 4.207$, $pK_2 = 5.635$ listed by Christensen et al.[4] for the dissociation constants at high dilution. Nunes et al. did not specify the succinic acid concentration at which the NMR data were recorded, but these concentrations were undoubtedly relatively high. The error in the estimate of $\alpha_2$ due to this factor is believed to be minor.

[12] Mariano, J. S.; Gil, V. M. S. *Mol. Phys.* **1969**, *17*, 313.

[13] Ascenso, J.; Gil, V. M. S. *Can. J. Chem.* **1980**, *58*, 1376.

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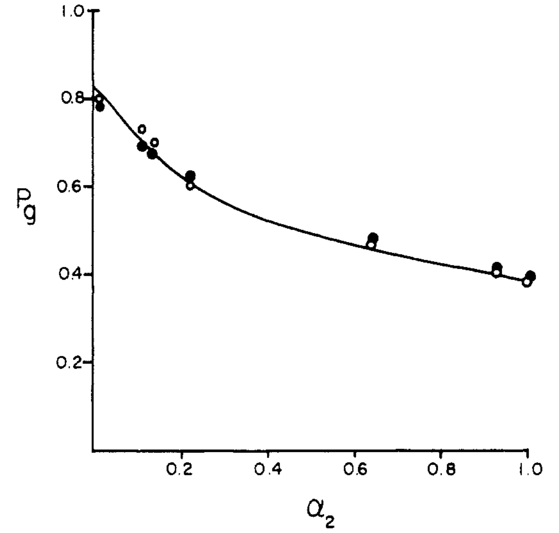


**Figure 1.** Fraction of succinic acid in the gauche conformation as a function of the fraction of the acid in the doubly ionized state: (○) experimental points; (●) calculated points using $K_c = 0.22$ and $K_{2g}/K_{2t} = 0.13$.

equilibrium constant $K_c$. We obtain then for the apparent second ionization constant

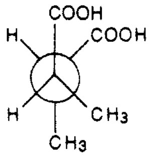
$$K_2^{\text{app}} = \frac{(\text{H}^+)[(\text{A}^{2-})_g + (\text{A}^{2-})_t]}{(\text{HA}^-)_g + (\text{HA}^-)_t} = \frac{K_{2g} + K_c K_{2t}}{1 + K_c} \quad (2)$$

Also, within the pH range in which the concentration of the un-ionized species is negligible

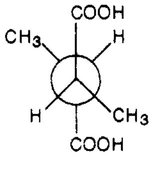
$$P_g = [(\text{HA}^-)_g + (\text{A}^{2-})_g]/[(\text{HA}^-)_g + (\text{A}^{2-})_g + (\text{HA}^-)_t + (\text{A}^{2-})_t] = [(\text{H}^+) + K_{2g}]/[(\text{H}^+) + K_{2g} + K_c((\text{H}^+) + K_{2t})] \quad (3)$$

At full ionization (H$^+$) is negligible compared with $K_{2g}$ and $K_{2t}$ and $P_g = K_{2g}/[K_{2g} + K_c K_{2t}]$. The NMR data of Nunes et al.[10] for the conformational equilibrium of un-ionized and fully ionized succinic acid lead then to $K_c = 0.22$ and $K_{2g}/K_{2t} = 0.13$.

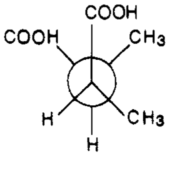
The conformational transition during the ionization of 2,3-dimethylsuccinic acid (which we determined, as described by Bothner-By and Naar-Colin[14] for other 2,3-disubstituted butanes from the spin–spin coupling of protons on adjacent carbons) leads to quite different results for the two stereoisomers. In the meso compound V the conformer with the methine hydrogens trans to each other has also the carboxyls in the trans position; the other two conformers are equivalent to each other. Ionization should favor conformer b, in which both the electrostatic energy and steric restraints are minimized:



Va

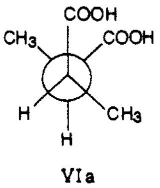


Vb

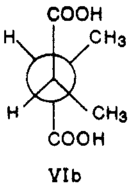


Vc

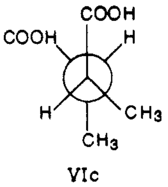
On the other hand, in the racemic isomer VI the conformer c with the methine hydrogens trans to each other should be favored for the un-ionized and singly ionized species, while the transition to conformer b, favored for the doubly ionized acid because it minimizes the electrostatic energy, is opposed by steric crowding:



VIa



VIb



VIc

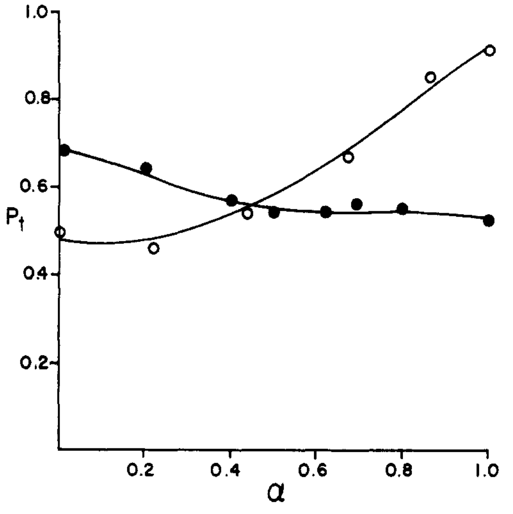


**Figure 2.** Fraction of 2,3-dimethylsuccinic acids in the conformation with the methines trans to each other as a function of the degree of ionization: meso isomer (○); *d,l* isomer (●).

**TABLE I: Conformational Transition during the Ionization of 2,3-Dimethylsuccinic Acids**

| | | | coupling constant, Hz | | fract *trans*-methine ($P_t$) | |
|---|---|---|---|---|---|---|
| isomer | deg ionization | pH | methine–methyl | methine–methine | exptl[a] | calcd[b] |
| meso[c] | 0.00 | 2.51 | 6.65 | 5.93 | 0.49 | 0.49 |
| | 0.22 | 3.78 | 6.55 | 5.56 | 0.46 | 0.52 |
| | 0.44 | 4.49 | 6.68 | 6.44 | 0.54 | 0.57 |
| | 0.67 | 5.17 | 6.41 | 7.65 | 0.67 | 0.68 |
| | 0.86 | 5.88 | 6.15 | 9.48 | 0.85 | 0.81 |
| | 1.00 | 12.74 | 6.13 | 10.13 | 0.91 | 0.91 |
| rac[d] | 0.00 | 2.21 | 6.89 | 7.77 | 0.68 | |
| | 0.20 | 3.91 | 6.92 | 7.38 | 0.64 | |
| | 0.40 | 4.58 | 6.96 | 6.80 | 0.57 | |
| | 0.50 | 5.01 | 6.96 | 6.41 | 0.54 | |
| | 0.62 | 5.35 | 6.96 | 6.41 | 0.54 | |
| | 0.69 | 5.58 | 6.98 | 6.65 | 0.56 | |
| | 0.80 | 5.97 | 6.71 | 6.45 | 0.55 | |
| | 1.00 | 13.02 | 6.71 | 6.23 | 0.52 | |

[a] It was assumed[14] that methine–methine coupling constants for gauche and trans conformations are 1 and 11 Hz, respectively. [b] Calculated from eq 3 using $K_c = 0.96$, $K_{2g} = 2 \times 10^{-6}$, $K_{2t} = 2 \times 10^{-5}$. [c] 0.085 M. [d] 0.42 M.

We should, therefore, expect a much less pronounced conformational transition during the ionization of the racemic acid. This is in agreement with our experimental results represented in Figure 2. The coupling constants on which the estimate of the fraction $P_t$ of compound V in conformation b and compound VI in conformation c are based are listed in Table I.

Applying to *meso*-2,3-dimethylsuccinic acid the same analysis as used above for the dependence of the conformational equilibrium on the ionization of succinic acid, we obtained $K_c = 0.96$ and $K_{2g}/K_{2t} = 0.095$. It is to be expected that $K_c$ should be substantially larger than for the unsubstituted succinic acid, since a transition from conformers Va and Vc to Vb leads to a relief of steric strain.

We attempted also fitting the conformational transitions derived from NMR data to predictions based on eq 3 with assumed values of $K_c$, $K_{2g}$, and $K_{2t}$. For succinic acid, $K_c = 0.22$, $K_{2g} = 3 \times 10^{-6}$, and $K_{2t} = 2.1 \times 10^{-5}$ led to an excellent fit as shown in Figure 1. For *meso*-2,3-dimethylsuccinic acid, titration yielded $K_1 = 1.2 \times 10^{-4}$, $K_2^{\text{app}} = 1.5 \times 10^{-5}$,[15] and the observed conformational transition was in reasonable agreement with predictions based on

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[14] Bothner-By, A. A.; Naar-Colin, C. *J. Am. Chem. Soc.* **1962**, *84*, 743.

[15] Our titrations were carried out with 0.26 M acid, and the dissociation constants were much higher than the $K_1 = 1.16 \times 10^{-4}$, $K_2 = 0.65 \times 10^{-6}$ reported by Gane and Ingold (*J. Chem. Soc.* **1931**, 2153) at the highest acid dilution of 0.00125 M. Since the NMR data were obtained in 0.095 M acid, the apparent dissociation constants found by us seem more appropriate for comparison.

$K_c = 0.96$, $K_{2g} = 2 \times 10^{-6}$, and $K_{2t} = 2 \times 10^{-5}$ (see Table I). We could not apply the same analysis to the racemic 2,3-dimethylsuccinic acid, since the methine–methine coupling does not distinguish between conformer VIa, with the carboxyls gauche, and conformer VIb, with the carboxyls trans to each other.

Finally, we used the stereoisomers of cyclohexane-1,2-dicarboxylic acid as model compounds for the gauche and trans conformer of succinic acid. Titration of 0.094 M acids yielded apparent second ionization constants of $6.2 \times 10^{-6}$ for the cis and $3.2 \times 10^{-5}$ for the trans isomers.[16] This corresponds to $K_{2g}/K_{2t} = 0.19$. These model compounds have conformations analogous to VIc and VIb, and the deviation from the $K_{2g}/K_{2t}$ ratio estimated from NMR data for succinic and *meso*-2,3-dimethylsuccinic acid is, therefore, not surprising.

## Experimental Section

*Materials.* All chemicals were obtained from the Aldrich Chemical Co. *meso*-2,3-Dimethylsuccinic acid was recrystallized from water: mp 210–211 °C (lit.[17] 197–201 °C). *trans*-1,2-Cyclohexanedicarboxylic acid was recrystallized from water: mp 229–231 °C (lit.[16] 215 °C). The racemic 2,3-dimethylsuccinic acid as received contained about 10% of the meso isomer; since this is much less water soluble, it was removed by filtration after the addition of a small volume of water. The product thus obtained exhibited only small $^{13}$C NMR peaks characteristic of the meso isomer; mp 122–123 °C (lit.[17] 121–122 °C). *cis*-1,2-Cyclohexanedicarboxylic acid was obtained by refluxing its anhydride in water for 5 h: mp 199–201 °C (lit.[16] 190 °C).

*Spectroscopy.* The $^1$H NMR spectra of $D_2O$ solutions of the 2,3-dimethylsuccinic acids were recorded by A. Malz at the College of Staten Island, City University of New York, on a WP-200 IBM NMR spectrometer at 25 °C.

*Acknowledgment.* We are grateful to the National Science Foundation for their support of this work through Grant DMR 85-00712, Polymers Program.

**Registry No.** Succinic acid, 110-15-6; *meso*-2,3-dimethylsuccinic acid, 608-40-2; *cis*-cyclohexane-1,2-dicarboxylic acid, 610-09-3; *trans*-cyclohexane-1,2-dicarboxylic acid, 2305-32-0.

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[16] Kuhn and Wassermann (*Helv. Chim. Acta* **1928**, *11*, 50) obtained $K_2 = 0.17 \times 10^{-6}$ for the cis and $K_2 = 1.2 \times 10^{-6}$ for the trans isomer. We cannot account for the large discrepancy between these and our values.

[17] Eberson, L. *Acta Chim. Scand.* **1959**, *13*, 40.

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# CHEMICAL KINETICS

## Deuterium Kinetic Isotope Effect in the Thermal Decomposition of 1,3,5-Trinitro-1,3,5-triazacyclohexane and 1,3,5,7-Tetranitro-1,3,5,7-tetraazacyclooctane: Its Use as an Experimental Probe for Their Shock-Induced Chemistry[†]

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An isothermal thermogravimetric analysis (TGA) study of the decomposition of RDX, HMX, and the respective deuterated analogues, RDX-$d_6$ and HMX-$d_8$, has been carried out. In RDX, a kinetic isotope effect (KIE) ($K_h/K_d$) of 1.5 was observed for the first time in the temperature range 199–216 °C. In the HMX decomposition, an isotope effect of $\sim$2.0 was consistently obtained in the temperature range 237–282 °C with *no* apparent temperature dependence. In both substances the KIE produced a small but definite decrease in shock sensitivity measured by the exploding metal foil method. These results indicate that the rate-determining steps in the processes of thermal decomposition and the chemical process of initiation are likely to be the same. Thus, the kinetic isotope effect served as a novel experimental probe to test the similarity, or otherwise, of the rate-limiting steps of the slow decomposition and the rapidly accelerating reactions of the initiation. Possible rate-limiting steps and reaction mechanisms are discussed.

### Introduction

1,3,5-Trinitro-1,3,5-triazacyclohexane (RDX) and 1,3,5,7-tetranitro-1,3,5,7-tetraazacyclooctane (HMX), both secondary cyclic nitramines, are well-known as high explosives and chemically interesting materials. They both undergo thermal decomposition in the solid state below their respective melting points and give rise mostly to low molecular weight gaseous products. In the solid state, HMX, which is the higher melting of the two nitramines, has four conformational isomers ($\beta$, $\alpha$, $\gamma$, and $\delta$),[1,2] while RDX has been shown[3,4] to have one metastable conformer ($\beta$) in addition to the room-temperature stable one ($\alpha$). The unique conformational properties and polymorphic transformations have been extensively studied recently by Brill and co-workers[5] using FT-IR, laser Raman, $^{14}$N NQR, and $^1$H NMR (solid state) spectroscopies.

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[†] Presented at the 8th International Symposium on Detonation, Albuquerque, NM, July 15–19, 1985, and the Symposium on the Role of Chemistry in Shock Phenomena, 190th National Meeting of the American Chemical Society, Chicago, IL, Sept. 8–13, 1985.

[1] Cady, H. H.; Smith, L. C. Report No. LAMS-2652; Los Alamos Scientific Laboratory: Los Alamos, NM, 1962.

[2] Bedard, M.; Huber, H.; Myers, J. L., Wright, G. F. *Can. J. Chem.* **1962**, *40*, 2778.

[3] McCrone, W. C. *Anal. Chem.* **1950**, *22*, 954.

[4] Karpowicz, R. J.; Sergio, S. T.; Brill, T. B. *Ind. Eng. Chem. Prod. Res. Dev.* **1983**, *22*, 363.

[5] Landers, A. G.; Apple, T. M.; Dybowski, Cecil; Brill, T. B. *Magn. Reson. Chem.* **1985**, *23*, 158 and additional references therein.

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