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Intramolecular Hydrogen Bonding in *cis*-Cyclopropanepolycarboxylic Acids[1]

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Acid dissociation constants and specific rates of reaction between a base and an intramolecularly hydrogen-bonded proton in monoanions of dicarboxylic acids have been determined at 10 and 25° in 0.1 M ionic strength aqueous solution for the following acids: cis-3,3-dimethylcyclopropane-1,2-dicarboxylic acid, cis-3,3-diphenylcyclopropane-1,2-dicarboxylic acid, and spiro[cyclopropane-1,9′-fluorene]-cis-2,3-dicarboxylic acid. The kinetic data obtained with the temperature-jump relaxation method permit an assignment of relative strengths of intramolecular hydrogen bonds in agreement with K_{a_1}/K_{a_2} data. Rough values of E_a, ΔH^*, and ΔS^* are calculated, and their significance is considered. Kinetic data are also reported for N,N-dimethyl-o-aminobenzoic acid at 25° and cis-cyclopropane-1,2,3-tricarboxylic acid at 10 and 25°.

Large values of the ratio K_{a_1}/K_{a_2} have been ascribed to intramoleular hydrogen bonding in the monoanions of dicarboxylic acids.[3] Fast reaction kinetic data substantiate this point of view; the temperature-jump relaxation method[4,5] frequently permits a determination of specific rates of forward and backward reactions in equilibria involving intramolecularly hydrogen-bonded species.[6,7] The bond strength is presumed to be, at least approximately, inversely proportional to the specific rate of proton abstraction from the intramolecular hydrogen bond. The work reported here compares potentiometric titration results with temperature-jump data for a series of structurally closely related cyclopropanepolycarboxylic acids: *cis*-caronic acid (*cis*-3,3-dimethylcyclopropane-1,2-dicarboxylic acid), *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid, spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid, and *cis*-cyclopropane-1,2,3-tricarboxylic acid. Figure 1 depicts the monoanion of the spiro acid and suggests the geometry of the intramolecular hydrogen bond in the ions of all four of these acids.

Experimental

cis-Caronic acid was prepared by the procedure of Perkin and Thorpe[8] but with the modification that β,β-dimethylglutaric acid was prepared from methone[9] rather than by the reported method. The synthetic *cis*-caronic acid had m.p. 176–178° (lit.[8] m.p. 176°).

cis-3,3-Diphenylcyclopropane-1,2-dicarboxylic acid was synthesized according to the method of van Alphen[10] to give white needles, m.p. 201–204° (lit.[10] m.p. 204°).

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[2] National Science Foundation undergraduate research participant.

[3] For a bibliography see L. Eberson and I. Wadsö, *Acta Chem. Scand.*, **17**, 1552 (1963).

[4] G. Czerlinski and M. Eigen, *Z. Elektrochem.*, **63**, 652 (1959).

[5] M. Eigen and L. DeMaeyer, "Technique of Organic Chemistry," Vol. VIII, Part II, S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1963, Chapter 18.

[6] M. Eigen and W. Kruse, *Z. Naturforsch.*, **18b**, 857 (1963).

[7] M. Eigen, W. Kruse, G. Maass, and L. DeMaeyer, "Progress in Reaction Kinetics," Vol. 2, G. Porter, Ed., Pergamon Press Ltd., Oxford, England, 1964, Chapter 6.

[8] W. H. Perkin and J. F. Thorpe, *J. Chem. Soc.*, **75**, 48 (1899).

[9] W. T. Smith and G. L. McLeod, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p. 345.

[10] J. van Alphen, *Rec. trav. chim.*, **62**, 210 (1943).

Table I. Mixed[a] Acid Dissociation Constants Determined Potentiometrically

	Temp.,[b] °C.	μ, M[c]	p$K_{a_1}{}^M$	p$K_{a_2}{}^M$	K_{a1}/K_{a_2}
N,N-Dimethyl-*o*-aminobenzoic acid	25	0.105	8.51 ± 0.02		
cis-Caronic acid	10.3	0.111	2.61 ± 0.04	8.17 ± 0.02	
	25	0.115	2.30 ± 0.05	8.01 ± 0.03	513,000
cis-3,3-Diphenylcyclopropane-1,2-dicarboxylic acid	10.7	0.115	2.25 ± 0.07	9.04 ± 0.03	
	25	0.115	2.22 ± 0.02	8.96 ± 0.01	5,500,000
Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid	10.5	0.097	2.91 ± 0.02	6.66 ± 0.04	
	24.9	0.095	2.90 ± 0.08	6.54 ± 0.03	4,360

[a] $K_{a_2}{}^M = a_{H^+}[A^{-2}]/[HA^-]$, where a_{H^+} denotes the activity of hydrogen ion and $[A^{-2}]$ the dianion concentration, etc. [b] Sample solution temperature ±0.1°. [c] μ = ionic strength adjusted with reagent grade KNO_3.

Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid was obtained by a procedure patterned after that of Staudinger and Gaule[11] except that, in place of diethyl fumarate, we used maleic anhydride. The product obtained in 40% yield was a white crystalline material, m.p. 229°.

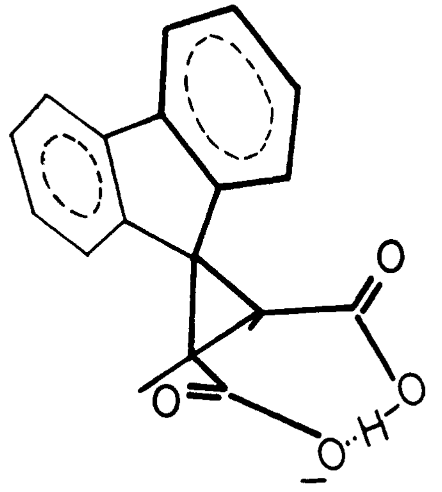


Figure 1. Schematic of the monoanion of spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid showing an intramolecular hydrogen bond between the two carboxyl groups.

Anal.[12] Calcd. for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32; neut. equiv., 140. Found: C, 72.70; H, 4.63; neut. equiv., 140.

A few milligrams of *cis*-cyclopropane-1,2,3-tricarboxylic acid was generously supplied by Dr. Martin G. Ettlinger.[13]

N,N-Dimethyl-*o*-aminobenzoic acid was prepared by the method of Edsall and Wyman[14] to give white crystals, m.p. 71.5° (lit.[14] m.p. 68°).

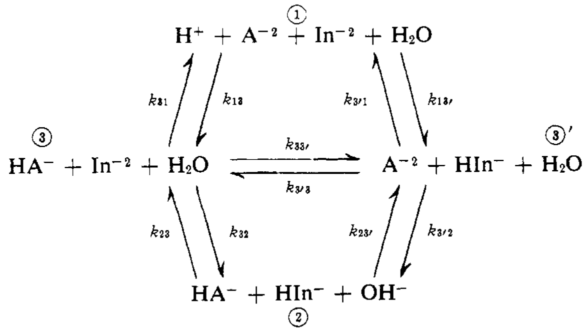
Values of pH and the acid dissociation constants shown in Table I were obtained with a Radiometer TTT-1 titrimeter, a Type G202B glass electrode, Type K4312 calomel electrode, and Type PHA 630T scale expander. Sample solutions were prepared from boiled, distilled water and the ionic strength was adjusted with reagent grade KNO_3. The titrant was carbonate-free 0.1 *N* KOH added under a nitrogen atmosphere with the temperature of the sample maintained to within 0.1° by a Forma-Temp refrigerated, circulating constant temperature bath. Our procedures for calculating the acid dissociation constants are those described by Albert and Serjeant.[15]

Our temperature-jump equipment closely resembles that described by Hammes and Fasella[16] modified for single beam operation.[17] The approximately 8° temperature jump was always effected in solutions thermostated either at 2 or 17°. Samples for the temperature-jump studies were prepared from freshly boiled, distilled, demineralized water. The ionic strength $\mu = 0.1$ *M* was attained in all cases with reagent grade KNO_3, and the pH was adjusted with reagent grade KOH. The two acid–base indicators used in this study were cresol red (*o*-cresolsulfonephthalein) for which the acid p*K* in 0.1 *M* ionic strength aqueous solution was taken to be $pK^M = -\log a_H [In^{-2}]\cdot[HIn^-]^{-1} \approx 8.58$ at 10° and 8.40 at 25°, and phenolphthalein for which $pK^M \approx 9.79$ at 10° and 9.63 at 25°.[18] The monochromator was adjusted to transmit at 580 mμ for those experiments involving cresol red and at 552 mμ for phenolphthalein. In Tables II through IV, we give concentrations and measured relaxation times for our temperature-jump experiments.

The data on N,N-dimethyl-*o*-aminobenzoic acid are included in Table II to permit a comparison of kinetic results obtained on our temperature-jump apparatus with those obtained previously on another at lower temperature (~12°).[19]

Results and Discussion

The complete reaction scheme for our sample systems is[20]



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(11) H. Staudinger and A. Gaule, *Ber.*, **49**, 1957 (1916).

(12) The carbon and hydrogen analyses were performed by the Australian Microanalytical Service.

(13) M. G. Ettlinger and J. Kagan, *Chem. Ind.* (London), 1574 (1962).

(14) J. T. Edsall and J. Wyman, *J. Am. Chem. Soc.*, **57**, 1964 (1935).

(15) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley and Sons, Inc., New York, N. Y., 1962.

(16) G. G. Hammes and P. Fasella, *J. Am. Chem. Soc.*, **84**, 4644 (1962).

(17) G. G. Hammes and J. I. Steinfeld, *ibid.*, **84**, 4639 (1962).

(18) I. M. Kolthoff and C. R. Rosenblum, "Acid-Base Indicators," The Macmillan Co., New York, N. Y., 1937.

(19) M. Eigen and E. M. Eyring, *J. Am. Chem. Soc.*, **84**, 3254 (1962).

(20) M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, **3**, 1 (1964).

where HA^- denotes, for instance, the monoanion of *cis*-caronic acid and In^{-2} the pink form of the phenolphthalein indicator. Since our temperature-jump experiments with all the sample acids except spiro-[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid were run in fairly alkaline solution (see Table II), we would not expect protolysis steps involving the state 1 to make significant contributions to our observed relaxation times.

Eigen, *et al.*,[7] have reported values of the specific rate k_{23} for the reaction $HIn^- + OH^- \rightarrow$ of $\sim 1 \times 10^{10}$ and 4×10^9 M^{-1} sec.$^{-1}$ for phenolphthalein and cresol red, respectively, at 12° and an ionic strength $\mu = 0.1$ adjusted with KNO_3. The phenolphthalein relaxation time is too short for reliable measurement with our temperature-jump apparatus, but confirmatory data on *o*-cresol red is shown in Table III for two temperatures. Both indicators give rise to relaxation times substantially shorter than those reported for our sample acids. This fact still does not permit us to neglect a small indicator contribution when we interpret our experimental relaxation times.

Let us make the reasonable approximation in the case of the experiments with *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid that we are dealing with only two coupled equilibria

$$HA^- + OH^- \underset{k_{3'2}}{\overset{k_{23'}}{\rightleftharpoons}} A^{-2} + H_2O \qquad (1)$$

$$HIn^- + OH^- \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} In^{-2} + H_2O \qquad (2)$$

For simplicity we will omit ionic charges in our subsequent notation. The instantaneous concentration of the monoanion of the sample acid we will denote by HA, and its equilibrium concentration by HA in place of $[HA^-]$. δHA will then be the small deviation of the concentration of the monoanion from its equilibrium value, *i.e.*, $HA \equiv \overline{HA} + \delta HA$, etc. The conservation relations

$$\delta HA = -\delta A \qquad (3)$$

$$\delta HIn = -\ \delta In \qquad (4)$$

and

$$\delta OH = \frac{\delta HA}{1 + \delta In/\delta OH} \equiv \frac{\delta HA}{1 + \alpha} \qquad (5)$$

and the presumption that the indicator equilibrium adjusts very rapidly compared to the sample equilibrium lead to the following expression for the relaxation time τ

$$\tau^{-1} = k_{23'}\left(\frac{\overline{HA}}{1 + \dfrac{\overline{HIn}}{K' + \overline{OH}}} + \overline{OH}\right) + k_{3'2} \qquad (6)$$

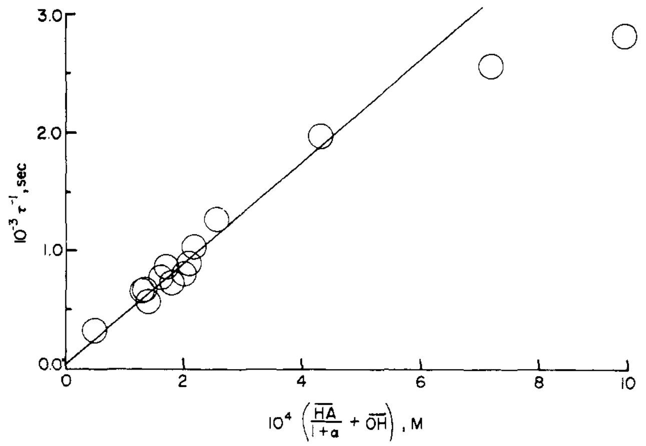

Figure 2. Plot of the reciprocal of the experimental relaxation times *vs.* $(\overline{HA}/(1 + \alpha) + \overline{OH})$ for *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid at 25° in 0.1 M ionic strength solution from the data of Table II.

where $K' \equiv \overline{HIn}\ \overline{OH}/\overline{In}$. Hereafter, the symbol α denotes the factor $\overline{HIn}/(K' + \overline{OH})$. Equation 6 is identical with an equation previously reported.[6] In Figure 2 we have plotted τ^{-1} *vs.* the parenthesized quantity in eq. 6 for the *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid data of Table II. The linearity of the plot provides a check on our assumed reaction order. The deviation at high concentrations probably indicates a change in mechanism. The intercept $k_{3'2} = 50$ sec.$^{-1}$ divided by the slope $k_{23'} = 4.3 \times 10^6$ M^{-1} sec.$^{-1}$ gives an equilibrium constant $K = 1.1 \times 10^{-5}$ M identical with the potentiometrically determined quotient $K_w/\gamma_{H^+}K_{a_2}{}^M$, where $K_w = a_{H^+}a_{OH^-} = 10^{-14.00}$, $\gamma_{H^+} = 0.83$, and from Table I $K_{a_2}{}^M = a_{H^+}\overline{A}/\overline{HA} = 10^{-8.96}$ M for $\mu = 0.1$ M at 25°. Since the potentiometric dissociation constant was used in calculating the concentrations, this identity of equilibrium constants is less significant than the linearity of the plot. The values of $k_{23'}$ (cor.) shown in Table II for the diphenyl acid were calculated from

$$\tau^{-1} = k_{23'}\left(\frac{\overline{HA}}{1 + \alpha} + \overline{OH} + \frac{K_w}{\gamma_{H^+}K_{a_2}{}^M}\right) \qquad (7)$$

and the values of $k_{23'}$ (uncor.) from this same equation with α omitted. There is a definite tendency for α to overcorrect when the indicator concentration is large, *i.e.*, when α exceeds about 0.5. With or without the correction factor, the precision of the calculated $k_{23'}$ is about the same. Both $k_{23'}$ (cor.) $= 4.30 \times 10^6$ M^{-1} sec.$^{-1}$ and $k_{23'}$ (uncor.) $= 3.61 \times 10^6$ M^{-1} sec.$^{-1}$ for *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid at 298°K. are substantially smaller than previously reported values for two other intramolecularly hydrogen-bonded monoanions of dicarboxylic acids: maleic acid, 7.4×10^8 M^{-1} sec.$^{-1}$; and di-*n*-propylmalonic acid, 5.3×10^7 M^{-1} sec.$^{-1}$ (presumably at 285°K.).[6] These acids have values of K_{a_1}/K_{a_2} of 20,400 and 155,000, respectively. Neither the monoanion of *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid nor that of di-*n*-propylmalonic acid is conjugated so that conjugation in the monoanion of an intramolecularly hydrogen-bonded acid may make a less important contribution to the stability of such a bond than has been inferred.[21]

Temperature-jump experiments were run with *cis*-caronic acid in total concentrations ranging from 1 to 40×10^{-4} M at pH values in the neighborhood of 9 using phenolphthalein as indicator. Employing eq. 7 again with the appropriate equilibrium constants, we calculate the specific rates $k_{23'} = (5.50 \pm 0.66) \times 10^7$ and $(2.26 \pm 0.34) \times 10^7$ M^{-1} sec.$^{-1}$ for 25 and 10°,

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[21] M. Eigen and G. G. Hammes in "Advances in Enzymology," Vol. 25, F. F. Nord, Ed., Interscience Publishers, New York, N. Y., 1963, p. 22.

Table II. Relaxation Spectra and Rate Constants for the Reaction $HA + OH \overset{k_{23}'}{\rightleftharpoons} A + H_2O$

C_0, 10^{-4} M[c]	C_0', 10^{-5} M[d]	pH	$\overline{OH}$, 10^{-5} M	$\overline{HA}$, 10^{-4} M[e]	$\overline{HIn}$, 10^{-5} M[f]	α[g]	τ, msec.[h]	k_{23}'(uncor.),[i] 10^6 M^{-1} sec.$^{-1}$	k_{23}' (cor.),[j] 10^6 M^{-1} sec.$^{-1}$
HA ≡ *cis*-3,3-Diphenylcyclopropane-1,2-dicarboxylic Acid Monoanion, 25°[a] (phenolphthalein)[b]									
1.0	3.0	9.30	2.41	0.31	2.05	0.27	3.10	4.90	5.40
5.0	4.5	9.30	2.41	1.57	3.07	0.41	1.48	3.52	4.60
5.0	3.5	9.50	3.82	1.12	2.01	0.22	1.50	4.14	4.75
5.0	1.0	9.55	4.27	1.02	0.55	0.06	1.75	3.68	3.81
7.0	3.8	9.30	2.41	2.20	2.59	0.34	0.970	4.04	5.17
7.0	3.0	9.50	3.82	1.57	1.72	0.19	1.16	4.18	4.76
7.0	1.0	9.53	4.07	1.48	0.06	0.06	1.372	3.74	3.80
7.3	4.4	9.30	2.41	2.28	3.00	0.30	1.24	3.06	3.83
7.3	2.0	9.90	9.58	0.75	0.70	0.05	1.30	4.24	4.30
7.3	5.0	9.10	1.52	3.06	3.86	0.58	1.125	2.67	4.04
10.	4.0	9.30	2.41	3.14	2.73	0.36	0.790	3.63	4.82
20.	2.3	9.50	3.82	4.48	1.32	0.15	0.508	3.97	4.48
30.	4.0	9.30	2.41	9.40	2.73	0.36	0.390	2.64	3.54
40.	4.0	9.30	2.41	12.5	2.73	0.36	0.355	2.19	2.96
								Av. 3.61 ± 0.57	4.30 ± 0.55
3.0	20.	8.8	0.76	1.78	17.4	2.94	1.56	3.27	10.03
7.0	19.	8.8	0.76	4.14	16.5	2.74	0.90	2.57	8.65
7.3	25.	8.9	0.96	3.88	21.1	3.45	1.05	2.32	8.65
7.3	20.	8.7	0.60	4.70	17.9	3.11	0.97	2.12	7.85
HA ≡ *cis*-3,3-Diphenylcyclopropane-1,2-dicarboxylic Acid Monoanion, 10° (phenolphthalein)									
1.1	1.0	9.68	1.68	0.21	0.56	0.15	5.67	2.20	2.27
2.0	1.0	9.26	6.40	0.796	0.78	0.28	4.82	2.30	2.83
3.8	1.0	9.65	1.57	0.81	0.58	0.16	4.24	1.70	1.85
5.0	1.0	9.83	2.38	0.76	0.48	0.10	3.62	1.95	2.05
7.0	1.0	9.83	2.38	1.06	0.48	0.10	2.01	2.89	3.06
8.0	1.0	9.66	1.61	1.67	0.58	0.15	2.55	1.74	2.02
10.2	1.0	9.64	1.53	2.2	0.59	0.16	2.11	1.70	1.91
15.0	1.0	9.65	1.57	3.18	0.58	0.16	2.20	1.35	1.54
20.0	1.0	9.35	7.88	7.0	0.74	0.25	1.12	1.25	1.56
								Av. 1.93 ± 0.39	2.14 ± 0.38
HA ≡ *cis*-Caronic Acid Monoanion, 25° (phenolphthalein)									
								10^7 M^{-1} sec.$^{-1}$	10^7 M^{-1} sec.$^{-1}$
1.0	3.0	9.30	2.41	0.049	2.04	0.27	0.545	6.08	6.29
3.0	1.0	9.23	2.05	0.170	0.72	0.10	0.435	5.94	6.20
5.0	1.0	9.33	2.57	0.228	0.667	0.09	0.332	6.06	6.29
7.0	1.0	9.05	1.35	0.585	0.791	0.12	0.290	4.71	5.17
9.0	1.0	9.00	1.21	0.836	0.810	0.13	0.255	4.04	4.48
11.0	1.0	8.94	1.05	1.160	0.807	0.13	0.201	3.90	4.34
20.0	5.0	9.30	2.41	0.975	3.40	0.45	0.176	4.64	5.49
25.0	4.0	9.00	1.21	2.32	3.24	0.51	0.110	3.71	5.57
42.5	4.0	9.30	2.41	2.08	2.72	0.36	0.113	3.79	4.96
								Av. 4.76 ± 0.84	5.49 ± 0.66
HA ≡ *cis*-Caronic Acid Monoanion, 10° (phenolphthalein)									
3.0	1.0	8.90	0.279	7.71	0.885	0.36	1.055	1.96	2.60
5.0	1.0	8.93	0.299	7.41	0.879	0.36	0.675	1.91	2.55
7.0	1.0	9.05	0.394	8.16	0.845	0.33	0.633	1.84	2.40
9.0	1.0	9.04	0.385	10.70	0.849	0.33	0.535	1.69	2.21
12.0	1.0	8.93	0.299	17.80	0.876	0.35	0.546	1.01	1.36
								Av. 1.68 ± 0.27	2.26 ± 0.34
HA ≡ Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic Acid Monoanion, 25° (cresol red)									
								10^8 M^{-1} sec.$^{-1}$	10^8 M^{-1} sec.$^{-1}$
3.0	1.0	7.87	0.0894	0.134	0.765	2.02	0.218	3.21	8.53
5.0	1.0	7.84	0.0834	0.238	0.776	2.08	0.196	2.06	5.93
7.0	1.0	7.84	0.0834	0.333	0.776	2.08	0.133	2.20	6.42
HA ≡ Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic Acid Monoanion, 10° (cresol red)									
3.0	1.0	7.98	0.0336	0.137	0.800	4.76	0.467	1.53	7.81
5.0	1.0	7.98	0.0336	0.228	0.800	4.76	0.334	1.30	6.96
7.0	1.0	8.00	0.0352	0.305	0.793	4.68	0.296	1.10	5.92
HA ≡ *cis*-Cyclopropane-1,2,3-tricarboxylic Acid Dianion, 25° (phenolphthalein)									
								10^6 M^{-1} sec.$^{-1}$	10^6 M^{-1} sec.$^{-1}$
5.63	3.5	9.50	3.81	4.36	1.85	0.21	0.792	2.13	2.48
20.0	6.0	9.50	3.81	15.90	3.17	0.35	0.405	1.41	1.84

Table II (*Continued*)

C_0, 10^{-4} M^c	C_0', 10^{-5} M^d	pH	$\overline{\text{OH}}$, 10^{-5} M	HA, 10^{-4} M^e	HIn, 10^{-5} M^f	α^g	τ, msec.^{h}	$k_{23'}$(uncor.), 10^8 M^{-1} sec.$^{-1}$	$k_{23'}$(cor.),^{j} 10^8 M^{-1} sec.$^{-1}$
HA ≡ N,N-Dimethyl-*o*-aminobenzoic Acid, 25° (phenolphthalein)									
3.0	1.0	9.12	1.59	0.592	0.765	0.11	0.0712	1.78	1.92
5.0	1.0	9.22	2.00	0.815	0.720	0.10	0.0605	1.57	1.68
3.0	2.0	9.00	1.20	0.74	1.62	0.25	0.114	0.98	1.31
5.0	2.0	8.83	0.82	1.62	1.73	0.29	0.0568	1.01	1.23

[a] Sample solution temperature immediately following capacitor discharge. [b] Indicator present in sample solution. [c] Total sample acid concentration, moles/l. [d] Total indicator concentration, moles/l. [e] Concentration of the protonated form of the sample acid calculated from the simultaneous equations $C_0 \approx \text{HA} + \overline{\text{A}}$ and $K_a{}^M = 10^{-\text{pH}}\overline{\text{A}}/\text{HA}$. [f] Concentration of protonated form of indicator, moles/l. [g] Correction factor calculated from $\alpha = \text{HIn}/(K' + \overline{\text{OH}})$. [h] Observed relaxation time, msec., in 0.1 M ionic strength solution. [i] Rate constant calculated from eq. 7 neglecting α. [j] Rate constant calculated from eq. 7.

Table III. Relaxation Spectra and Rate Constants for the Reaction $\text{HIn} + \overline{\text{OH}} \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} \overline{\text{In}} + H_2O$ Involving *o*-Cresol Red

C_0, 10^{-6} M^a	pH	$\overline{\text{OH}}$, 10^{-6} M^b	HIn, 10^{-6} M^c	τ, μsec.^{d}	Temp., °C.^{e}	k_{23},^{f} 10^9 M^{-1} sec.$^{-1}$	k_{32},^{g} 10^3 sec.$^{-1}$
4.0	7.70	0.604	3.31	28	25	6.03	12.1
4.0	8.68	1.68	1.78	56	10	4.05	3.74

[a] Total concentration of *o*-cresol red in all forms, moles/l. [b] Hydroxide ion concentration $= K_w/\gamma_{OH^-} \cdot 10^{-\text{pH}}$, where $\gamma_{OH^-} \approx 0.83$ according to extended Debye–Hückel theory in 0.1 M ionic strength aqueous solution, $pK_w = 14.00$ at 25° and $pK_w = 14.54$ at 10°. [c] Concentration of protonated form of *o*-cresol red calculated with $pK_{\text{HIn}} = -\log \overline{\text{HIn}}/\text{HIn} = 8.3$ and 8.5 at 10 and 25°, respectively. [d] Observed relaxation time, msec. [e] Temperature of sample solution immediately after capacitor discharge. [f] Rate constant calculated from $\tau^{-1} = k_{23}(\text{HIn} + \overline{\text{OH}} + K_w/\gamma^2 K_{\text{HIn}})$. [g] Rate constant of back reaction assuming H_2O constant.

Table IV. Relaxation Spectra and Rate Constants for the Reaction $\text{HA} + \overline{\text{In}} \underset{}{\overset{k_{33'}}{\rightleftharpoons}} \overline{\text{A}} + \text{HIn}$, where HIn is the Protonated Form of *o*-Cresol Red

C_0, 10^{-5} M^a	C_0', 10^{-5} M^b	pH	$\overline{\text{HA}}$, 10^{-5} M^c	$\overline{\text{HIn}}$, 10^{-5} M^d	τ, msec.^{e}	$k_{33'}$,^{f} M^{-1} sec.$^{-1}$
HA ≡ *cis*-Caronic Acid Monoanion, 25°						
5.0	5.0	7.65	3.48	4.22	0.305	4.90×10^7
5.0	5.0	7.14	4.20	4.73	0.275	5.33×10^7
8.0	8.0	7.26	6.80	7.44	0.136	6.66×10^7
10.0	10.0	7.15	7.25	9.45	0.130	5.20×10^7
HA ≡ Spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic Acid Monoanion, 25°						
5.0	5.0	7.20	0.898	4.69	0.144	5.17×10^8
6.9	4.0	6.96	1.89	3.81	0.078	6.18×10^8
8.0	8.0	7.23	1.52	7.48	0.120	4.65×10^8
10.0	10.0	7.33	1.40	9.18	0.100	4.03×10^8

[a] Total concentration of sample acid, moles/l. [b] Total concentration of *o*-cresol red, moles/l. [c] Concentration of sample acid monoanion, moles/l. [d] Concentration of protonated form of *o*-cresol red, moles/l. [e] Observed relaxation time, msec. [f] Rate constant calculated from eq. 9.

respectively. As was to be expected from the potentiometrically determined ratios K_{a_1}/K_{a_2} (see Table I), these larger values of $k_{23'}$ for *cis*-caronic acid than for *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid indicate a weaker intramolecular hydrogen bond in the monoanion of *cis*-caronic acid. These values of $k_{23'}$ for *cis*-caronic acid should be valid for the reaction of eq. 1 providing that competing bases such as In^{-2} are in lower concentration than OH^-. This condition is met by almost all of the experiments reported in Table II for *cis*-caronic acid.

Experiments involving *cis*-caronic acid were also run at or near pH 7 with *o*-cresol red as indicator. Results are shown in Table IV. At pH 7 we have a situation where $\overline{\text{In}} \gg \overline{\text{OH}},\text{H}$, and the equilibrium

$$\text{HA}^- + \text{In}^{-2} \underset{k_{3'3}}{\overset{k_{33'}}{\rightleftharpoons}} \text{A}^{-2} + \text{HIn}^- \qquad (8)$$

is primarily responsible for the experimental relaxation time. Thus we may write[17]

$$\frac{1}{\tau} \simeq k_{33'}(\text{HA} + \overline{\text{In}}) + k_{3'3}(\overline{\text{A}} + \text{HIn}) \qquad (9)$$

Additional small terms that we can neglect are given by Castellan's more complete eq. 60.[22] The value of $k_{33'}$ at 25° is about 5×10^7 M^{-1} sec.$^{-1}$ (see Table IV). These rate constants permit us to make a kinetic comparison of the strength of the hydrogen bond in the monoanion of *cis*-caronic acid with that in the monoanion of spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid for which a determination of $k_{23'}$ is virtually impossible. In principle, it is possible to determine $k_{23'}$ and $k_{3'2}$ for the latter acid from an equation[23] for the two relaxation times associated with the equilibria connecting states 2, 3, and 3′ of our reaction scheme and the rate constants $k_{33'}$, $k_{3'3}$, k_{23}, and k_{32} that are available for the spiro acid and *o*-cresol red using the data of Tables III and IV. In practice, however, quite large changes in assumed values of $k_{23'}$ do little to improve agreement between the calculated and the observed relaxation times. The value of $k_{33'} \cong 5 \times 10^8$ M^{-1} sec.$^{-1}$ at 25° for the proton exchange between the spiro acid and *o*-cresol red is definitely larger than that for the *cis*-caronic acid–*o*-cresol red combination. This is kinetic evidence for a much weaker intramolecular hydrogen bond in the monoanion of spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid than in that of *cis*-caronic acid.

A value of $k_{23'} = 2 \times 10^6$ M^{-1} sec.$^{-1}$ was calculated from the data of Table II for the reaction

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(22) G. W. Castellan, *Ber. Bunsenges. Physik. Chem.*, 67, 905 (1963).
(23) Reference 20, eq. 16, 17, and 28.

Table V. Approximate Values of E_a, ΔH^*, and ΔS^* at 298°K.

HA⁻ ≡ monoanion of	$k_{23'}$, M^{-1} sec.$^{-1}$		E_a, kcal./mole	ΔH^*, kcal./mole	ΔS^*, cal./mole deg.
	25°	10°			
	$HA^- + OH^- \xrightarrow{k_{23'}} A^{-2} + H_2O$				
3,3-Diphenylcyclopropane-1,2-dicarboxylic acid	$(4.30 \pm 0.55) \times 10^6$	$(2.14 \pm 0.38) \times 10^6$	7.8	7.2	−4.0
cis-Caronic acid	$(5.49 \pm 0.66) \times 10^7$	$(2.26 \pm 0.34) \times 10^7$	10.0	9.4	+8.5
	$A^{-2} + H_2O \xrightarrow{k_{32'}} HA^- + OH^-$				
	$k_{3'2}$, sec.$^{-1}$				
3,3-Diphenylcyclopropane-1,2-dicarboxylic acid	47.1 ± 6.0	9.06 ± 1.7	18.3	17.7	+8.9
cis-Caronic acid	67.9 ± 9.0	11.7 ± 1.9	19.6	19.0	+11.9

$$HA^{-2} + OH^- \overset{k_{23'}}{\rightleftharpoons} A^{-3} + H_2O \qquad (10)$$

where HA^{-2} is the dianion of *cis*-cyclopropane-1,2,3-tricarboxylic acid. The value of pK_{a_3} used was 10.0 (see ref. 11). We had too little of this acid for a redetermination of its pK values under our experimental conditions, much less a careful kinetic study over a wide range of concentrations. This value of $k_{23'}$ is significantly smaller than that for *cis*-caronic acid. Such a decrease is qualitatively predictable: in the tricarboxylic acid both a steric and an electronic effect must be considered, whereas in *cis*-caronic acid only a steric effect can strengthen the intramolecular hydrogen bond.

Since we have determined rate constants at two temperatures, it is possible, in principle, to report values of E_a, ΔH^*, and ΔS^*.[24] This we have done for the equilibrium $HA^- + OH^-$ $A^{-2} + H_2O$ with two of the acids (see Table V). Positive mean values of ΔS^* for the reverse reaction suggest a melting away of water molecules from the highly charged dianion as the intramolecular hydrogen bond reforms,[25] but an estimate of the number of melted water molecules based on such crude values of ΔS^* would be highly suspect.

The peaking in the strength of the monoanion intramolecular hydrogen bond in the series *cis*-caronic acid, *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid, spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid with the 3,3-diphenyl substitution is interesting since the attainment of such a maximum has been predicted by McCoy and Nachtigall[26] for the case where the *cis*-carboxyl groups are spread apart slightly more than in *cis*-caronic acid. The rigidity and the stereochemical positioning of the large 3,3-substituent in the spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid of Figure 1 apparently overdo this spreading of the *cis*-carboxyl groups with dramatic weakening of the intramolecular hydrogen bond as evidenced both by the downward shift in pK_{a_2} and by the increase in $k_{33'}$ for the spiro acid.

It is interesting to compare the experimental $k_{33'} = 5 \times 10^8$ M^{-1} sec.$^{-1}$ for the spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid with the theoretical value of 3×10^9 M^{-1} sec.$^{-1}$ estimated from Debye's equation[27] for the diffusion-controlled reaction between HA^- and In^{-2} in water at 25°. These two numerical values might be even closer if we knew what positive fraction the theoretical rate constant should be multiplied by to account for steric interference. This steric decrease in the theoretical $k_{33'}$ would be partially cancelled by the effect of the ionic strength.[28] In any case, the experimental and theoretical values of $k_{33'}$ are close enough to indicate little or no intramolecular hydrogen bonding in the monoanion of this acid, in good agreement with the conclusion of Eberson and Wadsö[3] that intramolecular hydrogen bonding can be neglected as a factor in determining ΔpK for dicarboxylic acids when $\Delta pK \leq 4$.

Goodman and Eastman[29] have shown that the geometric relationship between a cyclopropane ring which is conjugated to an aromatic system and the aromatic ring itself are of little consequence in terms of the electronic effects transmitted between them. To a first approximation, then, the electronic effects of the aromatic nuclei in the monoanions of 3,3-diphenylcyclopropane-1,2-dicarboxylic acid and spiro[cyclopropane-1,9′-fluorene]-*cis*-2,3-dicarboxylic acid will be the same, and any differences in the intramolecular hydrogen bonding would be attributable to a steric effect. The striking difference in intramolecular hydrogen-bond strength in the monoanions of these two acids clearly indicates a great difference in the geometrical relationship to one another of the benzene nuclei in the two kinds of ions. In the spiro case, the two benzene nuclei must be coplanar and at right angles to the plane of the cyclopropane ring. The preferred orientation of the phenyl groups in the 3,3-diphenylcyclopropane-1,2-dicarboxylic acid monoanion is almost certainly at 90° to their orientation in the spiro compound. Furthermore, it may well be that free rotation of the phenyl groups in the 3,3-diphenyl monoanion is restricted to the point where an appropriately substituted derivative may be resolvable into its optical enantiomers. While other physical methods such as n.m.r. or o.r.d. might yield information regarding the approximate orientation of the phenyl groups in the 3,3-diphenyl compound, only an X-ray analysis of the mono salt of a heavy metal could establish the exact orientation of these phenyl groups.

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