for 1.5 h more, and the mixture was cooled, diluted with water, and neutralized with $NaHCO_3$ solution. The solid separated was filtered, washed well with water, and air-dried. The crude product on recrystallization from benzene–methanol mixture afforded 170 mg (89.9%) of light yellow solid: mp 246–247 °C; ^1H NMR (DMSO-d_6) δ 7.28–7.48 (m, 2 H), 7.60–7.80 (m, 4 H), 8.28 (t, 2 H), 8.76 (s, 1 H), 9.28 (d, 1 H), 10.24 (s, 1 H). Anal. Calcd for $C_{17}H_{11}NO$: C, 83.2; H, 4.5; N, 5.7. Found: C, 83.1; H, 4.3; N, 5.5.

9-Hydroxybenz[*c*]acridine (6b). **5b** (191.1 mg, 7.3 mmol) on demethylation with 48% HBr as mentioned above for **6a** afforded 175 mg (96.8%) of **6b**: mp 208–211 °C; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 7.3–7.9 (m, 6 H), 8.1–8.2 (t, 2 H), 8.4 (s, 1 H), 9.3–9.4 (d, 1 H), 9.8 (s, 1 H); MS, *m/e* 245 (M^+).

3,4-Dioxo-3,4-dihydrobenz[*c*]acridine (7). To a stirred ice cooled solution of Fremy's salt (550 mg, 2.05 mmol) in 75 mL of water was added 0.16 M KH_2PO_4 buffer (6–8 mL). To this was added a solution of the phenol **6a** (100 mg, 0.408 mmol) in 25 mL of methanol–THF mixture and stirring continued for 2 h at 0–15 °C. The mixture was left in refrigerator for overnight. The green solid separated was filtered, washed well with water, and air-dried: yield, 90 mg (85%); mp of the crude product 266–268 °C dec; IR (Nujol) ν_{max} 1608, 1637, 1658 cm^{-1}.

8,9-Dioxo-8,9-dihydrobenz[*c*]acridine (8). The phenol **6b** (110.6 mg, 0.45 mmol) on oxidation with Fremy's salt (470 mg, 1.75 mmol) in a methanol (20 mL) and water (15 mL) mixture, after usual workup, afforded 88.4 mg (75.9%) of the quinone **8** as a reddish brown solid: mp >300 °C; IR (Nujol) ν_{max} 1675, 1700 cm^{-1}; MS, *m/e* 259 (M^+).

3,4-Dihydro-3,4-dihydroxybenz[*c*]acridine (9). To a stirred suspension of the quinone **7** (30 mg, 0.116 mmol) in 15 mL of ethanol was added 75 mg of $NaBH_4$ in four batches. Stirring was continued for 48 h at room temperature in presence of air, ethanol was evaporated at room temperature, and the residue was diluted with water and extracted with ethyl acetae. The usual workup and removal of solvent gave 28 mg of crude solid. This on purification by preparative TLC (silica gel) using ethyl acetate–petroleum ether mixture as eluent afforded 6 mg (19.7%) of the dihydrodiol **9** as a yellow solid (mp and mixed mp with authentic sample[6] was 200–201 °C) and 22 mg of phenol **6a** (mp and mixed mp with previous sample 246–247 °C). The dihydrodiol **9** was also characterized by ^1H NMR ($CDCl_3$ + DMSO-d_6): δ 4.47 (m, 1 H, H-3), 4.85 (m, 1 H, H-4 6.22 (m, 1 H, H-2), 7.5–8.3 (m, 7 H, H-1 and H-5, 6, 8–11), 9.09 (s, 1 H, H-7) ($J_{1,2}$ = 10 Hz) [lit.[6] ^1H NMR (DMSO-d_6, D_2O) δ 9.13 (s, 1 H, H-7), 7.9 (d, 1 H, H-1), 7.4–8.3 (m, 6 H, H-5, 6, 8–11), 6.28 (dd, 1 H, H-2), 4.89 (m, 1 H, H-4), 4.50 (m, 1 H, H-3) ($J_{1,2}$ = 9.9 Hz, $J_{2,3}$ = 2.7 Hz, $J_{3,4}$ = 10.2 Hz)].

8,9-Dihydroxy-8,9-dihydrobenz[*c*]acridine (10). The quinone **8** (100 mg, 0.4 mmol) in ethanol (6 mL) on reduction with $NaBH_4$ (82 mg) as per conditions mentioned above afforded 80 mg (80%) of the dihydrodiol **10**. It was purified by preparative TLC (silica gel; ethyl acetate–petroleum ether): mp 190–191 °C (lit.[7] mp 177–179 °C). The dihydrodiol **10** was characterized by ^1H NMR and its diacetate (pyridine/Ac_2O) showed a spot identical with that of an authentic sample[7] in TLC: ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 4.6 (d, 1 H), 5.0 (d, 1 H), 6.4 (d, 1 H), 6.8 (d, 1 H), 7.6–8.0 (m, 5 H), 8.3 (s, 1 H), 9.2–9.3 (d, 1 H) [lit.[7] ^1H NMR δ 4.46 (H-9), 4.88 (H-8), 6.43 (H-10), 6.80 (H-11), 7.66–8.14 (5 H), 8.38 (H-7), 9.06–9.28 (H-1).

Acknowledgment. We express our deep sense of gratitude to Dr. M. Schafer-Ridder, West Germany, for providing us with 1 mg of a sample of the dihydrodiol **9** for comparison and also to Dr. R. E. Lehr, U.S.A., for sending us few milligrams of the diacetae of the compound **10**. Thanks are also due to Dr. P. N. Moza, West Germany, for a few mass spectra and Dr. Malay Ghosh, U.S.A., for the NMR of **10**. C.S.I.R., New Delhi, deserves special thanks for financial assistance.

Registry No. **1a**, 1078-19-9; **1b**, 529-34-0; **2a**, 72019-91-1; **2b**, 3262-03-1; **3a**, 111378-92-8; **3b**, 111378-93-9; **4a**, 72019-93-3; **4b**, 111351-44-1; **5a**, 111351-45-2; **5b**, 111351-46-3; **6a**, 111351-47-4; **6b**, 111351-48-5; **7**, 111351-49-6; **8**, 111378-94-0; **9**, 77305-76-1; **10**, 85617-30-7; $PhNH_2$, 62-53-3; *p*-anisidine, 104-94-9.

^{13}C NMR Investigations on the Structure of α-Keto Acids in Aqueous Solution

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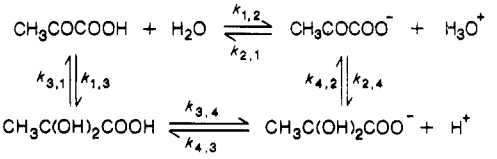
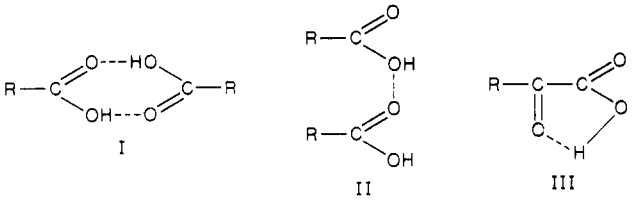
α-Keto acids play a central role as intermediates in the metabolism of carbohydrates and proteins, and their structure and reactivity under physiological conditions are therefore of interest. Pyruvic acid exists in aqueous solution as a mixture of four species: the hydrated and nonhydrated undissociated acids and anions.[1-4] In the equilibria among these species, $k_{1,2}$, $k_{2,1}$, $k_{3,4}$, and $k_{4,3}$ are fast on the NMR time scale relative to the ^{13}C chemical shifts.



The thermodynamics and kinetics of the hydration of pyruvic acid have been widely investigated, and the hydration equilibrium has been determined by UV absorption measurements at 320 nm and by ^1H NMR spectroscopy.[1,2,4,5]

Unsubstituted organic acids dimerize in nonpolar (I) and polar (II) solvents, whereas α-keto acids exist largely as monomers owing to formation of an intramolecular hydrogen bond (III) with the α-carbonyl group.[6-8] In aqueous solution, α-keto acids exist as monomers.



We here report on the ^{13}C chemical shifts of pyruvic acid and 2,2-dihydroxypropanoic acid in the pD range 2.0–5.5. The change in the hydration equilibrium was determined from the areas of the methyl C peaks of both molecules. Furthermore, the ^{13}C chemical shifts indicate an unusually high sensitivity of the α-carbon atom of pyruvic acid toward the prototropic equilibrium of the neighboring carboxyl group.

The ^{13}C NMR spectrum of a solution of pyruvic acid in D_2O at pD 2.0 contains six peaks which can be assigned to the carbon atoms of pyruvic acid and 2,2-dihydroxypropanoic acid. The ^{13}C chemical shifts in the pD range 2.0–5.5 ppm indicate a shift of the hydration equilibrium toward the keto form with increasing pD. This shift was determined from the ratio of the methyl carbon peak areas, which was 1.18 at pD 2.0 and 0.17 at pD 4.0 for 0.5 M pyruvic acid. The literature reports peak area ratios of 1.77 for 0.4 M pyruvic acid[9] and 1.67 for 2.0 M pyruvic acid,[2] in both cases for the undissociated acid.

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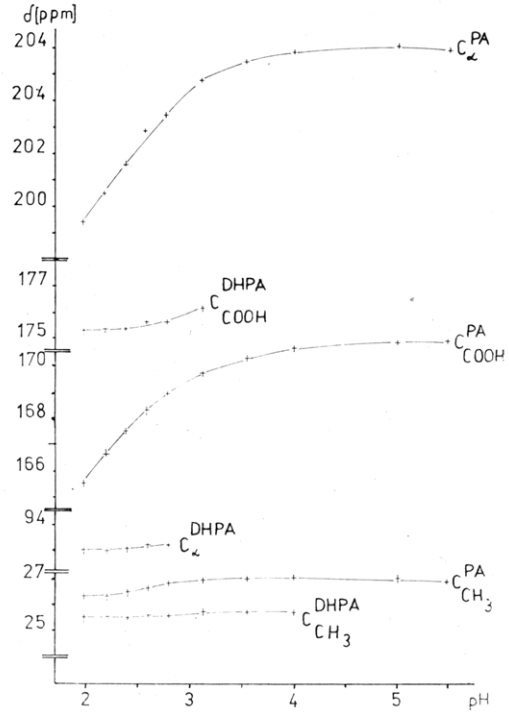


Figure 1. pD dependence of the ^{13}C chemical shifts of pyruvic acid (PA) and 2,2-dihydroxypropanoic acid (DHPA): pyruvic acid, 0.5 M in D_2O; T = 300 K.

The ^{13}C chemical shifts of pyruvic acid and 2,2-dihydroxypropanoic acid as functions of pH are shown in Figure 1. We obtained pK_a values for pyruvic acid and 2,2-dihydroxypropanoic acid by plotting $1/\Delta\delta$ vs $[OH^-]$.

	this work	lit.[10]	lit.[2]
pK_a (pyruvic acid)	1.56	1.5	2.07
pK_a (2,2-dihydroxypropanoic acid)	2.79	3.0	3.06

As can be seen from Figure 1, the deprotonation of pyruvic acid is accompanied by downfield shifts of the α-carbon and carboxyl carbon peaks, with $\Delta\delta_{C\alpha} = 1.2\Delta\delta_{C(COOH)}$. Generally, the deprotonation of carbon acids is signaled by a downfield shift in the carboxyl carbon peak. Yet the downfield shifts of the α- and β-carbon peaks in alkanoic acids are smaller than that of the carboxyl carbon.[11,12] In the α,β-unsaturated acrylic acid, the α-carbon downfield shift is also larger than that of the carboxyl carbon with transition to the anion.[13] This effect could be attributed to mesomeric influences or to formation of an intramolecular hydrogen bond, which is known to be formed in pyruvic acid in nonaqueous media.[6-8]

In order to investigate the effect of an intramolecular metal bridge on the ^{13}C chemical shifts of the carbon atoms

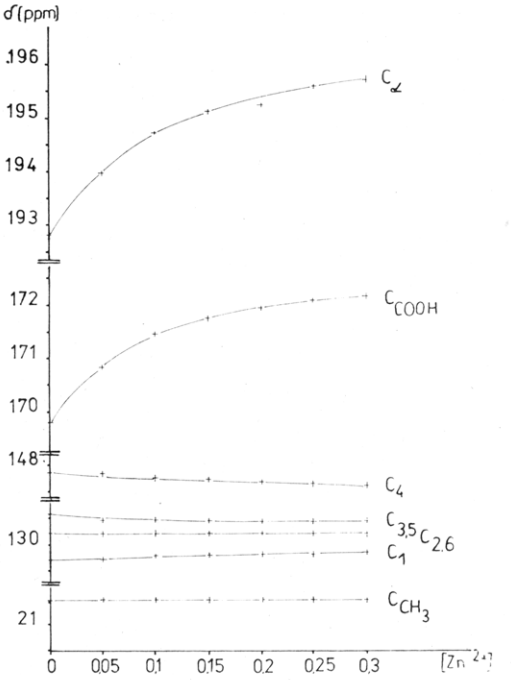


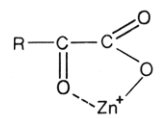
Figure 2. Zn^{2+} dependence of the ^{13}C chemical shifts of (4-methylphenyl)glyoxylic acid: (4-methylphenyl)glyoxylic acid, 0.1 M in D_2O; pD 1.9; T = 300 K.

Table I. NOE of the C Atoms of (4-Methylphenyl)glyoxylic Acid[a] in the Presence of Metal Ions Zn^{2+}, K^+, and Li^+

	NOE			
C atom	for free acid	for Zn complex	for anion (K salt)	for anion (Li salt)
C_α	3.0	1.9	1.48	1.4
C_{COOH}	2.0	0.9	1.70	1.3
C_4	2.8	2.8		2.7
$C_{3,5}$	2.5	2.5		2.4
$C_{2,6}$	2.4	2.5		2.4
C_1	1.4	1.5	1.8	1.7
C_{CH_3}	2.6	2.5	2.6	2.4

[a] (4-Methylphenyl)glyoxylic acid, 0.1 M in H_2O; pH 0.15 for the free acid; the Zn complex, pH 7.0, for the anion.

in an α-keto acid, the chemical shifts of (4-methylphenyl)glyoxylic acid were measured in the presence of Zn^{2+} ions. Whereas pyruvic acid can undergo self-condensation in the presence of divalent metal ions,[14] (4-methylphenyl)glyoxylic acid forms a Zn bridge. Figure



2 shows that the α-carbon and carboxyl carbon atoms of (4-methylphenyl)glyoxylic acid experience strong downfield ^{13}C chemical shifts as a function of Zn^{2+} concentration.

NOEs measured in the presence of monovalent metal ions (K^+ and Li^+) indicated that no intramolecular bridge was formed (Table I). A comparison of the NOE of (4-methylphenyl)glyoxylic acid in the presence and absence of Zn^{2+} ions allows a localization of the effect of the metal ion. Only the α-carbon and the carboxyl carbon showed a distinct decrease of the NOE in the presence of Zn^{2+} ions. Since Zn^{2+} lowers the NOE of both carbon atoms to the same degree, it appears that the metal ion replaces one or several protons within the range of the bridge between the

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Table II. NOE and T_1 Values of Pyruvic Acid[a] and 2,2-Dihydroxypropanoic Acid in D_2O

C atom	T_1, s	NOE
Pyruvic Acid		
C_{CH_3}	3.75	3.0
C_α	36.16	2.3
C_{COOH}	38.08	1.32
2,2-Dihydroxypropanoic Acid		
C_{CH_3}	3.22	1.57
C_α	28.20	1.33
C_{COOH}	31.68	0.90

[a] Pyruvic acid, 0.5 M in D_2O; pD 0.9; T = 300 K.

Table III. Correlation Times and Rotation Barriers for the Methyl Groups of Pyruvic Acid and 2,2-Dihydroxypropanoic Acid Calculated for the Isotropic Approximation Case of the Woessner Equation

	pyruvic acid	2,2-dihydroxypropanoic acid
overall correlation time of the methyl group, s	4.16×10^{-12}	1.40×10^{-12}
correlation time for the lattice molecule, s	15.57×10^{-12}	5.78×10^{-12}
overall diffusions coefficient, s^{-1}	4.00×10^{10}	11.88×10^{10}
diffusion coefficient for the lattice molecule, s^{-1}	10.70×10^{9}	28.83×10^{9}
inner diffusion coefficient of the methyl group, s^{-1}		
(a) stochastic diffusion	1.37×10^{11}	1.55×10^{12}
(b) methyl jump	2.00×10^{11}	2.14×10^{12}
rotation barrier for the methyl group, kJ/M		
(a) stochastic diffusion	10.4	4.3
(b) methyl jump	10.5	4.5

α-carbon and the carboxyl carbon. This is an additional argument for the existence of an intramolecular hydrogen bond in α-keto acids in aqueous solution.

Although intermolecular hydrogen bonding with the solvent should compete strongly with intramolecular bonding, such intramolecular hydrogen bonds in aqueous solution have been established in such molecules as cyclic nucleotides by thermodynamic and kinetic measurements.[15] ^{13}C NMR has established intramolecular hydrogen bonding in α-keto acids as yet only in nonpolar solvents. Our investigations show that NMR observations of the α-carbon of such acids in aqueous solution also indicate the formation of an intramolecular hydrogen bond, in particular by chemical shift changes and NOE.

Table II contains NOE factors and spin-lattice relaxation times T_1 of pyruvic acid and 2,2-dihydroxypropanoic acid. These data can be used to determine correlation times and rotation barriers of the methyl groups and therefore to characterize the mobility of these molecules. The method of Woessner[16,17] was applied to both acids for an isotropic approximation (Table III), using structural data from the literature.[18] The calculated values suggest limited mobility of the pyruvic acid molecule, indicated by a larger overall correlation time and a higher rotation barrier for the methyl group. This effect can be due in part to hyperconjugation of the methyl group with the π electrons of the carbonyl-carboxyl system. On the other hand, 2,2-dihydroxypropanoic acid appears to have a relatively high mobility. This result is not in agreement with that of Patting and Strehlow,[9] who infer a limited mobility of 2,2-dihydroxypropanoic acid from ^1H NMR line width measurements.

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Experimental Section

NMR spectra were obtained on a WP 200 spectrometer with samples at the normal probe temperature of 300 K at 50.32 MHz for ^{13}C. Spectra were recorded with broad band decoupling except those with inverse gated decoupling. Spin-lattice relaxation times were determined by the inversion recovery procedure with eight τ values. NOEs were calculated from the difference of integrals of ^{13}C peaks from spectra with broad band decoupling and spectra with inverse gated heterodecoupling. Under the conditions chosen the acids were essentially undissociated. Chemical shifts were referred to external TMS. Measurements of pH were made with a Radiometer Model 26 pH meter. The calculation of pD values was performed according to Wüthrich.[19]

$$pD = pH \text{ (meter reading)} + 0.40$$

Prior to the NOE and T_1 experiments, samples were degassed by five pump-freeze-thaw cycles.

Pyruvic acid was purchased from Fluka and freshly distilled. (4-Methylphenyl)glyoxylic acid was prepared according to Schellenberger.[13]

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Benzocyclopropene-*p*-quinone: Generation and Trapping

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Benzoquinones fused with small rings provide interesting insight into the effects of strain on the physicochemical properties of quinone systems and also have potential utility as synthetic intermediates. Although benzocyclobutenequinones have been synthesized,[1] no synthesis of the more highly strained benzocyclopropenequinones has been described. We here report the pyrolytic generation and trapping of benzocyclopropene-*p*-quinone (**1**).[2]

In view of the electrophilic nature of quinones and the enhanced Diels-Alder reactivity of the moderately strained benzocyclobutene-*p*-quinone (**2**) as a dienophile, the more highly strained quinone **1** should be a very reactive compound, particularly toward nucleophiles. On the other hand, **1** could be expected to be thermally, reasonably stable because it cannot undergo a symmetry-allowed, unimolecular thermal ring opening like that of the cyclobutene ring in **2**,[3,4] although ring opening of **1** by a radical mechanism may be possible with higher activation energy.

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(4) Compound **1** might undergo an intermolecular ene reaction to give a dimer, as does cyclopropene.

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