

Thermochemistry of Ionization Reactions for Glyoxylic Acid, Pyruvic Acid, and α -Ketobutyric Acid

GUNNEL ÖJELUND and INGEMAR WADSÖ

Thermochemistry Laboratory, University of Lund, Lund, Sweden*

Gross heats of ionization values have been determined calorimetrically at an ionic strength of 0.05 for glyoxylic acid (0.641 ± 0.004 kcal/mole), pyruvic acid (3.011 ± 0.006 kcal/mole), and α -ketobutyric acid (2.932 ± 0.008 kcal/mole). pK_a -values have been determined by a pH-metric procedure and NMR spectra have been recorded for the acids and their anions in D_2O solution. Results of the measurements are discussed and thermodynamic data for the hydration of pyruvic acid is calculated.

The structure of α -keto acids in aqueous solution has been the subject of several investigations in the past.¹ The results of these studies have been given rather contradictory interpretations. Recent UV and, in particular, NMR measurements,^{1,2} however, strongly indicate that pyruvic acid as well as other α -keto acids exist as hydrates to an appreciable extent in aqueous solution. It has also been demonstrated that there is a change in the degree of hydration when pyruvic acid is ionized; the acid anion is far less hydrated.

Bearing this in mind, it was thought to be of interest to determine heats of ionization for a few α -keto acids and to correlate the values obtained with changes in the degree of hydration accompanying the ionization process. This paper reports the results from calorimetric measurements of aqueous heats of ionization of glyoxylic acid, pyruvic acid, and α -keto butyric acid. NMR spectra in D_2O solution have been recorded for the acids as well as for the corresponding anions.

EXPERIMENTAL

Materials. Glyoxylic acid hydrate (BDH) was purified by recrystallising twice from water at room temperature. Crystals were allowed to dry at $30^\circ C$ *in vacuo* and afterwards were crushed and dried further *in vacuo* at room temperature for about 18 h. During the drying procedure the equivalent weight (as determined by potentiometric

* Sponsored by The Swedish Natural Science Research Council and The Swedish Technical Research Council.

titration with NaOH) fell below its theoretical value (3.4 %). This low value was presumably due to partial loss of hydrate water.

α -Keto propionic acid (pyruvic acid (Fluka, *puriss*)) was fractionally distilled at 18 mm Hg through a 10-plate column. A middle fraction was purified further by twice fractionally freezing out. The equivalent weight was 87.3 (calc. 88.07).

α -Keto butyric acid (Fluka, *puriss*) was purified by fractionally freezing out. The equivalent weight was 102.6 (calc. 102.09).

Water used in the preparation of the calorimetric liquids was glass distilled and freed from dissolved gases by boiling.

The ampoule content in the calorimetric experiments was constant boiling hydrochloric acid. Its exact concentration was determined by potentiometric titration.

Calorimetric experiments. The calorimetric experiments were carried out in an isothermal-jacket glass calorimeter which has been described in detail elsewhere.³ Electrical calibrations were performed on the system before the reaction had taken place and closely followed the temperature range of the reaction experiments. The final temperature for all experiments was $25.00 \pm 0.05^\circ\text{C}$. In calculating the calorimetric results, mean values from the calibration experiments were used.

The calorimetric liquid was prepared by neutralizing a 0.05 M NaOH solution with the appropriate α -keto acid.

The calorimeter was charged with 100 ml solution and the sealed glass ampoule contained about 2 mmoles constant boiling hydrochloric acid (20.22 %) by weight. pH was measured after each calorimetric experiment.

In addition to the protonization experiments, the heat of solution of the hydrochloric acid was determined in aqueous solution having ionic strength 0.05 (NaCl).

Determination of pK_a -values. The pH-metric procedure described in Ref. 4 was used. pH measurements were made by means of a Radiometer pH meter, Type PHM22p. The equipment was standardized with NBS standard samples (potassium biphthalate and potassium hydrogen tartrate). During the measurements the solutions were thermostated to $25.00 \pm 0.05^\circ\text{C}$.

Spectroscopic measurements. NMR spectra were recorded by use of a Varian A60 instrument. Spectra were taken for 10–20 % deuterium oxide solutions of the investigated keto acids as well as for corresponding solutions of their potassium salts, *cf.* Ref. 1. The temperature in the spectroscopic cell was $30 \pm 1^\circ$ during the measurements.

RESULTS AND DISCUSSION

Results from the calorimetric experiments are summarized in Table 1. In the table, data are given for the composition of the calorimetric liquid before the reaction has taken place and for the amount of HCl contained in the ampoule. It is seen that the acid anion was always in excess. But since there was a pH lowering during the reaction, some HCl was not consumed in the protonation reaction. From the measured change in pH-value the amount of HCl used to protonate the acid anion was calculated; this is designated HCl (corr). Q_{exp} given in Table 1 is the heat evolved in the experiment. Q_{dil} is the heat of dilution of the hydrochloric acid contained in the ampoule. Q_{dil} was calculated from the mean value of a number of separate heat of dilution measurements over the same concentration range as the protonization experiments ($\Delta H_{\text{dil}} = 1.639 \pm 0.003$ kcal/mole). The heat of ionization for the keto acids under the conditions of the experiment, ΔH_1 , was calculated from the difference ($Q_{\text{exp}} - Q_{\text{dil}}$) divided by the corrected amount of HCl. The uncertainties are the standard deviation of the mean to which estimates of possible systematic errors are added.

Table 1. Heats of ionization of α -keto acids at 25°C.

Calorimetric liquid	Ampoule content mmole HCl	pH after	mmole HCl (corr)	Q_{exp} (cal)	Q_{dil} (cal)	ΔH_i kcal/mole
Glyoxylic acid	1.8223	3.49	1.7903	4.1377	2.9874	0.643
buffer	1.8450	3.49	1.8130	4.1833	3.0240	0.639
$\mu = 0.05$						
$\varepsilon = 2692 \pm 2$	2.2789	3.35	2.2346	5.1601	3.7351	0.638
$\text{pH}_{\text{start}} = 5.46$	2.3401	3.32	2.2925	5.2933	3.8354	0.636
	1.3190	3.70	1.2994	3.0063	2.1618	0.650
						Mean 0.641 \pm 0.004
Pyruvic acid	1.9123	2.70	1.7130	8.2776	3.1342	3.003
buffer	1.8053	2.73	1.6194	7.8518	2.9589	3.022
$\mu = 0.05$	1.6876	2.79	1.5257	7.3469	2.7659	3.003
$\varepsilon = 2695 \pm 2$	1.9636	2.67	1.7501	8.5058	3.2183	3.021
$\text{pH}_{\text{start}} = 5.55$	1.8165	2.72	1.6263	7.8680	2.9773	3.007
						Mean 3.011 \pm 0.006
α -Ketobutyric acid, buffer	1.7644	2.65	1.5412	7.4064	2.8918	2.929
$\mu = 0.05$	1.7371	2.66	1.5164	7.3084	2.8471	2.942
$\varepsilon = 2699 \pm 2$	2.2337	2.49	1.9107	9.2674	3.6610	2.934
$\text{pH}_{\text{start}} = 5.20$	1.6601	2.68	1.4518	6.9843	2.7209	2.937
$^*\text{pH}_{\text{start}} = 5.08$	1.5907	2.74	1.4072	6.7501	2.6071	2.944
	1.6419 *	2.70	1.4432	6.8840	2.6910	2.905
						Mean 2.932 \pm 0.008

The following $\text{p}K_a$ -values were obtained from the pH-metric measurements: glyoxylic acid, 3.46 ± 0.06 ; pyruvic acid 2.60 ± 0.05 , and α -ketobutyric acid 2.50 ± 0.05 (the uncertainties are the overall standard deviation).

The obtained $\text{p}K_a$ -values agree reasonably well with earlier measurements at 25°C. For glyoxylic acid Strehlow⁵ (quoting a value by Becker) gives $\text{p}K_a = 3.3$. For pyruvic acid Pedersen⁶ made a careful study and found $\text{p}K_a = 2.49$ in agreement with the early value by Böeseken *et al.*⁷ Strehlow gives the value 2.5. For α -ketobutyric acid Strehlow found $\text{p}K_a = 2.5$ and Schellenberger⁸ reports 2.31.

No earlier calorimetric determinations of the heat of ionization of α -keto acids seem to have been reported. From Pedersen's $\text{p}K_a$ -determinations for pyruvic acid at 25° and 37° an enthalpy value similar to the present result may be calculated, ΔH_i (31°C) = 2.44 kcal/mole.

Results from NMR measurements are recorded in Fig. 1. The position of signals refers to the external TMS standard. For all the spectra, the large signal around 5 ppm downfield TMS is ascribed to the presence of some H_2O in the D_2O and to protons originally present in carboxylic acid groups and hydrate water (the latter being in rapid exchange with D_2O).

Glyoxylic acid and its anion are reported^{1,2} to be completely hydrated in aqueous solution. The present NMR spectra (for 10 % and 20 % acid in D_2O solutions) are in agreement with this statement as only one methin

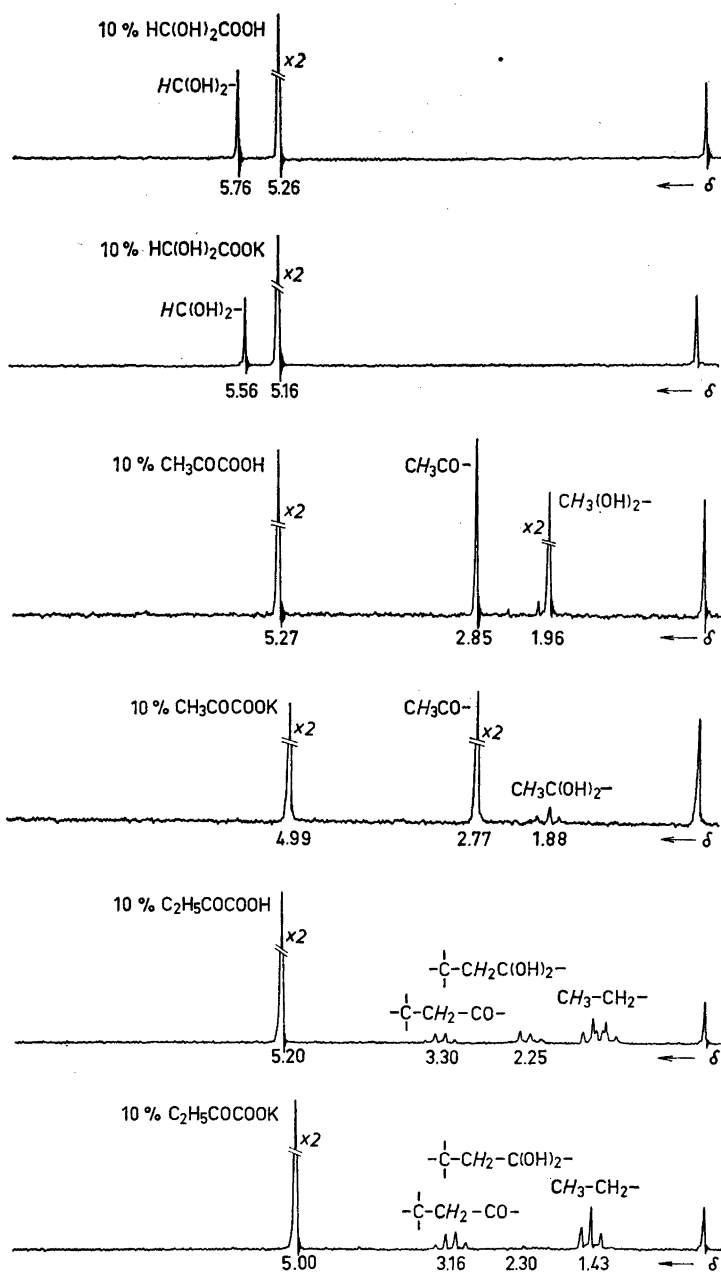


Fig. 1.

group signal is observed for both the acid and the salt solution. NMR spectra have earlier been reported by Becker¹ and by Gold *et al.*⁹ for aqueous pyruvic acid and pyruvate solutions. The present spectra agree with these previous investigations and the interpretation of the spectra by these workers is verified by the calorimetric results obtained in this work.

For pyruvic acid the two signals at $\delta = 2.85$ and $\delta = 1.96$ are ascribed to the methyl group for the nonhydrated acid and the hydrated acid, respectively (*cf.* Ref. 1). The ratio of the peak areas indicates that 60 % of the acid is hydrated in a 10 % D₂O solution and 50 % in a 20 % solution. From the anion spectra the corresponding ratio indicates that only 6 % of the anion is hydrated in 10 % D₂O solution and 5 % in 20 % solution. Becker reports 63 % hydration for 1 M (*ca.* 9 %) acid solution in H₂O and 5 % hydration for the anion solution. Gold *et al.* report 70 % hydrate in very dilute solution (31°C). Strehlow and Becker obtained the same value from measurements of UV spectra.

For a 10 % solution of α -ketobutyric acid in D₂O, calculation shows that 59 % is hydrated (55 % in 20 % D₂O solution), whereas for the anion the amount hydrated is found to be 20 % (17 % in 20 % solution). Strehlow (quoting a value by Becker) reports 58 % hydration of a 0.1 M α -ketobutyric acid solution.

Thermodynamics of the ionization process

Thermodynamic data for the ionization reaction at 25°C of the α -keto acids investigated are summarized in Table 2. Data are also given for some non-keto acids for comparison.

pK_a -values for glyoxylic acid and for α -ketobutyric acid reported in this work have been used in the calculation of the ΔG_i° -values. For pyruvic acid the pK_a -value given by Pedersen, $pK_a = 2.49$, was judged to be the most reliable and was used in the calculation. The calorimetrically determined ΔH_i° -values which refer to an ionic strength of $\mu = 0.05$ have been corrected to zero ionic strength using the expression¹⁰ $\Delta H_i^\circ = \Delta H_i^\circ - 0.5 \sqrt{\mu}$.

A comparison between glyoxylic acid and formic acid shows that introduction of a (hydrated) α -keto group slightly increases the acid strength. From Table 2 it is evident that this effect is the result of a rather small negative

Table 2. Thermodynamic data for ionization of α -keto acids and carboxylic acids at 25°C.

Acid	pK_a	ΔG_i° kcal/mole	ΔH_i° kcal/mole	ΔS_i° e.u.
Glyoxylic	3.46	4.72	0.53	-14
Pyruvic	2.49	3.40	2.90	-1.7
α -Ketobutyric	2.50	3.41	2.82	-2.0
Formic ^a	3.77	5.14	-0.13	-18
Acetic ^a	4.76	6.49	-0.07	-22
Propionic ^a	4.88	6.65	-0.08	-23

^a Data are taken from the compilation given in Ref. 11.

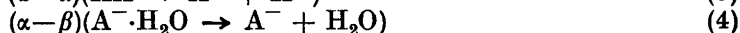
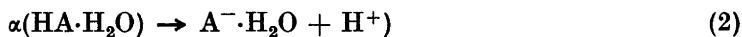
entropy change in the ionization of glyoxylic acid. Most of this acid strengthening effect, however, is cancelled by a positive enthalpy change. The comparatively small entropy change when the hydrated keto acid is ionized may be explained by an orientation effect on the neighbouring water molecules exerted by the hydrated keto group. The formation of a negative charge during the ionization is thus expected to cause a greater orientation effect in the case of, for example, formic acid than for glyoxylic acid.

Pyruvic acid and α -ketobutyric acid are markedly stronger than corresponding non-keto acids. It is important to note that the enthalpy values are quite large and positive, *i.e.* they work in an acid-weakening direction. Thus the very small entropy change accounts for the fact that these acids are relatively strong.

It must be remembered, when discussing data for ionization of pyruvic acid and α -ketobutyric acid, that values given in Table 2 are gross values. They consist of two different ionization reactions, involving the acids HA and HA·H₂O. In addition to the ionization process a change in the degree of hydration takes place. The gross process may be depicted by



Formally reaction (1) may be considered as two ionization reactions (2) and (3) and a dehydration process (4).



For a dilute solution of pyruvic acid α and β have been determined¹ as 0.65 and 0.05, respectively. By careful analysis of NMR spectra for pyruvic acid Becker deduced $\text{p}K_{\text{a}}$ -values for both the hydrated ($\text{p}K_{\text{a}} = 3.6$) and for the keto form ($\text{p}K_{\text{a}} = 2.1$) of the acid. From these data changes in free energy associated with reactions (2) and (3) may be calculated.

By comparing the difference between the heat of ionization of the hydrated glyoxylic acid and formic acid ($\Delta(\Delta H_i^\circ) = 0.66$ kcal/mole) and between formic acid and acetic acid ($\Delta(\Delta H_i^\circ) = -0.06$) we can estimate the heat of ionization of hydrated pyruvic acid as approximately 0.6 kcal/mole. From the empirical relationship between $\text{p}K_{\text{a}}$ and ΔS_i for carboxylic acids¹¹ we estimate ΔS_i for non-hydrated pyruvic acid to be about -11 e.u. and corresponding enthalpy change is thus -0.4 kcal/mole. Values for the dehydration reaction (4) may be obtained from the difference between data for the gross change (Table 2) and the sum of values for reactions (2) and (3). The molar changes for the dehydration of pyruvic acid anion were calculated to be $\Delta G = -1.3$ kcal/mole, $\Delta H = 4.5$ kcal/mole, and $\Delta S = 20$ e.u. These data combined with values for reaction (2) and reaction (3) lead to data for the dehydration of the acid form of pyruvic acid: $\Delta G = 0.7$ kcal/mole, $\Delta H = 5.5$ kcal/mole, and $\Delta S = 16$ e.u.

Becker¹ derived enthalpy values for the dehydration process of the acid form of pyruvic acid from results of NMR measurements at different temperatures (22 and 43°) in reasonable agreement with the result presented here,

6.7 kcal/mole (2 M solution) and 7.1 kcal/mole (3.5 M solution). The present results are in very good agreement with data for the dehydration of acetaldehyde,¹² $\Delta H = 5.1$ kcal/mole and $\Delta S = 16.8$ e.u.

REFERENCES

1. Becker, M. *Z. Elektrochem.* **68** (1964) 669.
2. Becker, M. and Strehlow, H. *Z. Elektrochem.* **64** (1960) 813.
3. Sunner, S. and Wadsö, I. *Acta Chem. Scand.* **13** (1959) 97.
4. Rose, J. In *Advanced Physico-Chemical Experiments*, Sir Isaac Pitman & Sons Ltd., London 1964, p. 133.
5. Strehlow, H. *Z. Elektrochem.* **66** (1962) 392.
6. Pedersen, K. J. *Acta Chem. Scand.* **6** (1952) 243.
7. Böeseken, J., Hansen, L. W. and Bertram, S. H. *Rec. Trav. Chim.* **35** (1916) 318.
8. Schellenberger, A. and Langguth, K. L. *Z. Chem.* **1964** 228.
9. Gold, V., Socrates, G. and (in part) Crampton, M. R. *J. Chem. Soc.* **1964** 5888.
10. Cottrell, T. L., Drake, G. W., Levi, D. L., Tully, K. J. and Wolfenden, J. H. *J. Chem. Soc.* **1948** 1016.
11. Ebersson, L. and Wadsö, I. *Acta Chem. Scand.* **17** (1963) 1552.
12. Bell, R. P. and Clunie, J. C. *Trans. Faraday Soc.* **48** (1952) 439.

Received February 28, 1967.