ANOMALOUS BEHAVIOUR OF 2,3-DICARBOXYPYRIDINE IN THE CALORIMETRIC BASICITY SCALE FOR SOME PYRIDINE AND ANILINE ISOMERS. THE INFLUENCE OF THE INTERNAL HYDROGEN BOND ON THE STERIC EFFECT

F. RODANTE and M.G. BONICELLI

Dipartimento di Ingegneria Chimica dei Materiali, delle Materie Prime e Metallurgia, Università di Roma, Via del Castro Laurenziano 7, Roma (Italy)

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ABSTRACT

The anomalous behaviour of $2,3\text{-}(COOH)_2py$ in a calorimetric basicity scale found for six anilines and two pyridines, is studied.

A feature of this compound is the prevalence of the primary steric effect in water-rich solutions and of the substituent effect in DMSO-rich solutions. This allows the comparison of $2,3\text{-}(COOH)_2py$ in different positions of the basicity scale, as a function of the medium.

INTRODUCTION

A study on a calorimetric basicity scale for six anilines and two pyridines in liquid phase has recently been carried out in our laboratory [1].

The substantial effects influencing the aniline and pyridine isomers were found to be: (1) substituent effect, (2) steric effect, (3) tautomeric effect, and (4) hydrogen bond effect.

This scale was also useful to emphasize the prevalence of one effect compared with the rest at the various solvent compositions (DMSO–water solutions).

The order based on the protonation enthalpy is: $m\text{-}OHphNH_2 > p\text{-}OHphNH_2 > o\text{-}OHphNH_2 > m\text{-}COOHphNH_2 > 3\text{-}COOHpy > p\text{-}COOHphNH_2 > o\text{-}COOHphNH_2 \simeq 2\text{-}COOHpy$. Furthermore, a systematic study of the ionization processes of disubstituted benzoic acid derivatives [2–5] and disubstituted phenol derivatives [6,7], in water–dimethylsulfoxide (DMSO) mixtures, has recently commenced.

As previously shown [2], the additivity principle is partially valid for 3,5-dinitrobenzoic acid, while for 2,6-dihydroxybenzoic acid it cannot be applied [3]. This is due to the two internal hydrogen bonds formed between the carboxyl and the hydroxyl groups. The introduction of the second hydroxyl group in the *meta* position destabilizes the benzene ring [4] to a

lesser degree than the (second) hydroxyl group in the *ortho* position.

The second hydroxyl group in the *para* position stabilizes the benzene ring [5]. Finally, a calorimetric study of 2,4- and 2,5-dinitrophenol shows that the second group in the *para* and *meta* positions, respectively, represents the key factor in the ionization process of the two compounds.

This work is aimed at investigating the behaviour of a disubstituted carboxyl pyridine and comparing it with the monosubstituted derivatives.

First, it seemed interesting to understand the effect of an additional carboxyl group on the interactions between the first carboxyl and the nitrogen atom, and where 2,3-dicarboxypyridine appears on the calorimetric scale of basicity.

EXPERIMENTAL

The calorimetric apparatus has been previously described [1–7]. DMSO (Carlo Erba RP grade) was purified according to the procedure of Synnot and Butler [8] and DMSO–water mixtures were prepared by weight from purified DMSO and CO_2-free twice distilled water. The mole fraction of DMSO in these mixtures ranged from 0.0 to 0.8. Aqueous solutions of 1 M HCl and 0.1 M NaOH were prepared from standard solutions; their concentrations were checked by potentiometric titrations. The 2,3-dicarboxy-pyridine (Merck) was recrystallized from water–alcohol mixtures; its m.p. was checked before use. The compound was handled in a dry-box containing dry nitrogen. The weighing of the compound was also performed in the dry-box.

The ionization process of the 2,3-dicarboxypyridine ion, $2,3$-$(COOH)_2pyH^+$, in the various water–DMSO mixtures at X mole fraction can be represented as

$$[2,3\text{-}(COOH)_2pyH^+]_X \rightarrow (H^+)_X + [2,3\text{-}(COOH)_2py]_X \tag{1}$$
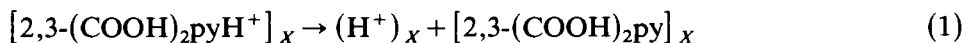
The molar enthalpy of ionization, $\Delta \overline{H}_1$, of $2,3$-$(COOH)_2pyH^+$ was obtained by measuring the molar enthalpy of solution, $\Delta \overline{H}_2$, of the 2,3-di-carboxypyridine in the mixed solvent of X mole fraction

$$2,3\text{-}(COOH)_2py_{(c)} \rightarrow [2,3\text{-}(COOH)_2py]_X \tag{2}$$
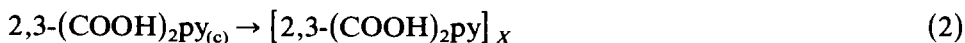
and the molar enthalpy of neutralization, $\Delta \overline{H}_3$, of the same compound in the same mixtures containing an excess of HCl

$$2,3\text{-}(COOH)_2py_{(c)} + (H^+)_X \rightarrow [2,3\text{-}(COOH)_2pyH^+]_X \tag{3}$$

The molar enthalpy, $\Delta \overline{H}_1$, of process (1) can be obtained by subtracting the two values $\Delta \overline{H}_2$ and $\Delta \overline{H}_3$.

In processes (2) and (3), concentrations ranging from 2×10^{-3} to 4×10^{-3}

TABLE 1

Enthalpy values of processes (1)–(3) for 2,3-dicarboxypyridine in DMSO–water mixtures of various mole fraction at 25°C

X_{DMSO}	ΔH_1^0	ΔH_2^0	ΔH_3^0
0.0	0.74	3.74	3.00
0.1	.2.98	7.38	4.40
0.2	1.87	7.77	5.90
0.3	0.98	6.58	5.60
0.4	0.36	4.17	3.81
0.5	0.08	2.91	2.83
0.6	0.07	2.27	2.20
0.7	0.06	1.67	1.61
0.8	0.05	1.31	1.26

m were used. Therefore, the $\Delta \overline{H}_1$ values can be considered at infinite dilution [1–7].

For all water–DMSO mixtures at X mole fraction, these values refer to the ionization process of one mole of 2,3-$(COOH)_2 pyH^+$, dissolved at infinite dilution in 1000 g of the mixed solvent, yielding one mole of 2,3-$(COOH)_2 py$ molecules and one mole of protons solvated in the same amount of solvent.

RESULTS

Table 1 shows the ΔH_1^0, ΔH_2^0 and ΔH_3^0 values of processes (1), (2) and (3) obtained for the 2,3-dicarboxypyridine ion.

For the sake of comparison, it is convenient to express the ionization enthalpy values, ΔH_1^0, of the 2,3-dicarboxypyridine ion as the difference between the values obtained in the mixed solvent at X mole fraction and in pure water so that

$$\delta \Delta H_1^0 = \left(\Delta H_1^0 \right)_X - \left(\Delta H_1^0 \right)_{X=0}$$

These values are relative to the transfer of the ionization process, while the $\delta \Delta H_2^0$ and $\delta \Delta H_3^0$ values represent the transfer enthalpy of the disubstituted pyridine and disubstituted pyridine ion, respectively, from pure water to mixed solvent.

All these data are plotted against X_{DMSO} in Fig. 1.

DISCUSSION

It can be noted that (Fig. 1), in water-rich solutions, the difference in solvation enthalpy between the undissociated molecule and the ion is greater
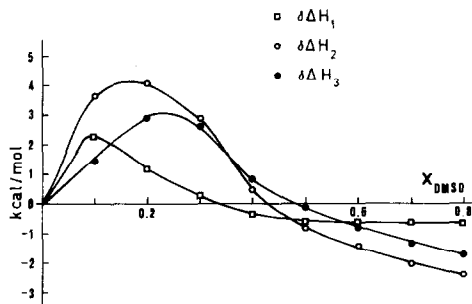
Fig. 1. Enthalpy for the transfer of the ionization and transfer enthalpies of the undissociated molecule and the ion of 2,3-dicarboxypyridine vs. mole fraction.

for the 2,3-dicarboxypyridine than for the mono-carboxy ones [9,10].

As previously shown [9,10] the electron-withdrawing effect of the carboxyl group reduces the lone-pair electron-density and the interactions between the water molecules and the N atom are weakened, while the positive charge density at the NH^+ group of the pyridinium ion will be enhanced and the solute–solvent interactions will be strengthened. It is clear that the addition of a second carboxyl group enhances the opposite substituent effects and, thus, the difference in solvation between the undissociated molecule and the ion.

By comparing the 2- and 3-dicarboxypyridines with the 2,3-dicarboxypyridine by means of the difference in the enthalpy of deprotonation, $\Delta H^0_{[2,3(COOH)_2pyH^+]} - \Delta H^0_{(3\text{-}COOHpyH^+)}$, $\Delta H^0_{[2,3(COOH)_2pyH^+]} - \Delta H^0_{(2\text{-}COOHpyH^+)}$ (Fig. 2), it can be inferred that the last is a more effective base up to 0.5 mole fraction: $2,3\text{-}(COOH)_2py > 3\text{-}COOHpy > 2\text{-}COOHpy$. Beyond 0.5 mole fraction the reverse is true: $3\text{-}COOHpy > 2\text{-}COOHpy > 2,3\text{-}(COOH)_2py$. This can be related to a cyclic structure (with six terms), stable mostly in water-rich mixtures, which diminishes the steric effect of the substituent group in the *ortho* position by means of an internal hydrogen bond between the two carboxyl groups.

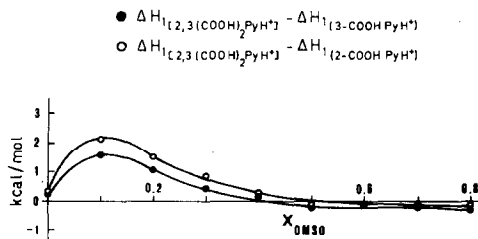In DMSO-rich solutions the basicity of the 2,3-dicarboxypyridine be-

Fig. 2. Differences in the enthalpies of ionization of 2,3-, 2- and 3-carboxypyridine in various DMSO–water mixtures.
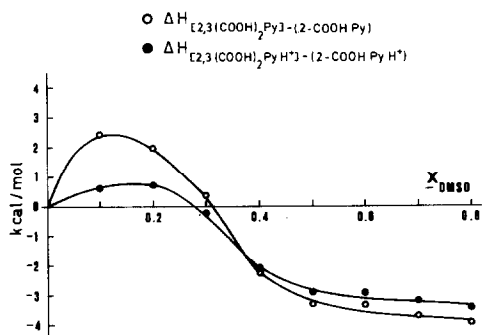
Fig. 3. Differences in solvation enthalpies between the undissociated molecule couples and the anion couples of the 2,3- and 2-carboxy pyridines in various DMSO–water mixtures.

comes slightly weaker than that of monocarboxyl pyridines. This is accounted for by the following considerations:

(a) the DMSO molecules compete with the internal hydrogen bond so that the cyclic form is broken and the increased primary steric effect diminishes the basicity;

(b) the large dipole of the 2,3-dicarboxypyridine molecule allows the onset of dipole–dipole interactions which prevail on the hydrogen bonding of the pyridinium ion to the DMSO molecules;

(c) the decrease of the number of hydrogen bonds between the NH^+ ions and the water molecules.

All these contribute in creating a solvation trend for the undissociated molecule which is opposite to that shown by the ions of the $2,3\text{-}(COOH)_2py$, $3\text{-}COOHpy$ and $2\text{-}COOHpy$. As shown in Figs. 3 and 4 the differences in solvation enthalpy between the ions, $\Delta H^0_{[2,3(COOH)_2pyH^+]_x-(2\text{-}COOHpyH^+)_x}$ − $\Delta H^0_{[2,3(COOH)_2pyH^+]-(3\text{-}COOHpyH^+)_x}$, and undissociated molecules, $\Delta H^0_{[2,3(COOH)_2py]_x-(2\text{-}COOHpy)_x}$ − $\Delta H^0_{[2,3(COOH)_2py]_x-(3\text{-}COOHpy)_x}$, show that in water-rich solutions the relative solvation of the ions is weaker than that of the undissociated molecules, while in DMSO-rich solutions the reverse is
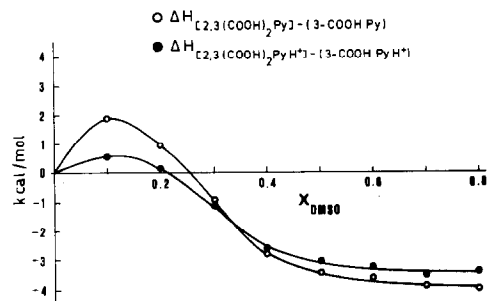

Fig. 4. Differences in solvation enthalpies between the undissociated molecule couples and anion couples of 2,3- and 3-carboxy pyridines in various DMSO–water mixtures.

true. In the latter solutions the solvations are substantially equivalent so that the basicities become very similar.

It is again noteworthy (Fig. 1) that in water-rich solutions (0.0–0.1) the cyclic form allows the absence of a zwitterion form and a maximum in the enthalpy of solution.

A feature of this compound, with respect to the monocarboxyl pyridines, is the prevalence of different effects in water-rich and DMSO-rich solutions. Therefore, in the former, the primary steric effect prevails while in the latter the substituent effect is more significant. This also brings about a reversal in the basicity strength of the di- and mono-carboxyl pyridines. Another comparison can be made with the *meta* and *ortho* anilines.

Again, in water-rich solutions, the steric effect of the 2,3-dicarboxypyridine is smaller, by virtue of the internal hydrogen bond, than that of the *ortho*-carboxyaniline. Thus, the latter displays a lower basicity strength. In DMSO-rich solutions the cyclic form is broken and the dipole–dipole interactions, due to the larger dipole of the 2,3-dicarboxypyridine, make this compound less basic than the *ortho*-carboxyaniline. This can be seen in Fig. 5 where the differences in enthalpy of deprotonation between $2,3$-$(COOH)_2pyH^+$, 2-$COOHphNH_3^+$ and 3-$COOHphNH_3^+$ are plotted vs. X_{DMSO}. Furthermore, this figure shows that the *meta*-carboxyaniline is always a stronger base than the $2,3$-$(COOH)_2py$. This can be related to the absence of the steric effect and to the smaller σ-electron-withdrawing effect in the *meta* position.

The relative solvation curves of the ions and the undissociated molecules (Figs. 6 and 7) show that the ion and the undissociated molecule of the $2,3$-$(COOH)_2py$ are more desolvated than those of the *meta* and *ortho* carboxy anilines. This means that the destabilization effect of the carboxyl groups in 2 and 3 position is greater than that of the carboxyl in the *meta* and *ortho* positions.

For these reasons, the $2,3$-$(COOH)_2py$ can be set in different positions in the basicity scale, as a function of the medium. In the water-rich solutions the order of basicity is the following: m-$COOHphNH_2 > 2,3$-$(COOH)_2$-
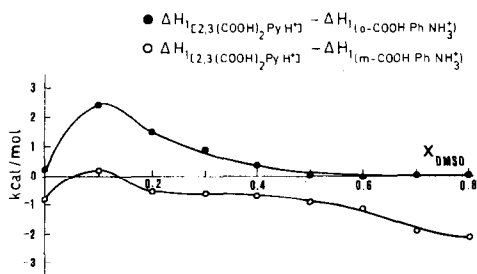

Fig. 5. Differences in the enthalpies of ionization of 2,3-dicarboxypyridine, *ortho*- and *meta*-carboxyaniline.
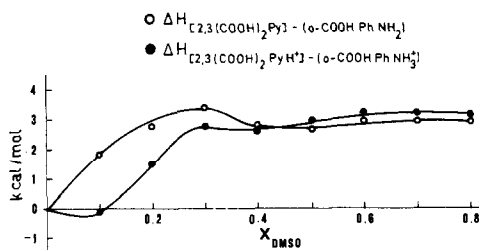
Fig. 6. Differences in solvation enthalpies between the undissociated molecule couples and anion couples of the 2,3-dicarboxypyridine and *ortho*-carboxyaniline.
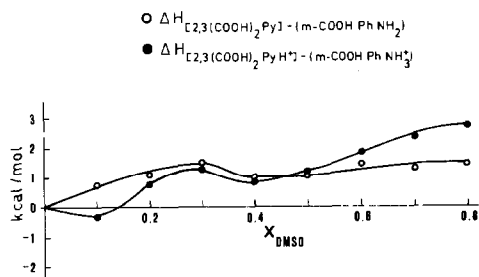

Fig. 7. Differences in solvation enthalpies between the undissociated molecule couples and anion couples of the 2,3-dicarboxypyridine and *meta*-carboxyaniline.

py > 3-COOHpy > o-COOHphNH$_2$ ≃ 2-COOHpy, while in DMSO-rich solutions the order is: m-COOHphNH$_2$ > 3-COOHpy > o-COOHpyNH$_2$ ≃ 2-COOHpy > 2,3-(COOH)$_2$py. This confirms the prevalence of different effects influencing the basicity strength of 2,3-(COOH)$_2$py as the composition of the medium is changed.

ACKNOWLEDGEMENT

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