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CALORIMETRIC STUDY OF THE IONIZATION PROCESS FOR *META*-METHOXY + BENZOIC ACID. A CALORIMETRIC ACIDITY SCALE FOR METHOXY-SUBSTITUTED BENZOIC ACIDS

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ABSTRACT

A calorimetric investigation of the ionization of *meta*-hydroxy benzoic acid is presented. The ionization and solution enthalpies of this compound have been measured in water-dimethylsulfoxide mixtures. A comparison between the *ortho*, *meta* and *para* isomers of methoxy and hydroxy benzoic acids allows a calorimetric acid strength scale to be made.

INTRODUCTION

A complete thermodynamic analysis of the ionization of *ortho*- and *para*-methoxy benzoic acids has been carried out in our laboratory [1,2].

The ionization and solution enthalpies have been measured in water-dimethylsulfoxide (DMSO) mixtures.

In the same solutions, the ΔG^0 values for the ionization, the enthalpic and entropic contributions to the substituent and reaction constant effects, and the proton transfer process from the methoxy derivatives to benzoic acid compared with the same process in the gaseous phase were also studied. Thus, a sufficiently complete thermodynamic analysis of the ionization of the above compounds in water-DMSO mixtures at 25°C is presented.

The methoxy group (R^+I^-), as well as the hydroxyl group (R^+I^-), in the *para* and (partially) *ortho* positions shows a large electron-releasing resonance effect. The difference between the two groups was related to the different degree of resonance.

Thus, the *ortho*- and *para*-methoxy were compared to the *ortho*- and *para*-hydroxy derivatives.

For the couple methoxy/hydroxy *para* derivatives a greater electron-releasing resonance effect was found for the hydroxy derivative [1], while for

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the methoxy/hydroxy *ortho* derivatives couple the contrary is true [2]. The *ortho*-methoxy derivative also shows a partial steric inhibition of resonance in water-rich solutions.

In the present work the behaviour of *meta*-methoxy benzoic acid is examined.

EXPERIMENTAL AND PROCEDURE

The calorimetric measurements were performed by means of (a) a Tronac 450 titration calorimeter, and (b) an LKB 8721-1 reaction and solution calorimeter.

DMSO (Carlo Erba, RP grade) was purified according to the procedure of Synnot and Butler [3], DMSO–water mixtures were prepared by weighing 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 0.98 M HCl and 0.098 M NaOH were prepared from standard solutions and their concentrations were checked by potentiometric titrations.

The *m*-methoxy benzoic acid (K & K) was purified by crystallization from water–ether mixtures and its melting point checked before use. The $CH_3OPhCOONa$ solutions were prepared by adding an NaOH solution of known molarity to the *m*-methoxy acid dissolved in the mixed solvent. As a result, 100 g of the DMSO–water solution at X' mole fraction were obtained. The concentration of the sodium salt was always in the range 2×10^{-4} to 4×10^{-4} m.

A certain amount of acid (about 4–5% of the original content) was not converted into the salt and remained as free acid to avoid the presence of free alkali.

The ionization process of $CH_3OPhCOOH$ in the various H_2O–DMSO mixtures of X mole fraction can be represented as

$$(CH_3OPhCOOH)_X \rightarrow (CH_3OPhCOO^-)_X + (H^+)_X \tag{1}$$

The molar enthalpy of ionization, $\Delta\overline{H}_1$, of $CH_3OPhCOOH$ was obtained by experimental measurement of:

(a) the molar enthalpy of reaction, $\Delta\overline{H}_2$, of $CH_3OPhCOONa$ dissolved in the mixed solvent of X' mole fraction, with 0.98 M HCl

$$(CH_3OPhCOO^-)_{X'} + (Na^+)_{X'} + (H^+)_{aq.} + (Cl^-)_{aq.} \rightarrow (CH_3OPhCOOH)_X + (Na^+)_X + (Cl^-)_X \tag{2}$$

(b) The molar enthalpy of solution, $\Delta\overline{H}_3$, of the same amount of 0.98 M HCl in the same solvent mixture at X' mole fraction

$$(H^+)_{aq.} + (Cl^-)_{aq.} \rightarrow (H^+)_X + (Cl^-)_X \tag{3}$$

From the dissocition constants of water [4] and *m*-methoxy benzoic acid (this work) it can also be inferred that the salt undergoes very little hydrolysis ($\beta < 0.02\%$). Therefore, it is not necessary to correct the experimental $\Delta\bar{H}_2$ values for hydrolysis.

The molar enthalpy process (1) can be obtained [1,2] by subtracting the two values $\Delta\bar{H}_3$ and $\Delta\bar{H}_2$ and by adding to this difference the $\Delta\bar{H}_4$ values relating to the molar transfer enthalpy of $CH_3OPhCOONa$ (at infinite dilution) from solvent X' to solvent X, viz.

$$(CH_3OPhCOO^-)_{X'} + (Na^+)_{X'} \rightarrow (CH_3OPhCOO^-)_X + (Na^+)_X \qquad (4)$$

It should be noted that the difference ($X - X'$) is very small for each couple. In the most unfavourable case, it was 2×10^{-4} when the final mole fraction of DMSO was 0.8. The thermal effect of process (4) was calculated using the data obtained in this work. For each of the water–DMSO mixtures at X mole fraction the $\Delta\bar{H}_1$ values refer to the ionization of 1 mole of $CH_3OPhCOOH$ dissolved at infinite dilution in 1000 g of the mixed solvent yielding 1 mole of protons and 1 mole of $CH_3OPhCOO^-$ ions solvated in the same amount of solvent.

In order to refer process (1) to only one initial thermodynamic state, the solution enthalpies of the crystalline *m*-methoxy benzoic acid, ΔH_s, in the various solvent mixtures were measured

$$CH_3OPhCOOH_{cry.} \rightarrow (CH_3OPhCOOH)_X \qquad (5)$$

so that the $\Delta\bar{H}_6 = \Delta\bar{H}_5 + \Delta\bar{H}_1$ values obtained for the process

$$CH_3OPhCOOH_{cry.} \rightarrow (H^+)_X + (CH_3OPhCOOH)_X \qquad (6)$$

refer to an identical thermodynamic state.

In processes (1) and (5), concentrations ranging from 2×10^{-3} to 4×10^{-4} *m* were used. Therefore, the $\Delta\bar{H}$ values related to these processes were assumed to be equal to ΔH^0 values [5]. All these mesurement were carried out at 25°C, the average thermal jump in the cell during the experiments being about 2×10^{-2}°C.

RESULTS AND DISCUSSION

Table 1 shows the ΔH^0 values of processes (1), (5) and (6) obtained for *meta*-methoxy benzoic acid. For comparison, it is convenient to express the ionization enthalpy as the difference between the values obtained in the mixed solvent of X mole fraction and in pure water so that

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

These values are relative to the transfer of the ionization process, while the $\delta\Delta H_5^0$ and $\delta\Delta H_6^0$ values represent the transfer enthalpy of the undissociated molecules, and of the two ions H^+ and $CH_3OPhCOO^-$, respectively, from

TABLE 1

Enthalpy values of processes (1), (5) and (6) for *meta*-methoxy benzoic acid in DMSO–water solutions of various mole fraction at 25°C (kcal mol^{-1})

X_{DMSO}	ΔH_1^0	ΔH_5^0	ΔH_6^0
0.0	0.660	7.048	7.708
0.1	0.615	8.209	8.824
0.2	0.983	8.247	9.230
0.3	1.652	7.487	9.131
0.4	2.508	6.253	8.761
0.5	3.439	4.871	8.310
0.6	4.332	3.665	7.917
0.7	5.074	2.961	8.035
0.8	5.553	3.084	8.637

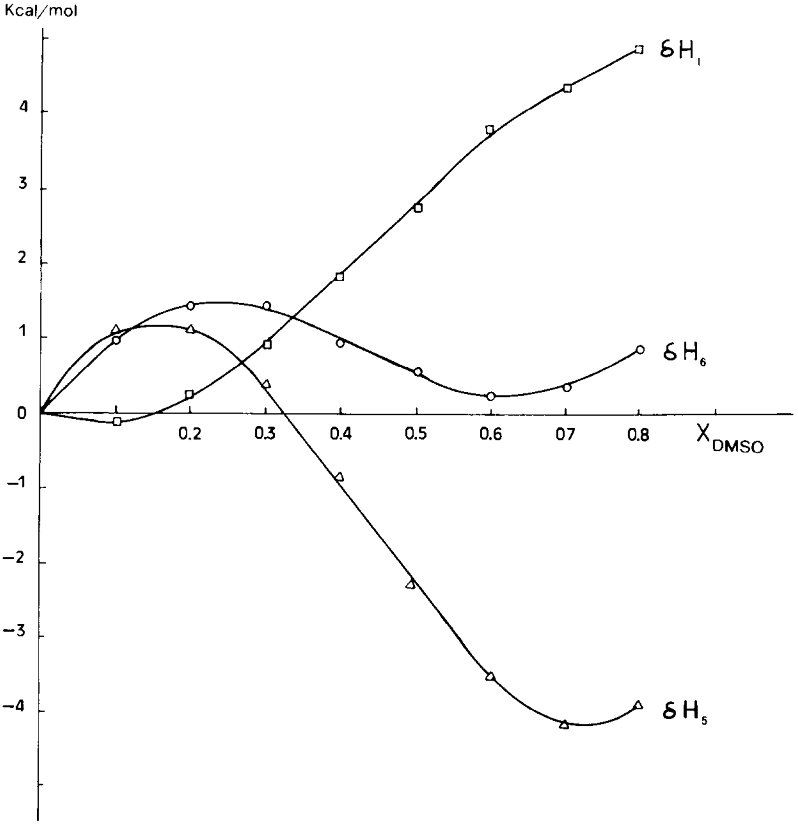

Fig. 1. Enthalpy for the transfer of the ionization and transfer enthalpies of the undissociated molecule and the ion of *meta*-methoxy benzoic acid in various DMSO–water mixtures.

TABLE 2

Ionization enthalpy values of *ortho, meta* and *para*-methoxy benzoic acids in various water–DMSO mixtures at 25°C (kcal mol^{-1})

X_{DMSO}	*o*-Methoxy	*m*-Methoxy	*p*-Methoxy
0.0	0.05	0.660	0.60
0.1	0.84	0.615	0.910
0.2	2.530	0.983	2.580
0.3	4.810	1.652	4.890
0.4	7.380	2.508	7.230
0.5	9.950	3.439	10.080
0.6	12.200	4.332	12.760
0.7	13.850	5.074	14.130
0.8	14.590	5.553	13.600

pure water to the mixed solvent. All these data are plotted against X_{DMSO} in Fig. 1, from which one may gather that, mostly in DMSO–rich solutions, the desolvation of the undissociated molecule plays a prevalent role in the ionization process.

By comparing the ΔH^0 ionization values of the *meta-*, *para* and *ortho*-methoxy derivatives (Table 2) the calorimetric scale $m > o > p$ is found over the whole mole fraction range, with the exception of pure water, where the scale becomes $o > p > m$. It can be noted that beyond $X_{DMSO} = 0.2$ the *m*-methoxy derivative is, with respect to the *para* and *ortho* derivatives, a very strong acid, while in pure water the *meta* derivative is the weakest acid. The different ionization of the three methoxy benzoic acids can be ascribed to the different solvation which the molecules and the ions undergo in the mixtures. The difference in solvation between the *meta* and *para* solvated ions was calculated as

$$\Delta \overline{H}_{(m\mathrm{CH_3O{-}PhCOO^-})_X-(p\mathrm{CH_3C{-}PhCOO^-})_X} = \Delta H_{6(m\mathrm{CH_3O{-}PhCOOH})}$$

$$-\Delta H_{6(p\mathrm{CH_3O{-}PhCOOH})} + \Delta H_{(m\mathrm{CH_3OPhCOO^-})_{aq}-(p\mathrm{CH_3OPhCOO^-})_{aq}} \tag{7}$$

while the difference in the solvation enthalpy between the undissociated molecule is

$$\Delta \overline{H}_{(m\mathrm{CH_3OPhCOOH})-(p\mathrm{CH_3OPhCOOH})} = \Delta H_{5(m\mathrm{CH_3OPhCOOH})} - \Delta H_{5(p\mathrm{CH_3OPhCOOH})}$$

$$+\Delta \overline{H}_{(m\mathrm{CH_3OPhCOOH})_{aq}-(p\mathrm{CH_3OPhCOOH})_{aq}} \tag{8}$$

The last term on the right-hand side of eqns. (7) and (8) was arbitrarily assumed to be equal to zero and the resulting $\Delta \overline{H}_{(m\mathrm{CH_3OPhCOO^-})_X-(p\mathrm{CH_3OPhCOO^-})_X}$ and $\Delta \overline{H}_{(m\mathrm{CH_3OPhCOOH})_X-(p\mathrm{CH_3OPhCOOH})_X}$ values are plotted in Fig. 2 as a function of the solvent composition. These values are supposed to approach the true values very closely [6]. The differences in the other couples were calculated in the same way and are plotted in Figs. 3 and 4.

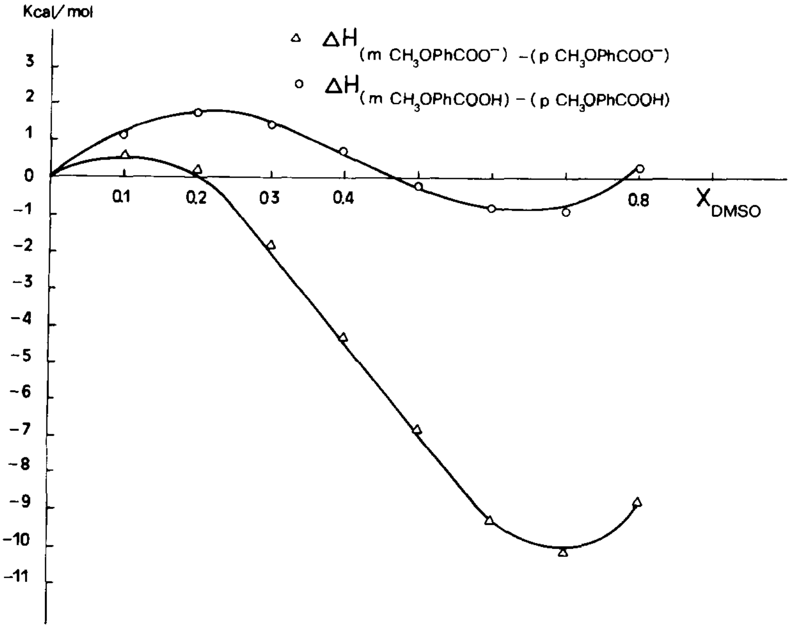

Fig. 2. Differences in the solvation enthalpy between the anions and the undissociated molecules of the *meta*- and *para*-methoxy derivatives in various DMSO–water mixtures. The differences in the hydration enthalpy both between the anion couple and the undissociated molecule couple are arbitrarily set equal to zero.

The order of the transfer of the ions is $m > p > o$ with the exception of the 0.1–0.2 mole fractions where the order is $p > m > o$.

The methoxy group in the *para* position attracts the negative charge of the carboxylate group more weakly than that in the *ortho* position because of the steric inhibition of the resonance of the latter. It is clear that in water-rich solutions the resonance effect for the *para* derivative is very strong so that the *para* anion interacts with the solvent molecules to a greater extent than the *meta* anion.

For the undissociated molecules the order of the transfer is $p > m > o$ up to $X_{\mathrm{DMSO}} = 0.4$, while beyond this mole fraction the sequence is $m > p > o$. Again, in water-rich solutions the resonance effect is very strong in the *para* derivative and allows a strong interaction with the solvent molecules.

In previous works [7–9] a study of the behaviour of *meta, para* and *ortho* hydroxy isomers was carried out.

In Table 3 the ionization enthalpy values of hydroxy isomers are given so that comparison between various methoxy/hydroxy couples is possible (Table 4).

The *ortho*-hydroxy is a stronger acid, from the enthalpic point of view, than the *ortho*-methoxy compound. This is because in the *o*-hydroxy isomer, both the COOH and OH groups have been shown [9] to take part in a strong

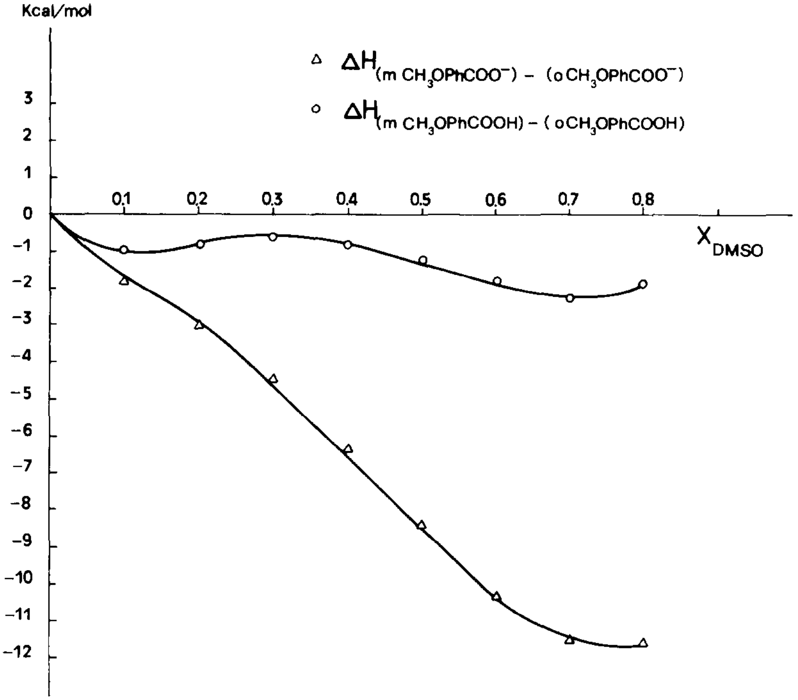

Fig. 3. Differences in the solvation enthalpy between the anions and the undissociated molecules of the *meta*- and *ortho*-methoxy derivatives in various DMSO–water mixtures. The differences in the hydration enthalpy both between the anion couple and the undissociated molecule couple are arbitrarily set equal to zero.

internal hydrogen bond. This fact, in turn, allows a greater desolvation, over the whole mole fraction range, of the hydroxy with respect the methoxy undissociated molecule [2].

As regards the *para* couple it can be noted that there is a sharp inversion in the relative acid strength of the two acids, as a function of the solvent composition. Indeed, in the water-rich solution the *para*-methoxy derivative shows a greater acidity strength, while in the DMSO-rich solutions the contrary is true. This can be related to the solvation inversion of the hydroxy and methoxy ions [1].

For the *meta* couple a greater acidity strength of the *meta*-methoxy compound is noted: the weaker inductive effect (I^-) allows a greater solvation of the methoxy anion. It is possible to give the calorimetric acidity scale: $m\mathrm{CH_3O} > o\mathrm{OH} > o\mathrm{CH_3O} > p\mathrm{CH_3O} > p\mathrm{OH} > m\mathrm{OH}$.

It is noteworthy that the *meta*-methoxy compound (the strongest) and the *meta*-hydroxy compound (the weakest) are affected by the inductive effect. For the *para* derivatives, for which the resonance is the prevalent effect, the acid strength varies with the solvent composition.

Finally, in the comparison of the *ortho* compounds the key-factor is the

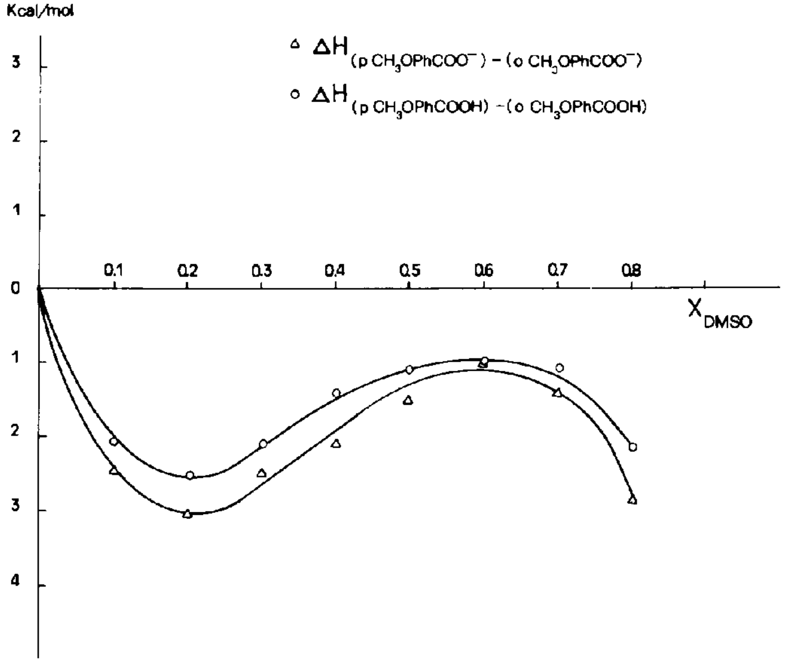

Fig. 4. Differences in the solvation enthalpy between the anions and the undissociated molecules of the *para-* and *ortho-*methoxy derivatives in various DMSO–water mixtures. The differences in the hydration enthalpy both between the anion couple and the undissociated molecule couple are arbitrarily set equal to zero.

internal hydrogen bond between the carboxyl and hydroxyl groups of the undissociated molecule.

It can be concluded that the trend in ionization of both the *para* and *meta* derivatives of the methoxy and hydroxy, and of the *ortho* (only) of the methoxy compounds is that typical of all mono-substituted benzoic deriva-

TABLE 3

Ionization enthalpy values of *ortho, meta* and *para-*hydroxy benzoic acids in various water–DMSO mixtures at 25°C (kcal mol^{-1})

X_{DMSO}	*o*-Hydroxy	*m*-Hydroxy	*p*-Hydroxy
0.0	0.73	0.16	0.37
0.1	0.79	1.46	1.16
0.2	1.94	4.36	4.64
0.3	3.36	3.74	6.14
0.4	8.15	7.12	8.58
0.5	8.27	9.97	9.57
0.6	8.45	12.34	10.04
0.7	11.59	15.63	8.56
0.8	9.96	13.80	11.89

TABLE 4

Differences in ionization enthalpies of methoxy and hydroxy benzoic acids in various water–DMSO mixtures at 25°C

X_{DMSO}	$\Delta H_{o\mathrm{CH_3O}-o\mathrm{OH}}$	$\Delta H_{m\mathrm{CH_3O}-m\mathrm{OH}}$	$\Delta H_{p\mathrm{CH_3O}-p\mathrm{OH}}$
0.0	−0.68	0.50	0.23
0.1	0.05	−0.845	−0.25
0.2	0.59	−3.377	−2.06
0.3	2.87	−2.088	−1.25
0.4	−0.77	−4.61	−1.35
0.5	1.68	−6.53	0.51
0.6	3.74	−8.008	2.72
0.7	2.26	−10.556	5.57
0.8	4.63	−8.247	1.71

tives [2], i.e., the solvation of the ions plays the principal role.

The *o*OH compound differs from the more likely behaviour of the mono-substituted derivatives because of the strong internal hydrogen bond.

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