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Potentiometric Determination of Some Solution Thermodynamic Parameters of Three Hydroxypyrone Derivates.

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In this paper, a potentiometric study on the thermodynamic acid base properties and solubility of three hydroxypyrones (successively indicated as maltols), namely maltol (H*ma*), ethylmaltol (H*ema*) and kojic acid (H_2*ka*), is reported. The acid base properties of these O-donor ligands have been investigated in NaCl ($0.10 \leq I$ / mol $L^{-1} \leq 5.00$), KCl ($0.15 \leq I$ / mol $L^{-1} \leq 2.90$) and $(C_2H_5)_4NI$ ($0.15 \leq I$ / mol $L^{-1} \leq 1.10$) aqueous solutions in the temperature range $283.15 \leq T$ / K ≤ 318.15. According to the nature of the side chain of maltols, log K^H (H*ema*) > log K^H (H*ma*) >> log K^H (H_2*ka*). The values at $I = 0$ mol L^{-1} and $T = 298.15$ K are log $K^H = 8.764\pm0.002$, 8.686 ± 0.002 and 7.933 ± 0.005 for H*ema*, H*ma* and H_2*ka*, respectively. The dependence on ionic strength of protonation constants was interpreted with the Debye-Hückel and the Specific ion Interaction Theory (SIT) equations, in this last case specific interaction coefficients were also provided. In general, protonation constants decrease with increasing temperature and ionic strength until $I = 1.5$ mol L^{-1}. The differences between the protonation constants of the maltols in the three ionic media were interpreted in terms of activity coefficients variation and weak complexes formation (with Na^+ and K^+ cations). Tetraethylammonium iodide has been considered as a baseline electrolyte. In NaCl and KCl media, the Na*L* and the K*L* (*L* = ligand) species were found and the interaction of the three ligands with sodium is stronger than that with potassium, as an example, for maltol: $\log K^{K} = -0.12 \pm 0.05$ and $\log K^{Na}$ 0.001 ± 0.030 at $T = 298.15$ K and $I = 0$ mol L^{-1}. The interaction between maltols and the cation of the supporting electrolyte lowers the apparent protonation constants and the trend is: log K^H ($(C_2H_5)_4NI$) > log K^H (KCl) > log K^H (NaCl). Enthalpy changes for the protonation of these ligands have been also determined and resulted negative in all cases ($\Delta H^0 = -15.0\pm0.1$, -14.2 ± 0.2 and -12.1 ± 0.3 kJ mol^{-1} for H*ema*, H*ma* and H_2*ka*, respectively at $T = 298.15$ K and $I = 0$ mol L^{-1}). Between the three ligands the trend of the ΔH^0 values is opposite to that observed for the protonation constants, ΔH (H*ema*) < ΔH (H*ma*) << ΔH (H_2*ka*). The major contribution in the protonation reaction is entropic in nature. Solubility and distribution measurements at $T = 298.15$ K in NaCl, allowed us to determine the salting coefficient (Setschenow parameter) of the neutral species and then to calculate the activity coefficients of the H*L* species of the three hydroxypyrone derivatives. The values of Setschenow parameters are $k_m = 0.10\pm0.01$, 0.13 ± 0.01 and 0.04 ± 0.01 for maltol, ethylmaltol and kojic acid, respectively, therefore salting out effect was evidenced for the three maltols.

Keywords: Hydroxypyrone derivatives, solution thermodynamics, potentiometry, solubility, activity coefficients.

1. INTRODUCTION

The hydroxypyrone derivatives studied in this paper are widely used by many food, cosmetics, tobacco and pharmaceutical companies for the manufacture of essences for foodstuffs, cigarettes, perfumes and other consumer goods. In particular, kojic acid (5-hydroxy-2-hydroxymethyl-4H-pyran-4-one, H_2*ka*) is added to food for its antibacterial and fungicidal properties [1], and it is widely used in dermatology for its ability to absorb free radicals and to inhibit the production of melatonin whitening the skin [2]. Maltol (3-hydroxy-2-methyl-4H-pyran-4-one, H*ma*) and ethylmaltol (3-hydroxy-2-ethyl-4H-pyran-4-one, H*ema*) are mainly used for their flavour properties. The structure of maltol, ethylmaltol and kojic acid is reported in Figure 1.

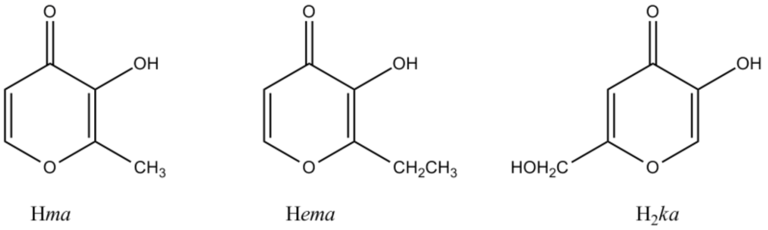

Figure 1. Structure of Maltol, Ethylmaltol and Kojic acid.

In general, hydroxypyrone derivatives are the subject of an intense research [3-13], due to their ability to bind metal cations with the formation of ML_n species. As an example, the paper of Enyedy et al. [6] regards a study on the property of some hydroxyl (thio) pyrone ligands to prevent the hydrolysis of Ga^{3+} in the anti cancer therapy, showing a very good ability of maltol to hamper Ga^{3+} hydrolysis. The authors also reported the protonation constant of maltol in KCl at T = 298.15 K and I = 0.2 mol L^{-1}. The oxovanadium complex with maltol is the leading insulin-mimetic agent [14, 15] and, in general, the vanadium complexes of maltol, ethylmaltol and kojic acid are considered important agents for the normalization of the glucose level [16].

In the study of solution equilibria, one of the most important aspect regards the modelling of the solubility and the thermodynamic acid base properties of a class of ligands. For this reason, in the past, similar studies allowed us to determine the most important properties of some relevant classes of ligands, such as amino acids, aromatic amines, carboxylates and resorcinols [17-20].

In the light of the previous considerations, maltol and its derivates hold an important role in a wide field of applications, therefore, the knowledge and the understanding of the distribution of these molecules in a system is fundamental to predict and describe their behaviour in the presence or in the absence of a metal cation.

Sodium and potassium are the most important cations in all biological fluids and in natural waters, therefore the hydroxypyrone derivatives were studied in $NaCl_{(aq)}$ and $KCl_{(aq)}$, using $(C_2H_5)_4NI$ as baseline electrolyte.

Potentiometry is regarded as the primarily technique for the study of solution equilibria, because of its precision, accuracy, reliability, experienced data analysis and relatively cheap instrumentation required. Recently, many techniques, such as voltammetry [21], spectrophotometry [22] and NMR [23], have been used with good results for equilibrium studies, but still potentiometry (e.g. [24, 25]) maintains its role as principal analytical technique in this field.

In this paper, the potentiometric study of the thermodynamic acid base properties of maltol, ethylmaltol and kojic acid is reported. The protonation constants of the maltols have been studied in NaCl, KCl and $(C_2H_5)_4NI$ aqueous solutions at different ionic strengths and temperatures. The Debye-Hückel equation and Specific ion Interaction Theory (SIT) [26-29] were used for modelling the ionic strength dependence of thermodynamic acid base properties. Formation constants for the weak interactions between the three ligands and the cations of the supporting electrolytes (Na^+ and K^+) were determined; their temperature and ionic strength dependence was also studied. Solubility and distribution measurements (2-methyl-1-propanol/water) were carried out in NaCl solutions at different ionic strengths to determine the salting and the activity coefficients of the neutral species (HL) for the three ligands.

2. EXPERIMENTAL SECTION

2.1. Chemicals

Maltol, ethylmaltol and kojic acid solutions were prepared weighing the pure compound without further purification. The purity and the concentration of the ligand solutions were determined by alkalimetric titrations using the Gran method for the calculations [30]. Hydrochloric acid and hydroxide solutions (NaOH, KOH and $(C_2H_5)_4NOH$) were prepared diluting concentrated ampoules and were standardized. NaCl and KCl aqueous solutions were prepared weighing the pure salts, previously dried in an oven at 383.15 K for two hours. $(C_2H_5)_4NI$ solutions were prepared weighing, after re-crystallization from methanol [31], the pure salt. Grade A glassware and twice distilled water ($R = 18$ MΩ cm^{-1}) were used to prepare all the solutions. Distribution measurements were performed in mixtures water/2-methyl-1-propanol.

All chemicals were purchased from Sigma-Aldrich (Italy) and its brands at the highest purity available.

2.2. Procedure

2.2.1. Potentiometric measurements

Potentiometric ISE-H^+ measurements, for the determination of protonation constants, were carried out titrating with NaOH, KOH and $(C_2H_5)_4NOH$ standard solutions. 25 mL of the solution containing the ligand and ionic medium at a pre-established ionic strength value. The ligand concentration used in the potentiometric measurements ranged between 0.001 and 0.010 mol L^{-1}. The potentiometric measurements were performed in NaCl, KCl and $(C_2H_5)_4NI$ aqueous solutions, at different ionic strengths, NaCl ($0.10 \leq I$ / mol L^{-1} ≤ 5.00), KCl ($0.15 \leq I$ / mol L^{-1} ≤ 2.90) and $(C_2H_5)_4NI$ ($0.15 \leq I$ / mol L^{-1} ≤ 1.10) and temperatures $283.15 \leq T$ / K ≤ 318.15 in thermostatted cells. All the potentiometric titrations were carried out under magnetic stirring and bubbling purified pre-saturated $N_{2(g)}$ through the solution, to exclude $O_{2(g)}$ and $CO_{2(g)}$ inside. For each temperature, various ionic strength values were investigated and for each ionic strength at least two measurements were performed. To avoid systematic errors, the measurements were carried out using two different apparatus, whose description has been reported elsewhere [32]. In any case, for both setups, the estimated precision was ±0.15 mV and ±0.001 mL for the e.m.f. and titrant volume readings, respectively.

For each experiment, independent titrations of strong acid solutions (HCl in our case) with standard base were performed in the same experimental conditions of the systems under investigation, to determine the standard electrode potential (E^0) and the acidic junction potential ($E_j = j_a [H^+]$). In this way, the free proton concentration scale, $pH \equiv -\log_{10}[H^+]$, can be used. For each titration, 80 to 100 data points were collected and the equilibrium state during titrations was checked adopting some usual precautions, such as checking the time required to reach equilibrium and performing back titrations.

2.2.2. Solubility and distribution measurements

The solubility measurements were performed as described in ref [17]. Briefly, different saturated solutions of hydroxypyrone derivatives were prepared in NaCl aqueous solutions at different concentrations at T = 298.15 K. The solutions were stirred for at least 24 h, preliminary conductivity tests established that longer stirring times were unnecessary and the pH value of each solution, measured when the solubility equilibrium was reached, remained constant. The saturated solutions were centrifuged and filtered through a cellulose membrane filter (Ø = 0.45 μm). A volume of 25 mL of the filtered solution was titrated with standard NaOH solution. For each titration, the ISE-H$^+$ electrode was calibrated as reported in the previous section.

The procedure followed for the distribution measurements is reported in previous paper [19], namely, 25 mL of an aqueous solution containing the ligand and the ionic media at a pre-established ionic strength value were mixed with 25 mL of 2-methyl-1-propanol (organic phase). Each mixture was shaken for at least four hours and after successive separation of two immiscible phases; potentiometric titrations were performed on the aqueous phase to determine the ligand concentration. The ligand concentration in the organic phase was calculated by difference between the total initial ligand concentration and its concentration in the aqueous phase after equilibrium. The distribution ratio of each ligand, at different ionic strengths in NaCl, was determined as explained in section 3.2.

2.3. Calculations

Protonation constants, analytical concentration of the ligands, standard electrode potential (E^0), acidic junction potential (E_j) and ionic product of water ($\log K_w$) of the systems studied in this paper were refined using the ESAB2M [33], BSTAC and STACO [34] computer programs. The formation constants of the weak complexes were calculated with the ES2WC computer program [35]. The least squares computer program LIANA [36] was used for the refinement of both the parameters for ionic strength and temperature dependence of both the protonation constants and the protonation enthalpy changes and to fit different equations.

The protonation constants of the three studied hydroxypyrone derivatives were determined employing three different computer programs: ESAB2M, STACO and BSTAC. The programs use the non linear least squares method, in particular data processing is done minimizing the error squares sum on the titrant volume for ESAB2M and STACO computer programs. For STACO computer program the minimizing objective function is:

$$U_v = \sum_i w_i \left(v_{exp,i} - v_{calc,i}\right)^2 \qquad (1)$$

whereas for BSTAC, data processing is done minimizing the of error squares sum on the e.m.f. readings:

$$U_E = \sum_i w_i \left(E_{exp,i} - E_{calc,i}\right)^2 \qquad (2)$$

The protonation constant (K^H) of the hydroxypyrone derivatives is given according to the following equilibria:

$$\mathrm{H}^+ + ma^- = \mathrm{H}ma \qquad (3)$$

$$\mathrm{H}^+ + ema^- = \mathrm{H}ema \qquad (4)$$

$$\mathrm{H}^+ + Hka^- = \mathrm{H}_2ka \qquad (5)$$

Conversion from molar to molal concentration scale have been performed using appropriate density values [37]. The thermodynamic protonation constants in the molal concentration scale can be determined subtracting the density factor 0.0013 (log *K* units) to the $\log {}^TK_\theta^H$ values in the molar concentration scale.

3. RESULTS AND DISCUSSION

3.1. Protonation constants

The protonation constants of maltols were determined in different ionic media at different ionic strengths: NaCl ($0.10 \leq I$ / mol L$^{-1} \leq 5.00$), KCl ($0.15 \leq I$ / mol L$^{-1} \leq 2.90$) and $(C_2H_5)_4NI$ ($0.15 \leq I$ / mol L$^{-1} \leq 1.10$), in the temperature range $283.15 \leq T$ / K ≤ 318.15.

The analysis of the experimental potentiometric data was performed with three different computer programs, namely ESAB2M, BSTAC and STACO [33, 34] and the results are reported as supplementary data (Tables 1S-7S). As an example in Tables 1-3, the experimental protonation constants of hydroxypyrone derivatives obtained from BSTAC computer program in NaCl, KCl and $(C_2H_5)_4NI$ at different ionic strengths and temperatures, are reported. As can be observed, the values for the different computer programs are in a very good agreement and the differences between the results obtained between ESAB2M and BSTAC are always lower than the experimental errors. In

Figure 2, the comparison between the results obtained with the three computer programs is depicted at different temperatures and ionic strengths for maltol in NaCl.

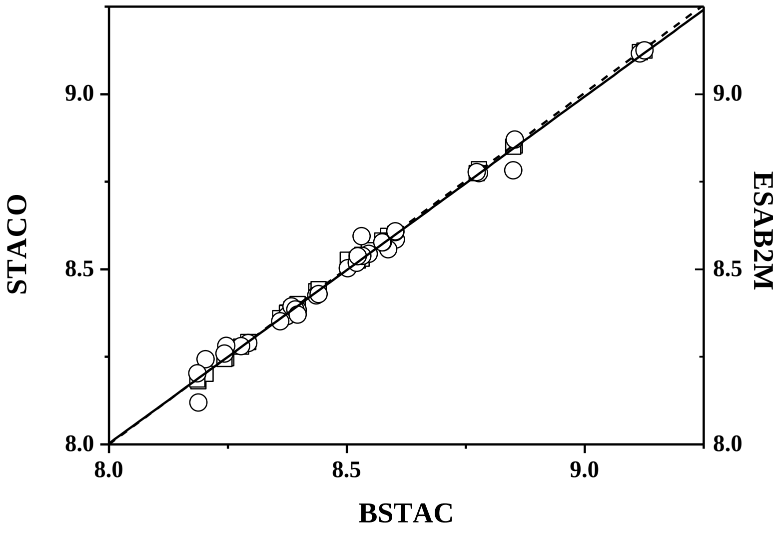

Figure 2. Comparison of the results obtained with three computer programs for maltol protonation constants in NaCl at different ionic strengths and temperatures. 1) BSTAC *vs.* STACO (□, continuous line) and 2) BSTAC *vs.* ESAB2M (○, dotted line) fitted with equation y = a + b·x. For 1) a = 1.003, b = 0.02 and r = 0.9995; for 2) a = 0.99, b = 0.07 and r = 0.995.

We fitted the experimental data considering those obtained with BSTAC as reference set. The accordance in the values is satisfactory, and for both fits the t-test (99% C.I.) performed for the existence of the intercept rejected the zero hypothesis.

The comparison of the results in Tables 1-3 shows that the protonation constants in NaCl are lower than the values in KCl, in turn lower than those in $(C_2H_5)_4NI$. In fact, the interaction between the cation of the supporting electrolyte and the ligand anion lowers the apparent protonation constant values. In Na^+ ionic media, this interaction is stronger than in K^+ ionic media, whereas it does not take place in $(C_2H_5)_4NI$ medium, which, in fact, is considered as baseline electrolyte [20, 38-40].

Table 1. Experimental protonation constants of hydroxypyrone derivatives in NaCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated by BSTAC program [34]

			log $K^{\mathrm{H}\ a)}$			
T / K	*I* / mol L^{-1}	Maltol	*I* / mol L^{-1}	Ethylmaltol	*I* / mol L^{-1}	Kojic acid
283.15	0.158	8.603±0.006$^{b)}$	0.197	8.665±0.006$^{b)}$	0.113	7.84±0.02$^{b)}$
283.15	0.158	8.587±0.006	0.198	8.661±0.006	1.036	7.76±0.02
283.15	0.480	8.502±0.005	0.966	8.629±0.004	1.813	7.67±0.03
283.15	0.489	8.521±0.005	0.972	8.621±0.004	4.903	8.40±0.06
283.15	0.990	8.546±0.005	1.932	8.727±0.004		
283.15	1.007	8.533±0.005	1.938	8.730±0.004		
283.15	1.419	8.576±0.005	2.899	8.869±0.006		
283.15	1.457	8.575±0.005	2.923	8.862±0.006		
283.15	2.861	8.778±0.007	3.848	9.048±0.011		

283.15	2.914	8.773±0.007	3.876	9.046±0.011		
283.15	4.858	9.116±0.014				
283.15	4.880	9.126±0.014				
298.15	0.157	8.436±0.005	0.197	8.491±0.005	0.111	7.71±0.02
298.15	0.158	8.441±0.005	0.197	8.493±0.005	0.513	7.61±0.01
298.15	0.479	8.375±0.004	0.950	8.447±0.004	1.064	7.61±0.01
298.15	0.486	8.374±0.004	0.950	8.452±0.004	1.624	7.68±0.02
298.15	0.947	8.397±0.004	1.917	8.515±0.005	2.030	7.73±0.02
298.15	0.964	8.384±0.004	1.927	8.518±0.005	4.057	7.87±0.05
298.15	1.422	8.397±0.004	2.936	8.641±0.006	4.862	7.95±0.06
298.15	1.446	8.392±0.004	4.019	8.775±0.010		
298.15	2.858	8.523±0.006	4.047	8.769±0.011		
298.15	2.916	8.531±0.006				
298.15	4.745	8.853±0.009				
298.15	4.826	8.850±0.009				
313.15	0.158	8.293±0.009	0.196	8.372±0.008		
313.15	0.158	8.278±0.009	0.197	8.351±0.008		
313.15	0.482	8.211±0.007	0.953	8.290±0.007		
313.15	0.483	8.188±0.007	0.959	8.287±0.007		
313.15	0.953	8.203±0.007	2.846	8.478±0.009		
313.15	0.967	8.186±0.007	2.863	8.460±0.010		
313.15	1.432	8.247±0.007	4.079	8.617±0.014		
313.15	1.449	8.243±0.007	4.204	8.631±0.014		
313.15	2.834	8.397±0.009				
313.15	2.886	8.360±0.009				
313.15	4.758	8.602±0.013				
313.15	4.816	8.602±0.014				
318.15					0.113	7.58±0.02
318.15					1.092	7.43±0.02
318.15					2.064	7.40±0.03
318.15					3.940	7.69±0.05
318.15					4.998	7.95±0.06

a) log K^{H} refers to eqs. (3) – (5); b)± 95 % C.I.

Table 2. Experimental protonation constants of maltol and ethylmaltol in KCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated by BSTAC program [34]

log K^{H} a)				
T / K	*I* / mol L^{-1}	Maltol	*I* / mol L^{-1}	Ethylmaltol
283.15	0.124	8.622±0.007 b)	0.153	8.672±0.006 b)
283.15	0.124	8.611±0.007	0.153	8.676±0.006
283.15	0.582	8.590±0.006	0.480	8.628±0.006
283.15	0.582	8.590±0.006	0.488	8.634±0.006
283.15	0.730	8.624±0.006	0.954	8.686±0.006
283.15	1.162	8.641±0.006	0.973	8.694±0.006
283.15	1.168	8.631±0.006	2.870	8.924±0.015
283.15	2.564	8.875±0.012	2.892	8.925±0.015
283.15	2.575	8.882±0.012		
298.15	0.148	8.468±0.006	0.153	8.515±0.006
298.15	0.148	8.481±0.006	0.153	8.534±0.006
298.15	0.252	8.444±0.005	0.479	8.471±0.005
298.15	0.586	8.431±0.004	0.486	8.473±0.005
298.15	0.589	8.433±0.004	0.954	8.458±0.005
298.15	1.165	8.469±0.004	0.968	8.466±0.005
298.15	1.170	8.468±0.004	2.867	8.730±0.008

298.15	1.944	8.585±0.006	2.886	8.732±0.008
298.15	2.562	8.697±0.008		
298.15	2.572	8.696±0.008		
313.15	0.129	8.359±0.009	0.152	8.373±0.008
313.15	0.129	8.347±0.009	0.153	8.367±0.008
313.15	0.627	8.313±0.007	0.487	8.330±0.007
313.15	0.630	8.279±0.007	0.493	8.348±0.007
313.15	1.121	8.318±0.007	0.623	8.369±0.006
313.15	1.125	8.312±0.007	0.972	8.344±0.006
313.15	1.940	8.425±0.008	0.983	8.338±0.006
313.15	2.676	8.579±0.011	2.913	8.546±0.003
313.15	2.742	8.542±0.011	2.925	8.568±0.003

[a] log K^{H} refers to eqs. (3) and (4); [b] ± 95 % C.I.

Table 3. Experimental protonation constants of hydroxypyrone derivatives in $(C_2H_5)_4NI$ aqueous solutions at different ionic strengths and temperatures (molar scale) calculated by BSTAC computer program [34]

			log K^{H} [a]			
T / K	I / mol L^{-1}	Maltol	I / mol L^{-1}	Ethylmaltol	I / mol L^{-1}	Kojic acid
283.15	0.148	8.638±0.006[b]	0.148	8.785±0.006[b]	0.146	7.90±0.02[b]
283.15	0.149	8.655±0.006	0.148	8.756±0.006	0.146	7.91±0.02
283.15	0.482	8.752±0.006	0.489	8.825±0.009	0.327	7.94±0.02
283.15	0.491	8.768±0.006	0.479	8.832±0.009	0.327	7.94±0.02
283.15	0.858	8.856±0.014	0.886	9.054±0.015	0.406	7.96±0.02
283.15	0.889	8.889±0.015	0.881	8.948±0.015	0.406	7.96±0.02
			0.880	9.010±0.015	0.619	8.02±0.02
			0.876	9.027±0.015	0.619	8.03±0.02
298.15	0.147	8.521±0.004	0.153	8.597±0.005	0.146	7.77±0.01
298.15	0.149	8.442±0.004	0.153	8.599±0.005	0.146	7.78±0.01
298.15	0.478	8.598±0.002	0.466	8.710±0.008	0.284	7.75±0.01
298.15	0.489	8.592±0.002	0.466	8.711±0.008	0.284	7.75±0.01
298.15	0.874	8.704±0.012	0.846	8.805±0.010	0.703	7.88±0.01
298.15	0.886	8.701±0.012	0.846	8.805±0.010	0.703	7.89±0.01
					0.948	7.97±0.02
					0.948	7.98±0.02
313.15	0.148	8.367±0.008	0.148	8.473±0.008		
313.15	0.149	8.405±0.008	0.149	8.426±0.008		
313.15	0.489	8.466±0.008	0.487	8.518±0.009		
313.15	0.494	8.494±0.008	0.478	8.532±0.009		
313.15	0.894	8.606±0.017	0.892	8.672±0.013		
313.15	0.896	8.599±0.017				
318.15					0.146	7.63±0.02
318.15					0.146	7.62±0.02
318.15					0.286	7.62±0.02
318.15					0.641	7.72±0.02
318.15					0.641	7.72±0.02
318.15					0.945	7.80±0.02

[a] log K^{H} refers to eqs. (3) – (5); [b] ± 95 % C.I.

From the analysis of the data, it can be observed that the protonation constant values decrease with increasing temperature and ionic strength, though for $I > 1.5$ mol L^{-1} the trend is opposite. As an example, in Figure 3 the ionic strength dependence of the protonation constant of ethylmaltol is reported in NaCl, KCl and $(C_2H_5)_4NI$ ionic media at T = 298.15 K.

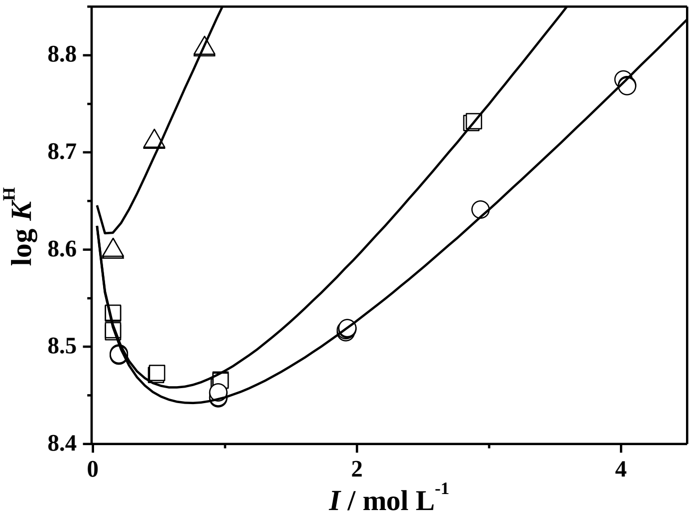

Figure 3. Ionic strength dependence (in the molar concentration scale) of the ethylmaltol protonation constants at T = 298.15 K in NaCl (○), KCl (□) and $(C_2H_5)_4NI$ (Δ).

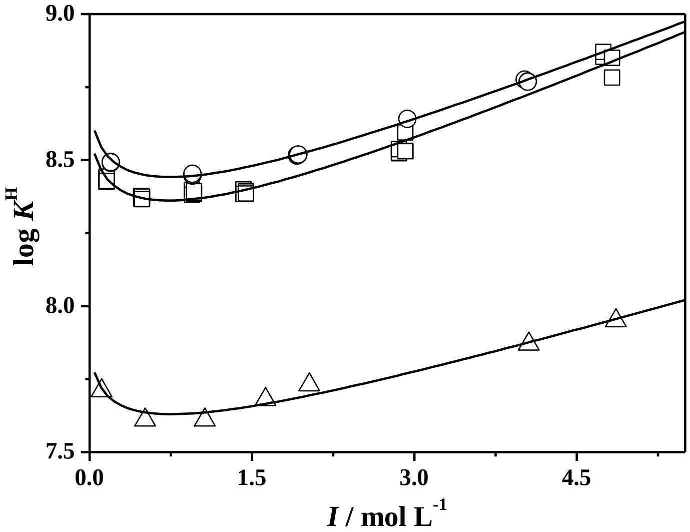

Figure 4. Ionic strength dependence (in the molar concentration scale) of ethylmaltol (○), maltol (□) and kojic acid (Δ) protonation constant, in NaCl at T = 298.15 K.

It can be noted that log K^H is higher in $(C_2H_5)_4NI$ than in KCl, in turn higher than in NaCl. According to the nature of the side chain of maltols, log K^H (H*ema*) > log K^H (H*ma*) >> log K^H (H_2*ka*). In Figure 4, the ionic strength dependence of the protonation constants of the three ligands is reported in NaCl ionic media at T = 298.15 K, whereas in Figure 5, the experimental protonation constants of H*ema*, H*ma* and H_2*ka* are reported at different temperatures in NaCl at I = 0.15 mol L^{-1}. In the figure, it can be observed that the lines are slightly curved, due to the same refined ΔC_p value (see below), and are parallel, indicating that enthalpy changes are close for three ligands studied.

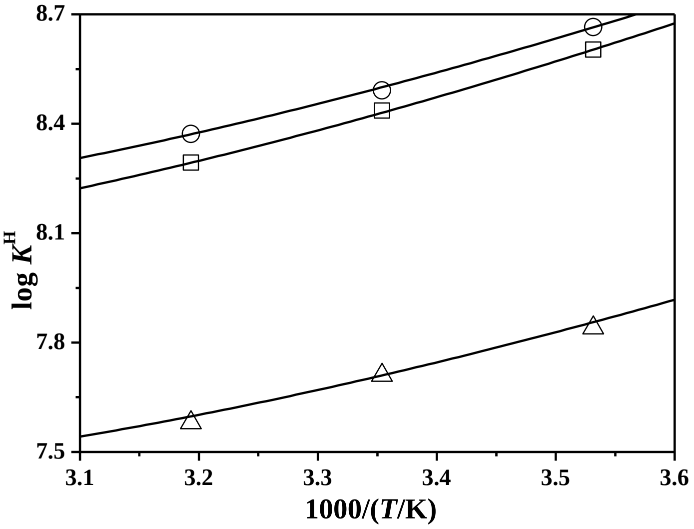

Figure 5. Temperature dependence of the ethylmaltol (○), maltol (□) and kojic acid (Δ) protonation constants in NaCl at I = 0.15 mol L^{-1}.

The dependence of the experimental data on ionic strength was interpreted in two ways: i) considering the variation of the activity coefficients with ionic strength and ii) considering the formation of weak complexes. In this last case, the implication and the necessary approximation have been widely discussed elsewhere [41].

The first issue has been performed using the Debye-Hückel equation and Specific ion Interaction Theory (SIT) [26-29], whereas the second in section 3.3.

The DH model is expressed by the following equation:

$$\log K^H = \log {}^T K^H - z^* \cdot A \frac{\sqrt{I}}{1+1.5\cdot\sqrt{I}} + C \cdot I \tag{6}$$

where: $\log {}^T K^H$ is the protonation constant at infinite dilution, C is an empirical parameter that takes into account the ionic strength dependence of the protonation constant;

$$z^* = \sum (\text{charges})^2_{\text{reag}} - \sum (\text{charges})^2_{\text{prod}} \tag{7}$$

and

$$A = \left(0.51 + \frac{0.856\cdot(T\text{-}298.15) + 0.00385\cdot(T\text{-}298.15)^2}{1000}\right) \tag{8}$$

when both the ionic strength and the protonation constants are expressed in the molal concentration scale, eq. (6) becomes the Specific ion Interaction Theory [26-29]:

$$\log K^H = \log {}^T K^H - z^* \cdot A \frac{\sqrt{I}}{1+1.5\cdot\sqrt{I}} + \Delta\varepsilon \cdot I \tag{9}$$

where the C parameter is substituted by $\Delta\varepsilon$.

Both C and $\Delta\varepsilon$ can be true constants or vary with ionic strength. Recently [42], the following equation was proposed:

$$P = p_\infty + \frac{p_0 - p_\infty}{I + 1} \tag{10}$$

where P can be C and $\Delta\varepsilon$.

If the protonation constant in eqs. (3-5) are written as a function of the activity coefficients, it can be written as follows:

$$\log K^H = \log {}^T K^H + \log \gamma_{H^+} + \log \gamma_{L^-} - \log \gamma_{HL} \tag{11}$$

and therefore, in NaCl:

$$\Delta\varepsilon = \varepsilon(H^+, Cl^-) + \varepsilon(Na^+, L^-) - k_m\,(NaCl) \tag{12}$$

where k_m is the Setschenow coefficient [43]. If given in the molar concentration scale, k_m is k_c and can be expressed as a function of ionic strength as in eq. (10).

The dependence of the protonation constant on temperature was modelled by Clarke and Glew's equation, as follows:

$$\log K^H = \log K^H_\theta + \Delta H^c \cdot \left(\frac{1}{\theta} - \frac{1}{T}\right) \cdot 52.23 + \Delta C^c_p \cdot (T - \theta) \tag{13}$$

where θ is the reference temperature (θ = 298.15 K in our case) and ΔH^c is the enthalpy variation in the molar concentration scale, whose dependence on temperature and ionic strength was taken into account by the following equation:

$$\Delta H^c = \Delta H^{c\,0} - z^* \cdot A' \cdot \frac{\sqrt{I}}{1 + 1.5 \cdot \sqrt{I}} + C' \cdot I + \Delta C^c_p \cdot (T - \theta) \tag{14}$$

where $\Delta H^{c\,0}$ is the protonation enthalpy at infinite dilution, $\Delta C_p^{\,c}$ and C' are the temperature and the ionic strength dependence parameters of $\Delta H^{c\,0}$, respectively.

In the molal scale, ΔH^c is ΔH, $\Delta H^{c\,0}$ is ΔH^0, $\Delta C_p^{\,c}$ is ΔC_p and C' is $\Delta\varepsilon'$. Therefore the eq. (14) becomes:

$$\Delta H = \Delta H^0 - z^* \cdot A' \cdot \frac{\sqrt{I}}{1 + 1.5 \cdot \sqrt{I}} + \Delta\varepsilon' \cdot I + \Delta C_p \cdot (T - \theta) \tag{15}$$

The A' and the $\Delta\varepsilon'$ quantities are related to A and $\Delta\varepsilon$ by the following equations:

$$A' = RT^2 \cdot \ln\ (10) \cdot \frac{\partial A}{\partial T} = 1.5 + 0.024 \cdot (T - 298.15) \tag{16}$$

$$\Delta\varepsilon' = RT^2 \cdot \ln\ (10) \cdot \frac{\partial \Delta\varepsilon}{\partial T} \tag{17}$$

Combining eq. (6) with eq. (14), the equations to which the experimental data were fitted, are given:

$$\log K^H = \log\ {}^T K^H_\theta - z^* \cdot A \cdot \frac{\sqrt{I}}{1 + 1.5 \cdot \sqrt{I}} + C \cdot I + \Delta H^c \cdot \left(\frac{1}{\theta} - \frac{1}{T}\right) \cdot 52.23 \tag{18}$$

in the molar concentration scale and

$$\log K^H = \log\ {}^T K^H_\theta - z^* \cdot A \cdot \frac{\sqrt{I}}{1 + 1.5 \cdot \sqrt{I}} + \Delta\varepsilon \cdot I + \Delta H \cdot \left(\frac{1}{\theta} - \frac{1}{T}\right) \cdot 52.23 \tag{19}$$

in the molal concentration scale.

In the fitting procedure, rough values of ΔC_p and $\Delta\varepsilon'$ were determined. ΔC_p = 0.062±0.016 kJ mol^{-1} K^{-1} for the three ligands in NaCl, KCl and $(C_2H_5)_4NI$, whereas $\Delta\varepsilon'$ resulted independent of the ligand and dependent on the ionic medium, namely $\Delta\varepsilon'$ = -1.1±0.2, -2.0±0.1 and -1.5±0.6 for KCl, NaCl and $(C_2H_5)_4NI$, respectively. To provide a complete set of thermodynamic parameters, the molar values of these last quantities are given: $\Delta C_p{}^c$ = 0.078±0.018 kJ mol^{-1} K^{-1} and C' = -1.1±0.2, -2.0±0.1 and -1.6±0.5 for KCl, NaCl and $(C_2H_5)_4NI$, respectively. Fitting experimental protonation data to eqs. (18)-(19), the ionic strength and temperature dependence parameters were determined and are listed in Table 4. The log ${}^TK_\theta^H$, $\Delta H^{c\,0}$ and ΔH^0 values have been constrained to be equal for all the ionic media, because at infinite dilution the enthalpy change should be equal in all ionic media.

Table 4. Ionic strength and temperature dependence parameters of maltol, ethylmaltol and kojic acid protonation constant in different ionic media in the molar and in the molal concentration scales

Ligand	NaCl	KCl	$(C_2H_5)_4NI$
Maltol			
$\log {}^TK_\theta^H$	8.686±0.002$^{a)}$	8.686±0.002$^{a)}$	8.686±0.002$^{a)}$
c_∞	0.166±0.001	0.238±0.002	0.41±0.02
c_0	0.011±0.003	0.082±0.003	0.57±0.02
$\Delta H^{c\,0}$ $^{b)}$	-14.2±0.2	-14.2±0.2	-14.2±0.2
$\Delta\varepsilon_\infty$	0.136±0.001	0.198±0.001	0.19±0.01
$\Delta\varepsilon_0$	0.030±0.001	0.092±0.001	0.53±0.01
ΔH^0 $^{b)}$	-14.4±0.2	-14.4±0.2	-14.4±0.2
Ethylmaltol			
$\log {}^TK_\theta^H$	8.764±0.002	8.764±0.002	8.764±0.002
c_∞	0.168±0.002	0.198±0.001	0.43±0.02
c_0	0.012±0.003	0.042±0.003	0.59±0.02
$\Delta H^{c\,0}$ $^{b)}$	-15.0±0.1	-15.0±0.1	-15.0±0.1
$\Delta\varepsilon_\infty$	0.139±0.001	0.160±0.001	0.21±0.01
$\Delta\varepsilon_0$	0.033±0.001	0.054±0.001	0.55±0.01
ΔH^0 $^{b)}$	-15.2±0.2	-15.2±0.2	-15.2±0.2
Kojic acid			
$\log {}^TK_\theta^H$	7.933±0.005	-	7.933±0.005
c_∞	0.157±0.003	-	0.39±0.02
c_0	0.001±0.003	-	0.55±0.02
$\Delta H^{c\,0}$ $^{b)}$	-12.1±0.3	-	-12.1±0.3
$\Delta\varepsilon_\infty$	0.128±0.003	-	0.17±0.01
$\Delta\varepsilon_0$	0.022±0.001	-	0.51±0.01

ΔH^0 [b)]	-11.8±0.5	-	-11.8±0.5

[a)]±95% C. I.; [b)]in kJ mol^{-1}.

Table 5. Thermodynamic parameters for hydroxypyrone derivatives protonation in different ionic media, at different ionic strengths and temperatures in the molal concentration scale

		$-\Delta G$			ΔH			$T\Delta S$		
					Maltol					
T / K	I / mol kg^{-1}	KCl	NaCl	$(C_2H_5)_4NI$	KCl	NaCl	$(C_2H_5)_4NI$	KCl	NaCl	$(C_2H_5)_4NI$
		±0.1[a)]	±0.1[a)]	±0.3[a)]	±0.4[a)]	±0.4[a)]	±0.4[a)]	±0.4[a)]	±0.4[a)]	±0.5[a)]
283.15	0.10	46.8	46.7	47.0	-15.9	-16.0	-16.0	30.9	30.7	31.0
283.15	1.00	46.6	46.3	47.8	-17.3	-18.2	-17.8	29.3	28.1	30.0
283.15	3.00	48.3	47.4		-19.7	-22.4		28.6	25.0	
283.15	5.00		48.8			-26.5			22.4	
298.15	0.10	48.4	48.3	48.6	-15.1	-15.2	-15.2	33.3	33.1	33.4
298.15	1.00	48.1	47.7	49.3	-16.7	-17.6	-17.1	31.4	30.1	32.2
298.15	3.00	49.7	48.6		-19.1	-21.8		30.6	26.8	
298.15	5.00		50.0			-25.9			24.1	
313.15	0.10	50.1	50.0	50.3	-14.3	-14.5	-14.4	35.7	35.5	35.9
313.15	1.00	49.6	49.2	50.9	-16.0	-16.9	-16.5	33.6	32.3	34.4
313.15	3.00	51.2	49.9		-18.5	-21.2		32.7	28.7	
313.15	5.00		51.1			-25.3			25.8	
					Ethylmaltol					
283.15	0.10	47.2	47.2	47.5	-16.8	-16.9	-16.8	30.5	30.4	30.7
283.15	1.00	46.8	46.8	48.3	-18.2	-19.1	-18.6	28.7	27.7	29.7
283.15	3.00	48.1	47.9		-20.6	-23.2		27.5	24.7	
283.15	5.00		49.4			-27.3			22.1	
298.15	0.10	48.8	48.8	49.1	-16.0	-16.1	-16.0	32.8	32.7	33.0
298.15	1.00	48.3	48.2	49.9	-17.5	-18.4	-18.0	30.8	29.7	31.9
298.15	3.00	49.5	49.1		-20.0	-22.7		29.5	26.5	
298.15	5.00		50.5			-26.7			23.8	
313.15	0.10	50.5	50.4	50.7	-15.2	-15.3	-15.3	35.2	35.1	35.5
313.15	1.00	49.8	49.6	51.4	-16.9	-17.8	-17.3	32.9	31.9	34.1
313.15	3.00	50.9	50.4		-19.4	-22.1		31.5	28.4	
313.15	5.00		51.6			-26.2			25.5	
					Kojic acid					
283.15	0.10		42.5	42.8		-13.4	-13.3		29.2	29.4
283.15	1.00		42.0	43.4		-15.6	-15.1		26.4	28.3
283.15	3.00		43.0			-19.7			23.3	
283.15	5.00		44.4			-23.8			20.6	
298.15	0.10		44.0	44.3		-12.6	-12.5		31.5	31.8
298.15	1.00		43.4	44.9		-14.9	-14.5		28.4	30.4
298.15	3.00		44.2			-19.2			25.0	
298.15	5.00		45.4			-23.2			22.2	
313.15	0.10		45.6	45.9		-11.8	-11.8		33.8	34.1
313.15	1.00		44.8	46.4		-14.3	-13.8		30.5	32.5
313.15	3.00		45.4			-18.6			26.8	
313.15	5.00		46.5			-22.7			23.8	

[a)]±95% C.I.

As a general trend, the enthalpy values (listed in Table 5) determined for kojic acid are less negative than those reported for maltol and ethylmaltol, respectively, whose values are very similar at any ionic strength value and at any temperature. This trend, in accordance with the nature of the side chain residue of the hydroxypyrone derivatives, confirms that the proton binding is exothermic, as expected for O-donor ligands [41].

Protonation enthalpies, at $I = 0$ mol L^{-1} and $T = 298.15$ K, are $\Delta H^0 = -14.4\pm0.2$, -15.2 ± 0.2 and -11.8 ± 0.5 for maltol, ethylmaltol and kojic acid, respectively. Using the ΔC_p and $\Delta\varepsilon'$ values, the ΔH values can be calculated at various temperatures and ionic strengths with eq. (15) and from the data obtained, it possible to note that the enthalpy values decrease with increasing ionic strength, whereas increase with increasing temperature. According to Hepler [44] the determination of the enthalpy of a generic reaction, should be given only in the molal concentration scale. ΔG and $T\Delta S$ values were also provided in the same conditions and the complete set of thermodynamic parameters is given in Table 5, in the molal concentration scale. The proton association process is entropic in nature, in fact the $T\Delta S$ contribution is higher than the ΔH one (see Table 5), although in NaCl solutions, the enthalpic contribution to the stability of the protonated species tends to become equal to the entropic one at high ionic strengths, generally $I > 3.0$ mol L^{-1}. In any case, the difference between of the ΔH values for these ligands is annulled by the entropic contribution, that is very similar in the three maltols.

Table 6. Analysis of the robustness of the proposed model, comparison of various refinement sets with eq. (19)

	ΔH^0				
N. of parameters	Maltol	Ethylmaltol	Kojic acid	σ_{fit}	m.d.$_{fit}$
17 [a)]	-14.4±0.2	-15.2±0.1	-11.8±0.3	0.028	0.018
14	-14.1±0.3	-14.9±0.2	-11.4±0.2	0.044	0.030
10	-14.1±0.2	-14.9±0.2	-11.7±0.3	0.045	0.031
7	-14.1±0.3	-16.5±0.5	-12.1±1.3	0.093	0.072

Different fitting attempts were performed to check the robustness of the proposed model. For this purpose, the variation of the protonation enthalpy (ΔH^0), considered as the test parameter, was studied using eq. (19) considering different constraints. In the chosen model, proposed in Table 4, the $\log {}^{T}K_{\theta}^{H}$ and ΔH^0 values were constrained for the three ionic media and the $\Delta\varepsilon_0$ values in NaCl and KCl have been considered equal for the three ligands; the $\Delta\varepsilon'$ values were equal for the three maltols in the same ionic medium and ΔC_p values have been constrained for all the ligands in all ionic media. This fit considered the refinement of 17 parameters showing $\sigma_{fit} = 0.028$ and m.d.$_{fit} = 0.018$. The second test consisted in the constrain, for each ligand, of the $\Delta\varepsilon_\infty$ in NaCl and KCl while the $\Delta\varepsilon_0$ and $\Delta\varepsilon'$ have been considered equal in NaCl and in KCl for all maltols; the number of parameters to be refined becomes 14 with $\sigma_{fit} = 0.044$ and m.d.$_{fit} = 0.030$. If $\Delta\varepsilon_\infty$ and $\Delta\varepsilon_0$ have been considered independent from the ligand, the total number of refined parameters is 10, $\sigma_{fit} = 0.045$ and m.d.$_{fit} = 0.031$, therefore no variation in the fitting parameters was observed. The last try has been performed fixing the same ionic strength dependence parameters independently of the ligand and the ionic medium. In this way, 7 parameters were refined and the fitting parameters worsened significantly, becoming σ_{fit} = 0.093 and m.d.$_{\mathrm{fit}}$ = 0.072. Even if the observed test parameters, represented by the ΔH^0, did not strongly vary, the analysis of the cited data evidenced that it is not possible to model the behaviour of the hydroxypyrone derivatives constraining the ionic strength dependence parameters of a not interacting medium (as $(C_2H_5)_4NI$) and weakly interacting media (NaCl and KCl). For a fast comparison, the fitting information and the values of the observed test parameters are summarized in Table 6.

3.2. Solubility and distribution measurements

The data treatment for the solubility measurements was widely explained in previous works [45-47], for this reason, the smoothing equation used to model the experimental data is only reported:

$$\log S_c^T = \log S_{0\,c}^T + a_c \cdot c_{\mathrm{NaCl}} \tag{20}$$

$$\log S_m^T = \log S_{0\,m}^T + a_m \cdot m_{\mathrm{NaCl}} \tag{20a}$$

where S_c^T, S_m^T, S_{0c}^T and S_{0m}^T are the total solubility at different ionic strengths and the total solubility in pure water in the molar and in the molal concentration scale, respectively, c_{NaCl} or m_{NaCl} are the molar and molal concentration of NaCl; a_c or a_m represent two empirical parameters for the ionic strength dependence in the molar or in the molal concentration scale.

The total solubility is related to the solubility of the neutral species (S_c^0 or S_m^0) by the ligand protonation constant (see [48] and references therein). On the basis of the results obtained from the analysis of solubility data using BSTAC computer program [34], it was observed that at the solubility pH, the protonated species (neutral) is predominant and the unprotonated species is present in negligible amounts. This allowed us to consider $S_c^T \equiv S_c^0$ and $S_m^T \equiv S_m^0$ in our calculations, therefore:

$$\log S_{0\,c}^0 = \log S_c^0 + k_c \cdot c_{\mathrm{NaCl}} \tag{21}$$

$$\log S_{0\,m}^0 = \log S_m^0 + k_m \cdot m_{\mathrm{NaCl}} \tag{21a}$$

and the activity coefficient of neutral species is given:

$$\log y_{\mathrm{N}} = k_c \cdot c_{\mathrm{salt}} \tag{22}$$

$$\log \gamma_{\mathrm{N}} = k_m \cdot m_{\mathrm{salt}} \tag{22a}$$

where k_c and k_m are the Setschenow coefficients in the molar or in the molal concentration scale. From the data analysis, a salting out effect was evidenced for all the three hydroxypyrone derivatives and the solubility decreases with increasing NaCl concentration.

As regards the distribution measurements, as already explained in previous papers [19], the chemical potential of a component in equilibrium between the two phases, aqueous and organic, is the same in both phases, so that [49]:

$$\exp\left(\frac{\mu_{aq}^0 - \mu_{org}^0}{RT}\right) = \frac{m_{org}\cdot\gamma_{org}}{m_{aq}\cdot\gamma_{aq}} = K_{D\,m}^T\,\frac{\gamma_{org}}{\gamma_{aq}} \tag{23}$$

where μ^0, m and γ are chemical potential, total concentration and activity coefficient of a component, respectively, in the molal concentration scale in aqueous (*aq*) and in organic phase; $K_{D\,m}^T$ is the distribution ratio of the component between the organic and the aqueous phase (this equation is also valid in the molar concentration scale, substituting “*m*” with “*c*” and γ with *y*). If, the aqueous phase is pure water, $K_{D\,m}^{T}$ becomes $K_{D\,0}^{T}$ and substituting $K_{D\,0}^{T}$ in eq. (23):

$$\frac{\gamma_{aq}}{\gamma_{org}} = \frac{K_{D\,m}^{T}}{K_{D\,0}^{T}} \qquad (24)$$

it can be assumed that, if the concentration of the component in the organic phase is low enough, the activity coefficient in this phase is $\gamma_{org} \approx 1$, therefore:

$$\log \gamma_{aq} = \log \gamma_{\mathrm{N}} = \log \frac{K_{D\,m}^{T}}{K_{D\,0}^{T}} \qquad (25)$$

considering the Setschenow coefficient [43]:

$$\log y_{\mathrm{N}} = k_c \cdot c_{\mathrm{salt}} \qquad (26)$$

$$\log \gamma_{\mathrm{N}} = k_m \cdot m_{\mathrm{salt}} \qquad (26a)$$

where y_{N} and γ_{N} are the activity coefficients of the neutral species, k_c and k_m represent the Setschenow parameters, in the molar (c_{salt}) and in the molal (m_{salt}) concentration scale, respectively. Rearranging eqs. (24-26) for NaCl:

$$\log K_{D\,c}^{T} = \log K_{D\,0\,c}^{T} + k_c \cdot c_{\mathrm{NaCl}} \qquad (27)$$

$$\log K_{D\,m}^{T} = \log K_{D\,0\,m}^{T} + k_m \cdot m_{\mathrm{NaCl}} \qquad (27a)$$

Also the Setschenow parameter can be expressed as a function of ionic strength in different ways [42], as in eq. (10); in this paper a good linearity was found and therefore k_m was considered a true constant.

The simultaneous analysis of the solubility and the distribution measurements performed in NaCl aqueous solutions at different concentrations, allowed us to determine the salt effect (salting in and salting out) of the neutral species. The experimental values of total solubility of the neutral species and distribution constants for the three ligands are reported, in NaCl at different concentrations, in Table 7.

Table 7. Experimental solubility of the neutral species and distribution constants at different ionic strengths in NaCl solutions at *T* = 298.15 K

Ligand	m_{NaCl} / mol kg^{-1}	$\log S_m^{0}$ a)	m_{NaCl} / mol kg^{-1}	$\log K_{D\,m}^{0}$ b)
Maltol	0.002	-0.94±0.04 c)	0.000	0.39±0.02 c)
	0.499	-1.09±0.04	0.100	0.44±0.02
	1.175	-1.18±0.02	1.022	0.57±0.02
	3.112	-1.36±0.02	2.691	0.70±0.02
	5.352	-1.59±0.04	4.671	0.83±0.04
Ethylmaltol	0.000	-0.91±0.02	0.000	0.92±0.02
	0.484	-0.99±0.02	0.100	0.94±0.02
	0.966	-1.08±0.02	1.022	1.09±0.02
	3.078	-1.38±0.02	3.199	1.36±0.04
	5.590	-1.69±0.04	5.606	1.55±0.06
Kojic acid	0.018	-0.56±0.02	0.002	-0.28±0.02
	0.528	-0.60±0.02	0.484	-0.21±0.01
	0.969	-0.62±0.01	1.052	-0.19±0.01
	3.168	-0.71±0.02	3.200	-0.13±0.01
	5.596	-0.77±0.02		

a) eq. (21a); b) eq. (27a); c) ±95% C.I.

Table 8. Log $S^0_{0\,c}$ and log $S^0_{0\,m}$ [a)]values in water, $\log K^T_{D\,0c}$ and $\log K^T_{D\,0m}$ [b)] values in 2-methyl-1-propanol/water, k_c and k_m (Setschenow coefficients) values in $NaCl_{(aq)}$ and at T = 298.15 K, in the molar (c) and molal (m) scale

Ligand	$\log S^0_{0c}$	$\log K^T_{D\,0c}$	k_c
Maltol	-1.03±0.04[c)]	0.41±0.02[c)]	0.12±0.01[c)]
Ethylmaltol	-0.95±0.01	0.92±0.02	0.15±0.01
Kojic acid	-0.58±0.02	-0.24±0.02	0.05±0.01
	$\log S^0_{0m}$	$\log K^T_{D\,0\,m}$	k_m
Maltol	-1.04±0.04[c)]	0.41±0.02[c)]	0.10±0.01[c)]
Ethylmaltol	-0.95±0.02	0.92±0.02	0.13±0.01
Kojic acid	-0.58±0.02	-0.24±0.02	0.04±0.01

[a)] eqs. (21) – (21a); [b)] eqs. (27) – (27a); [c)]±95% C.I.

The experimental values of $\log S^0_c$, $\log S^0_m$, $\log K^T_{D\,c}$ and $\log K^T_{D\,m}$ have been fitted to eqs. (21)-(21a) and eqs. (27)-(27a), respectively, to determine the $\log S^0_{0\,c}$, $\log S^0_{0\,m}$, $\log K^T_{D\,0c}$, $\log K^T_{D\,0\,m}$, k_c and k_m parameters. The Setschenow coefficients, calculated with the two methods, were not significantly different at the 95% of the confidence interval. The values of these parameters are listed in Table 8 and the activity coefficients of neutral species, calculated with eq. (26a) are reported in supplementary data (Table 8S). The ionic strength dependence of the activity coefficients for the three ligands is shown in Figure 6.

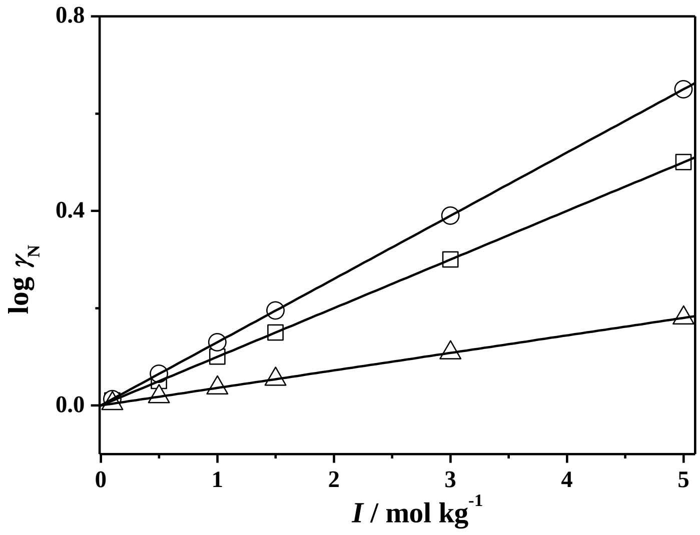

Figure 6. Activity coefficients ($\log \gamma_N$) of ethylmaltol (○), maltol (□) and kojic acid (Δ), at different ionic strengths (in the molal concentration scale) at T = 298.15 K in NaCl.

As can be seen, the log γ_N values of the neutral species increase more quickly for H*ema* than H*ma* and H$_2$*ka* with increasing ionic strength, in accordance with the nature of the side chain residue of the three maltols.

3.3 Specific interaction coefficients

Considering the ionic strength dependence parameters obtained in previous paragraph (i.e. $\Delta\varepsilon$), the solubility and the distribution measurements, which allowed us to determine the Setschenow coefficients of the neutral species, it was possible to determine the single specific interaction coefficients using eq. (12). Knowing that $\varepsilon(\mathrm{H}^+, \mathrm{Cl}^-)$ = 0.136 + (0.0839 - 0.136) / (I + 1) [50] and substituting the k_m values (Table 8) in the eq. (12), the single interaction coefficients $\varepsilon(\mathrm{Na}^+, ma^-)$, $\varepsilon(\mathrm{Na}^+, ema^-)$ and $\varepsilon(\mathrm{Na}^+, Hka^-)$ can be determined. The values are: $\varepsilon_\infty(\mathrm{Na}^+, ma^-)$ = 0.104±0.002, $\varepsilon_0(\mathrm{Na}^+, ma^-)$ = 0.029±0.006; $\varepsilon_\infty(\mathrm{Na}^+, ema^-)$ = 0.137±0.004, $\varepsilon_0(\mathrm{Na}^+, ema^-)$ = 0.068±0.008, $\varepsilon_\infty(\mathrm{Na}^+, Hka^-)$ = 0.043±0.014 and $\varepsilon_0(\mathrm{Na}^+, Hka^-)$ = -0.093±0.056.

The $\varepsilon_\infty(\mathrm{Na}^+, L^-)$ and $\varepsilon_0(\mathrm{Na}^+, L^-)$ values can be used to calculate the protonation constants of the three hydroxypyrone derivatives in a wide ionic strengths range using eqs. (9), (10) and (12). Data obtained are listed in Table 4.

Finally, considering all the data reported in this work, a complete set of suggested protonation constants was proposed for maltol, ethylmaltol and kojic acid in different ionic media, at different ionic strengths and temperatures, whose values are summarized in supplementary data (Tables 9S, 10S) in the molal and in the molar concentration scales, respectively.

3.3 Alkali metal weak ion pairs

The dependence of the protonation constants on ionic strength was interpreted in terms of variation of activity coefficient, using the Debye-Hückel and the SIT equation (see above), and in terms of formation of weak complexes between the anion of the ligand and the cation of the supporting electrolyte [41]. In this last case, two assumptions are necessary, i) the arbitrary choice of a baseline background electrolyte and ii) the implicit assumption the activity coefficients of the L^- and HL species are the same in a baseline electrolyte and in an interacting medium, corrected for ion pair formation [51] The first issue has been discussed elsewhere [20, 38-40] and it has been demonstrated that is reasonable to use tetraalkylammonium salts as baseline, when dealing with O-donor ligands. The second assumption is valid in the ionic strength range $0 \leq I$ / mol $\mathrm{L}^{-1} \leq 1.0$ and, in fact, this ionic strength window was selected in this paper for this purpose.

According to a previously proposed simple model [35, 38] it is possible to calculate weak complex formation constants from the differences in the protonation function [38], which for brevity is not shown.

The ionic strength and the temperature dependence of the weak complexes was taken into account with the following equation, using ES2WC computer program [35]:

$$\log K^{M} = \log K^{M\,0} + \frac{\partial \log K^{M\,0}}{\partial T} \cdot \Delta T - z^{*} \cdot \frac{\sqrt{I}}{2+3\cdot\sqrt{I}} + \left(C + \frac{\partial C}{\partial T}\cdot \Delta T\right)\cdot I + D \cdot I^{3/2} \tag{28}$$

where K^{M} and $K^{M\,0}$ are the formation constants of the weak species at different ionic strengths and temperatures and, the same quantity at infinite dilution and T = 298.15 K, the partial derivatives take into account the temperature dependence of the log $K^{M\,0}$ and C, respectively; C and D are empirical parameters for the ionic strength dependence and $\Delta T = (T - 298.15)$.

Table 9. Formation constants of weak complexes with Na^{+} and K^{+} and their dependence parameters on temperature and ionic strength at infinite dilution and T =298.15 K

Species	$K^{M\,0}$	log $K^{M\,0}$	∂ log $K^{M\,0}/\partial T$	C	$\partial C/\partial T$	D
Na(*ma*)	1.00±0.09$^{a)}$	0.001±0.02	0.004±0.002$^{a)}$	0.66±0.02$^{a)}$	-0.001±0.001$^{a)}$	-0.20±0.02$^{a)}$
K(*ma*)	0.76±0.09	-0.12±0.03	0.003±0.004	0.66±0.02	-0.001±0.001	-0.20±0.02
Na(*ema*)	1.26±0.05	0.11±0.01	0.002±0.002	0.72±0.02	-0.0017±0.0006	-0.20±0.02
K(*ema*)	1.15±0.05	0.06±0.01	0.002±0.002	0.72±0.02	-0.0017±0.0006	-0.20±0.02
Na(H*ka*)	1.00±0.10	0.004±0.03	0.002±0.004	0.68±0.03	-0.002±0.001	-0.20±0.02

$^{a)}$± 95% C.I.

The whole set of the parameters determined with this kind of analysis is summarized in Table 9, where for simplicity the $K^{M\,0}$ and K^{M} values are reported instead of the logarithm quantities. For the three hydroxypyrone derivatives only the M*L* species was determined and, as usual for O-donor ligands, the stability of the Na*L* complexes is higher than that of the K*L* ion pairs. In addition, as observed for the protonation constant, the values for ethylmaltol are higher than the values for maltol and kojic acid. The ionic strength dependence parameters are very close for the three ligands, in particular the value of D was equal in the experimental error range and was D = -0.20±0.02, for the three ligands. The temperature dependence of the weak complex is slightly positive, which implies an increase of the value with increasing temperature, for an endothermic process.

3.4 Literature comparison

The results reported in this work were critically compared with previous literature findings [52-54]. As regards the protonation constants at infinite dilution and T = 298.15 K, the literature values for the three hydroxypyrones are not significantly different compared to the results reported here (see Table 4), considering the 95% of C.I. The ionic strength dependence of literature values was also analyzed with the same model used in this work. The results obtained are in a very good agreement with our experimental findings. In fact, fitting the literature data to eqs. (6) and (10), the calculated c_{∞} values for maltol and ethylmaltol are c_{∞} = 0.162 and 0.180, respectively, compared to c_{∞} = 0.166 and 0.168 obtained in this work and reported in Table 4.

In the paper of Enyedy et al. [6], on the study of the anti cancer properties of some hydroxyl (thio) pyrone ligands, the protonation constant of maltol are given in KCl at T = 298.15 K and I = 0.2 mol L^{-1}. The authors found $\log K^{H}$ = 8.45, very close to our value of $\log K^{H}$ = 8.44 in the same experimental conditions.

The thermodynamic parameters reported in the literature are also in a good agreement with our experimental findings, the protonation enthalpy reported in Martell et al. [52] for maltol is ΔH^{0} = -18 kJ mol^{-1} whereas ΔH^0 = -14.4 kJ mol^{-1} was found in this work. In the case of kojic acid the literature protonation enthalpy is ΔH^0 = -14 kJ mol^{-1}, very close to those reported in this paper ΔH^0 = -11.8 kJ mol^{-1}. In Zborowski et al. [11] the structure of various hydroxypyrones has been deeply examined in the gas phase and in the presence of solvent, with computational studies. The authors found that in the case of kojic acid, the deprotonation is more probable from the hydroxyl group that is directly bound to the pyran ring.

As regards the weak complexes, the mean values, at infinite dilution and T = 298.15 K, reported in Daniele et. al [41] for the formation constants of the Na^+ and K^+ complexes of mono anions are $\log \overline{K}$ = 0.11±0.06 and 0.04±0.07 for Na*L* and K*L* ion pairs, respectively. In our case in the same experimental conditions, it was found that the mean values are: $\log \overline{K}$= 0.04±0.03 and -0.03±0.03 for Na*L* and K*L* complexes, which in the confidence interval (95%) cannot be considered significantly different with respect to the literature data. On the contrary, our values are higher than previous literature findings for another O-donor ligand class, namely resorcinols [19], for which the mean value for the formation constant of Na^+ complexes is $\log \overline{K}$ = -0.8±0.2 for the neutral NaH*L* species, at I = 0 mol L^{-1} and T = 298.15 K.

4. CONCLUSIONS

The results obtained in this work can be summarized as follows.

i) The protonation constants of three hydroxypyrone derivatives were obtained at different temperatures and ionic strengths in aqueous solutions of different ionic media (see Tables 1-3 and supplementary data 1S-7S).

ii) The corresponding temperature gradients allowed us to calculate the protonation enthalpy changes (Table 5).

iii) The protonation constants follow the order $Na^+ < K^+ << (C_2H_5)_4N^+$. These differences have been interpreted in terms of weak ion-pair formation, considering as baseline medium the tetraalkylammonium salt.

iv) From distribution and solubility measurements, in NaCl aqueous solution at different salt concentrations, Setschenow coefficients were obtained (Table 8), which, in turn, allowed us to calculate the activity coefficients of the neutral species (supplementary data Table 8S).

v) From the data of the points i) and iv) it was obtained a complete set of parameters of $\log K^H$ dependence on the ionic strength and on the ionic medium (Table 4).

The three compounds object of our study behave in a very similar way, in particular as regards the parameters of dependence on the ionic strength and, consequently, the stability constants of the weak ion pairs of Na^+ and K^+ (Table 9).

The protonation constants and protonation ΔH of maltol and ethylmaltol are very similar (with differences of borderline significance), while kojic acid shows highly significant differences: however, these differences are cancelled almost completely in the entropic contribution that appears to be very similar in the three compounds (Table 5).

Finally, it is remarkable that the technique used (the potentiometric one, both for the determination of the constants of protonation, and for the analysis in the distribution and solubility measurements) is able to provide a large number of information on the properties in solution of a class of ligands.

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Supplementary data:

Table 1S. Experimental protonation constants of maltol in NaCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with three computer programs [33, 34]

		log K^{H} a)		
T / K	I / mol L^{-1}	BSTAC	STACO	ESAB2M
283.15	0.158	8.603±0.006 b)	8.600±0.006 b)	8.585±0.006 b)
283.15	0.158	8.587±0.006	8.595±0.006	8.557±0.006
283.15	0.480	8.502±0.005	8.527±0.005	8.503±0.005
283.15	0.489	8.521±0.005	8.528±0.005	8.518±0.005
283.15	0.990	8.546±0.005	8.554±0.005	8.544±0.005
283.15	1.007	8.533±0.005	8.541±0.005	8.538±0.005
283.15	1.419	8.576±0.005	8.581±0.005	8.577±0.005
283.15	1.457	8.575±0.005	8.582±0.005	8.577±0.005
283.15	2.861	8.778±0.007	8.785±0.007	8.774±0.007
283.15	2.914	8.773±0.007	8.774±0.007	8.777±0.007
283.15	4.858	9.116±0.014	9.120±0.014	9.116±0.014
283.15	4.880	9.126±0.014	9.124±0.014	9.125±0.014
298.15	0.157	8.436±0.005	8.437±0.005	8.425±0.005
298.15	0.158	8.441±0.005	8.443±0.005	8.429±0.005
298.15	0.479	8.375±0.004	8.376±0.004	8.367±0.004
298.15	0.486	8.374±0.004	8.375±0.004	8.366±0.004
298.15	0.947	8.397±0.004	8.397±0.004	8.381±0.004
298.15	0.964	8.384±0.004	8.386±0.004	8.394±0.004
298.15	1.422	8.397±0.004	8.399±0.004	8.384±0.004
298.15	1.446	8.392±0.004	8.392±0.004	8.385±0.004
298.15	2.858	8.523±0.006	8.525±0.006	8.537±0.006
298.15	2.916	8.531±0.006	8.530±0.006	8.594±0.006
298.15	4.745	8.853±0.009	8.853±0.009	8.870±0.009
298.15	4.826	8.850±0.009	8.850±0.009	8.782±0.009
313.15	0.158	8.293±0.009	8.292±0.009	8.289±0.009
313.15	0.158	8.278±0.009	8.279±0.009	8.280±0.009
313.15	0.482	8.211±0.007	8.203±0.007	8.207±0.006
313.15	0.483	8.188±0.007	8.180±0.007	8.119±0.007
313.15	0.953	8.203±0.007	8.201±0.007	8.243±0.007
313.15	0.967	8.186±0.007	8.185±0.007	8.203±0.007
313.15	1.432	8.247±0.007	8.246±0.007	8.281±0.007
313.15	1.449	8.243±0.007	8.244±0.007	8.259±0.007
313.15	2.834	8.397±0.009	8.400±0.009	8.370±0.009
313.15	2.886	8.360±0.009	8.360±0.009	8.351±0.009
313.15	4.758	8.602±0.013	8.600±0.013	8.606±0.013
313.15	4.816	8.602±0.014	8.601±0.014	8.608±0.014

a) Refers to eq. (3); b) ± 95 % C.I.

Table 2S. Experimental protonation constants of maltol in KCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with two computer programs [34]

		log $K^{\mathrm{H}\ \mathrm{a)}}$	
T / K	I / mol L^{-1}	BSTAC	STACO
283.15	0.124	8.622±0.007[b)]	8.625±0.007[b)]
283.15	0.124	8.611±0.007	8.615±0.007
283.15	0.582	8.590±0.006	8.590±0.006
283.15	0.582	8.590±0.006	8.591±0.006
283.15	0.730	8.624±0.006	8.626±0.006
283.15	1.162	8.641±0.006	8.643±0.006
283.15	1.168	8.631±0.006	8.634±0.006
283.15	2.564	8.875±0.012	8.876±0.012
283.15	2.575	8.882±0.012	8.882±0.012
298.15	0.148	8.468±0.006	8.469±0.006
298.15	0.148	8.481±0.006	8.483±0.006
298.15	0.252	8.444±0.005	8.446±0.005
298.15	0.586	8.431±0.004	8.431±0.004
298.15	0.589	8.433±0.004	8.433±0.004
298.15	1.165	8.469±0.004	8.469±0.004
298.15	1.170	8.468±0.004	8.468±0.004
298.15	1.944	8.585±0.006	8.585±0.006
298.15	2.562	8.697±0.008	8.698±0.008
298.15	2.572	8.696±0.008	8.696±0.008
313.15	0.129	8.359±0.009	8.361±0.009
313.15	0.129	8.347±0.009	8.348±0.009
313.15	0.627	8.313±0.007	8.315±0.007
313.15	0.630	8.279±0.007	8.279±0.007
313.15	1.121	8.318±0.007	8.318±0.007
313.15	1.125	8.312±0.007	8.314±0.007
313.15	1.940	8.425±0.008	8.426±0.008
313.15	2.676	8.579±0.011	8.581±0.011
313.15	2.742	8.542±0.011	8.544±0.011

[a)] Refers to eq. (3); [b)] ± 95 % C.I.

Table 3S. Experimental protonation constants of maltol in $(C_2H_5)_4NI$ aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with two computer programs [34]

		log $K^{\mathrm{H}\ \mathrm{a)}}$	
T / K	I / mol L^{-1}	BSTAC	STACO
283.15	0.148	8.638±0.006[b)]	8.641±0.006[b)]
283.15	0.149	8.655±0.006	8.655±0.006
283.15	0.482	8.752±0.006	8.753±0.006
283.15	0.491	8.768±0.006	8.769±0.006
283.15	0.858	8.856±0.014	8.857±0.014
283.15	0.889	8.889±0.015	8.889±0.015
298.15	0.147	8.521±0.004	8.521±0.004
298.15	0.149	8.442±0.004	8.445±0.004
298.15	0.478	8.598±0.002	8.599±0.002
298.15	0.489	8.592±0.002	8.592±0.002

298.15	0.874	8.704±0.012	8.705±0.012
298.15	0.886	8.701±0.012	8.702±0.012
313.15	0.148	8.367±0.008	8.369±0.008
313.15	0.149	8.405±0.008	8.408±0.008
313.15	0.489	8.466±0.008	8.468±0.008
313.15	0.494	8.494±0.008	8.499±0.008
313.15	0.894	8.606±0.017	8.610±0.017
313.15	0.896	8.599±0.017	8.589±0.017

a) Refers to eq. (3); b) ± 95 % C.I.

Table 4S. Experimental protonation constants of ethylmaltol in NaCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with two computer programs [34]

		log K^{H} a)	
T / K	I / mol L^{-1}	BSTAC	STACO
283.15	0.197	8.665±0.006 b)	8.667±0.006 b)
283.15	0.198	8.661±0.006	8.662±0.006
283.15	0.966	8.629±0.004	8.629±0.004
283.15	0.972	8.621±0.004	8.621±0.004
283.15	1.932	8.727±0.004	8.728±0.004
283.15	1.938	8.730±0.004	8.730±0.004
283.15	2.899	8.869±0.006	8.869±0.006
283.15	2.923	8.862±0.006	8.863±0.006
283.15	3.848	9.048±0.011	9.050±0.011
283.15	3.876	9.046±0.011	9.048±0.011
298.15	0.197	8.491±0.005	8.491±0.005
298.15	0.197	8.493±0.005	8.492±0.005
298.15	0.950	8.447±0.004	8.448±0.004
298.15	0.950	8.452±0.004	8.453±0.004
298.15	1.917	8.515±0.005	8.517±0.005
298.15	1.927	8.518±0.005	8.519±0.005
298.15	2.936	8.641±0.006	8.641±0.006
298.15	4.019	8.775±0.010	8.775±0.010
298.15	4.047	8.769±0.011	8.768±0.011
313.15	0.196	8.372±0.008	8.372±0.008
313.15	0.197	8.351±0.008	8.351±0.008
313.15	0.953	8.290±0.007	8.290±0.007
313.15	0.959	8.287±0.007	8.289±0.007
313.15	2.846	8.478±0.009	8.478±0.009
313.15	2.863	8.460±0.010	8.460±0.010
313.15	4.079	8.617±0.014	8.617±0.014
313.15	4.204	8.631±0.014	8.636±0.014

a) Refers to eq. (4); b) ± 95 % C.I.

Table 5S. Experimental protonation constants of ethylmaltol in KCl aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with two computer programs [34]

		log $K^{\mathrm{H}\ a)}$	
T / K	*I* / mol L^{-1}	BSTAC	STACO
283.15	0.153	8.672±0.006[b]	8.679±0.006[b]
283.15	0.153	8.676±0.006	8.679±0.006
283.15	0.480	8.628±0.006	8.628±0.006
283.15	0.488	8.634±0.006	8.634±0.006
283.15	0.954	8.686±0.006	8.688±0.006
283.15	0.973	8.694±0.006	8.699±0.006
283.15	2.870	8.924±0.015	8.924±0.015
283.15	2.892	8.925±0.015	8.925±0.015
298.15	0.153	8.515±0.006	8.517±0.006
298.15	0.153	8.534±0.006	8.535±0.006
298.15	0.479	8.471±0.005	8.471±0.005
298.15	0.486	8.473±0.005	8.473±0.005
298.15	0.954	8.458±0.005	8.459±0.005
298.15	0.968	8.466±0.005	8.465±0.005
298.15	2.867	8.730±0.008	8.730±0.008
298.15	2.886	8.732±0.008	8.732±0.008
313.15	0.152	8.373±0.008	8.372±0.008
313.15	0.153	8.367±0.008	8.366±0.008
313.15	0.487	8.330±0.007	8.327±0.007
313.15	0.493	8.348±0.007	8.344±0.007
313.15	0.623	8.369±0.006	8.369±0.006
313.15	0.972	8.344±0.006	8.344±0.006
313.15	0.983	8.338±0.006	8.337±0.006
313.15	2.913	8.546±0.003	8.545±0.003
313.15	2.925	8.568±0.003	8.565±0.003

[a] Refers to eq. (4); [b] ± 95 % C.I.

Table 6S. Experimental protonation constants of ethylmaltol in $(C_2H_5)_4NI$ aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with three computer programs [33, 34]

			log $K^{\mathrm{H}\ a)}$	
T / K	*I* / mol L^{-1}	BSTAC	STACO	ESAB2M
283.15	0.148	8.785±0.006[b]	8.787±0.006[b]	8.786±0.006[b]
283.15	0.148	8.756±0.006	8.758±0.006	8.760±0.006
283.15	0.489	8.825±0.009	8.830±0.009	8.835±0.009
283.15	0.479	8.832±0.009	8.834±0.009	8.838±0.009
283.15	0.886	9.054±0.015	9.058±0.015	9.063±0.015
283.15	0.881	8.948±0.015	8.949±0.015	8.955±0.015
283.15	0.880	9.010±0.015	9.015±0.015	9.020±0.015
283.15	0.876	9.027±0.015	9.031±0.015	9.035±0.015

298.15	0.153	8.597±0.005	8.597±0.005	8.592±0.014
298.15	0.153	8.599±0.005	8.599±0.005	8.589±0.013
298.15	0.466	8.710±0.008	8.710±0.008	8.713±0.012
298.15	0.466	8.711±0.008	8.711±0.008	8.710±0.015
298.15	0.846	8.805±0.010	8.805±0.010	8.796±0.013
298.15	0.846	8.805±0.010	8.807±0.010	8.796±0.010
313.15	0.148	8.473±0.008	8.474±0.008	8.469±0.008
313.15	0.149	8.426±0.008	8.427±0.008	8.423±0.008
313.15	0.487	8.518±0.009	8.519±0.009	8.519±0.009
313.15	0.478	8.532±0.009	8.531±0.009	8.537±0.009
313.15	0.892	8.672±0.013	8.673±0.013	8.675±0.014

a)Refers to eq. (4); b)± 95 % C.I.

Table 7S. Experimental protonation constants of kojic acid in NaCl and $(C_2H_5)_4NI$ aqueous solutions at different ionic strengths and temperatures (molar scale) calculated with BSTAC computer program [34]

log K^{H} a)					
T / K	I / mol L^{-1}	NaCl	T / K	I / mol L^{-1}	$(C_2H_5)_4NI$
283.15	0.113	7.84±0.02 b)	283.15	0.146	7.90±0.02 b)
283.15	1.036	7.76±0.02	283.15	0.146	7.91±0.02
283.15	1.813	7.67±0.03	283.15	0.327	7.94±0.02
283.15	4.903	8.40±0.06	283.15	0.327	7.94±0.02
298.15	0.111	7.71±0.02	283.15	0.406	7.96±0.02
298.15	0.513	7.61±0.01	283.15	0.406	7.96±0.02
298.15	1.064	7.61±0.01	283.15	0.619	8.02±0.02
298.15	1.624	7.68±0.02	283.15	0.619	8.03±0.02
298.15	2.030	7.73±0.02	298.15	0.146	7.77±0.01
298.15	4.057	7.87±0.05	298.15	0.146	7.78±0.01
298.15	4.862	7.95±0.06	298.15	0.284	7.75±0.01
318.15	0.113	7.58±0.02	298.15	0.284	7.75±0.01
318.15	1.092	7.43±0.02	298.15	0.703	7.88±0.01
318.15	2.064	7.40±0.03	298.15	0.703	7.89±0.01
318.15	3.940	7.69±0.05	298.15	0.948	7.97±0.02
318.15	4.998	7.95±0.06	298.15	0.948	7.98±0.02
			318.15	0.146	7.63±0.02
			318.15	0.146	7.62±0.02
			318.15	0.286	7.62±0.02
			318.15	0.641	7.72±0.02
			318.15	0.641	7.72±0.02
			318.15	0.945	7.80±0.02

a)Refers to eq. (5); b)± 95 % C.I.

Table 8S. Activity coefficients of the neutral species in NaCl at T 298.15 K for the three investigated hydroxypyrone derivatives

I / mol kg^{-1}	log γ_N		
	Maltol	Ethylmaltol	Kojic acid
0.100	0.01±0.01 a)	0.01±0.01 a)	0.004±0.001 a)
0.500	0.05±0.01	0.07±0.01	0.018±0.001

1.000	0.10±0.01	0.13±0.01	0.036±0.002
2.000	0.20±0.01	0.26±0.01	0.072±0.004
3.000	0.30±0.02	0.39±0.02	0.108±0.006
5.000	0.50±0.03	0.65±0.03	0.180±0.010

a) ± 95% C.I.

Table 9S. Smoothed protonation constants of maltol, ethylmaltol and kojic acid in $KCl_{(aq)}$, $NaCl_{(aq)}$ and $(C_2H_5)_4NI_{(aq)}$ at different ionic strengths and temperatures in the molal concentration scale

Medium	T / K	I / mol kg^{-1}	log K^H		
			Maltol	Ethylmaltol	Kojic acid
KCl	283.15	0.100	8.630±0.003 a)	8.712±0.003 a)	
	283.15	0.500	8.560±0.003	8.627±0.003	
	283.15	1.000	8.590±0.003	8.638±0.004	
	283.15	3.000	8.899±0.008	8.871±0.007	
	298.15	0.100	8.478±0.000	8.552±0.000	
	298.15	0.500	8.398±0.002	8.457±0.002	
	298.15	1.000	8.420±0.002	8.460±0.002	
	298.15	3.000	8.706±0.006	8.670±0.004	
	313.15	0.100	8.351±0.003	8.418±0.003	
	313.15	0.500	8.260±0.003	8.312±0.002	
	313.15	1.000	8.275±0.003	8.307±0.002	
	313.15	3.000	8.537±0.006	8.494±0.002	
NaCl	283.15	0.100	8.624±0.003	8.711±0.003	7.845±0.005 a)
	283.15	0.500	8.534±0.003	8.621±0.003	7.751±0.005
	283.15	1.000	8.537±0.002	8.626±0.002	7.750±0.007
	283.15	3.000	8.740±0.004	8.836±0.004	7.936±0.016
	283.15	5.000	9.011±0.007	9.112±0.008	8.190±0.026
	298.15	0.100	8.472±0.000	8.550±0.000	7.718±0.001
	298.15	0.500	8.367±0.002	8.447±0.002	7.610±0.003
	298.15	1.000	8.359±0.002	8.440±0.002	7.597±0.005
	298.15	3.000	8.521±0.003	8.608±0.004	7.743±0.015
	298.15	5.000	8.753±0.005	8.846±0.007	7.957±0.024
	313.15	0.100	8.344±0.003	8.415±0.003	7.613±0.003
	313.15	0.500	8.226±0.003	8.298±0.002	7.492±0.003
	313.15	1.000	8.205±0.003	8.279±0.002	7.467±0.005
	313.15	3.000	8.329±0.005	8.409±0.005	7.574±0.014
	313.15	5.000	8.525±0.008	8.611±0.009	7.753±0.024
$(C_2H_5)_4NI$	283.15	0.100	8.669±0.003	8.757±0.003	7.889±0.005
	283.15	0.500	8.705±0.005	8.802±0.005	7.920±0.007
	283.15	1.000	8.807±0.008	8.915±0.007	8.017±0.010
	298.15	0.100	8.517±0.002	8.597±0.001	7.762±0.002
	298.15	0.500	8.541±0.004	8.630±0.003	7.782±0.004
	298.15	1.000	8.633±0.007	8.733±0.005	7.868±0.006
	313.15	0.100	8.390±0.003	8.463±0.002	7.659±0.003
	313.15	0.500	8.401±0.005	8.483±0.001	7.665±0.003
	313.15	1.000	8.484±0.009	8.577±0.006	7.742±0.005

a) ±95% C.I.

Table 10S. Smoothed protonation constants of maltol, ethylmaltol and kojic acid in $KCl_{(aq)}$, $NaCl_{(aq)}$ and $(C_2H_5)_4NI_{(aq)}$ at different ionic strengths and temperatures in the molar concentration scale

Medium	T / K	I / mol L^{-1}	log K^H		
			Maltol	Ethylmaltol	Kojic acid
KCl	283.15	0.100	8.630±0.004[a]	8.712±0.003[a]	
	283.15	0.500	8.566±0.003	8.632±0.002	
	283.15	1.000	8.608±0.003	8.655±0.003	
	283.15	3.000	8.985±0.009	8.953±0.008	
	298.15	0.100	8.477±0.003	8.551±0.004	
	298.15	0.500	8.403±0.002	8.461±0.003	
	298.15	1.000	8.438±0.002	8.477±0.003	
	298.15	3.000	8.791±0.006	8.751±0.004	
	313.15	0.100	8.354±0.005	8.421±0.005	
	313.15	0.500	8.269±0.004	8.320±0.004	
	313.15	1.000	8.296±0.004	8.328±0.003	
	313.15	3.000	8.627±0.008	8.580±0.005	
NaCl	283.15	0.100	8.623±0.004	8.710±0.003	7.850±0.012[a]
	283.15	0.500	8.534±0.002	8.621±0.003	7.757±0.012
	283.15	1.000	8.545±0.002	8.633±0.003	7.763±0.012
	283.15	3.000	8.795±0.004	8.887±0.006	7.995±0.019
	283.15	5.000	9.120±0.009	9.214±0.011	8.301±0.030
	298.15	0.100	8.469±0.003	8.548±0.004	7.716±0.009
	298.15	0.500	8.367±0.002	8.446±0.003	7.609±0.008
	298.15	1.000	8.366±0.003	8.446±0.003	7.604±0.008
	298.15	3.000	8.577±0.004	8.660±0.005	7.796±0.016
	298.15	5.000	8.863±0.007	8.950±0.009	8.064±0.027
	313.15	0.100	8.346±0.005	8.417±0.005	7.610±0.009
	313.15	0.500	8.230±0.004	8.302±0.004	7.490±0.008
	313.15	1.000	8.218±0.004	8.290±0.003	7.473±0.008
	313.15	3.000	8.391±0.005	8.466±0.006	7.627±0.015
	313.15	5.000	8.642±0.009	8.721±0.012	7.861±0.026
$(C_2H_5)_4NI$	283.15	0.100	8.676±0.004	8.765±0.003	7.902±0.011
	283.15	0.500	8.758±0.004	8.857±0.005	7.979±0.009
	283.15	1.000	8.940±0.010	9.051±0.010	8.155±0.010
	298.15	0.100	8.522±0.003	8.603±0.003	7.768±0.008
	298.15	0.500	8.592±0.004	8.683±0.004	7.833±0.006
	298.15	1.000	8.765±0.010	8.868±0.007	7.999±0.005
	313.15	0.100	8.399±0.005	8.473±0.004	7.662±0.008
	313.15	0.500	8.456±0.006	8.540±0.005	7.714±0.006
	313.15	1.000	8.618±0.012	8.714±0.009	7.870±0.008

[a] ±95% C.I.