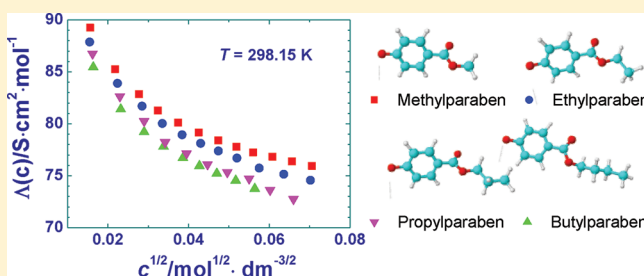


Dissociation Constants of Parabens and Limiting Conductances of Their Ions in Water

Ana Kroflič,[†] Alexander Apelblat,^{*,‡} and Marija Bešter-Rogač^{*,†}[†]Faculty of Chemistry and Chemical Technology, University of Ljubljana, SI-1000 Ljubljana, Slovenia[‡]Department of Chemical Engineering, Ben-Gurion University of the Negev, Beer Sheva, 84105, Israel

ABSTRACT: Precise measurements of electrical conductivities of methylparaben, ethylparaben, propylparaben, and butylparaben sodium salts in dilute aqueous solutions were performed from 278.15 to 313.15 K in 5 K intervals. Experimental conductivity data were analyzed applying the Quint–Viallard conductivity equations by taking into account the salt hydrolysis in aqueous solutions. These evaluations yield the limiting conductances of paraben anions and the dissociation constants of the investigated parabens in water. From temperature dependence of dissociation constants, the thermodynamic functions associated with the dissociation process were estimated. It was discovered that the contributions of enthalpy and entropy to the Gibbs free energy are quite similar. The Walden products of paraben anions in water are independent of temperature, indicating that the hydrodynamic radii are not significantly affected by temperature.



INTRODUCTION

Alkyl esters of 4-hydroxybenzoic acid (called parabens and denoted here as RPBOH) are widely used in food, cosmetic, and pharmaceutical industry due to their antimicrobial activity, low toxicity, and low cost. They often serve as food additives and preservatives in cosmetics and are common constituents of shampoos, moisturizers, deodorants, antiperspirants, shaving gels, lubricants, and toothpastes. Their bactericidal and fungicidal properties are also utilized in topical and parenteral pharmaceuticals. Parabens have been the subject of numerous studies that have established not only their broad spectrum of action against microorganisms^{1,2} but also their efficiency, stability, and their lack of side effects.^{3,4} Despite these studies, a controversy surrounding parabens has been mounting since late 1990s, when several studies suggested that parabens have an estrogenic activity.^{5–8} It has been even intensified in 2004 when Darbre et al. detected the traces of parabens in breast tumor tissue samples.⁹ Lately, it turned out that there is no proven link between parabens and breast cancer and that the estrogenic activity of parabens is immensely lower than that of estrogen.^{3,4,10–13}

Due to the solubility limitations, parabens as water-soluble antiseptics are used in a form of sodium salts. They are relatively stable over a wide range of temperature and pH. Commercial parabens are synthetically produced, although some of them are also found in plants, for example, methylparaben in blueberries.

Resistance of microorganisms to parabens^{14,15} and their degradation reactions^{16–18} as well as paraben behavior in micellar mixtures^{19,20} have been also investigated in the literature. From degradation reactions, the kinetic aspects of catalytic hydrolysis of parabens in alkaline solutions (temper-

ature and pH effect) were mainly reported.^{16–18} The base-catalyzed hydrolysis of methylparaben has also been proposed as a reference and test reaction for isothermal flow microcalorimeters used for determination of kinetic and thermodynamic parameters.²¹ Considering the importance of the interaction of parabens with micelles, a number of studies have been devoted to partitioning of parabens between water and micellar pseudophases and to the effect of micelles on the value of paraben dissociation constants.^{15,20}

In this work, the precise values of electrical conductivities in dilute aqueous solutions of paraben sodium salts (RPBONa), namely methylparaben (MePBONa), ethylparaben (EtPBONa), propylparaben (PrPBONa), and butylparaben (BuPBONa), in the 278.15–313.15 K temperature range are reported. A search in the literature failed to reveal any measurements of this kind so far. Applying the molecular model of hydrolysis of salt of weak organic base in water, it was possible to determine limiting conductances of paraben ions, $\lambda^0(RPBO^-, T)$, dissociation constants of parabens, $K(T)$, and thermodynamic functions associated with the dissociation process from the experimental conductivities.

EXPERIMENTAL SECTION

Materials. Methyl-4-hydroxybenzoate sodium salt (methylparaben sodium salt, MePBONa, Fluka, Germany, PhEur, $M = 174.13$ g/mol), ethyl-4-hydroxybenzoate sodium salt (ethylparaben sodium salt, EtPBONa, Chemo GmbH, Germany, PhEur, $M = 188.16$ g/mol), propyl-4-hydroxybenzoate sodium

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Table 1. Experimental Molar Conductances, Λ_{expt} of Paraben Sodium Salts in Aqueous Solution as a Function of Molality, m , and Temperature, T^a

$10^3 m$	Λ_{expt}							
	278.15 K	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
Methylparaben Sodium Salt: $b = 0.067 \text{ kg}^2 \cdot \text{dm}^{-3} \cdot \text{mol}^{-1}$								
0.2448	50.15	58.77	68.13	78.33	89.25	100.85	113.17	126.10
0.4766	48.42	56.61	65.48	75.07	85.27	96.15	107.58	119.55
0.7676	47.41	55.34	63.89	73.09	82.87	93.26	104.00	115.31
1.0543	46.85	54.60	62.94	71.78	81.29	91.38	101.96	112.93
1.4006	46.39	53.90	62.06	70.82	80.11	89.93	100.29	110.86
1.8129	45.94	53.42	61.45	70.05	79.16	88.78	98.89	109.18
2.2556	45.68	53.07	60.98	69.46	78.41	87.86	97.78	107.83
2.7064	45.44	52.76	60.58	68.96	77.80	86.97	96.71	106.68
3.1425	45.28	52.55	60.31	68.61	77.25	86.48	96.06	105.96
3.7060	45.10	52.31	60.00	68.16	76.84	85.94	95.43	105.16
4.3238	44.93	52.09	59.68	67.81	76.38	85.39	94.82	104.50
5.0049	44.75	51.83	59.40	67.47	75.95	84.87	94.20	103.75
Ethylparaben Sodium Salt: $b = 0.063 \text{ kg}^2 \cdot \text{dm}^{-3} \cdot \text{mol}^{-1}$								
0.2400	49.28	57.73	66.98	77.05	87.88	99.25	111.62	124.66
0.5027	47.45	55.53	64.35	73.78	83.90	94.68	106.14	118.25
0.8140	46.72	54.47	62.91	72.02	81.70	91.64	102.52	113.83
1.1239	46.05	53.71	62.02	70.58	80.03	90.01	100.55	111.56
1.4796	45.59	52.92	61.07	69.72	78.94	88.72	98.98	109.67
1.8543	45.16	52.56	60.52	69.08	78.12	87.67	97.56	108.03
2.2537	44.88	52.19	60.04	68.46	77.39	86.79	96.70	106.61
2.7139	44.60	51.85	59.61	67.93	76.70	85.74	95.52	105.63
3.3175	44.31	51.47	59.13	67.33	75.74	84.90	94.50	104.38
4.0577	44.03	51.13	58.57	66.64	75.15	84.13	93.61	103.33
4.9392	43.75	50.67	58.16	66.16	74.57	83.42	92.69	102.34
Propylparaben Sodium Salt: $b = 0.060 \text{ kg}^2 \cdot \text{dm}^{-3} \cdot \text{mol}^{-1}$								
0.2699	48.76	57.11	66.22	76.13	86.76	98.19	110.32	123.17
0.5390	46.88	54.82	63.41	72.73	82.65	93.23	104.45	116.15
0.8451	45.95	53.64	61.92	70.88	80.42	90.44	101.11	112.10
1.1477	45.41	52.93	61.04	69.72	79.00	88.86	99.22	109.94
1.4899	44.96	52.30	60.26	68.81	77.90	87.51	97.67	108.17
1.8237	44.61	51.89	59.74	68.18	77.11	86.54	96.49	106.75
2.2219	44.28	51.49	59.24	67.55	76.36	85.66	95.42	105.29
2.6784	44.00	51.15	58.81	67.03	75.69	84.88	94.30	104.16
3.1925	43.76	50.83	58.44	66.52	74.88	83.89	93.44	103.44
Butylparaben Sodium Salt: $b = 0.058 \text{ kg}^2 \cdot \text{dm}^{-3} \cdot \text{mol}^{-1}$								
0.2639	48.71	57.04	66.18	76.08	86.75	97.80	109.87	122.65
0.5302	46.73	54.70	63.33	72.65	82.65	93.13	104.12	115.79
0.8434	45.77	53.47	61.80	70.74	80.27	89.60	100.21	111.47
1.1704	45.10	52.64	60.78	68.96	78.24	88.05	98.34	109.25
1.5664	44.57	51.62	59.56	68.09	77.16	86.76	96.72	107.27
2.0087	43.88	51.09	58.93	67.24	76.10	85.47	95.35	105.73
2.4637	43.57	50.76	58.41	66.66	75.35	84.48	94.18	103.40
3.0336	43.31	50.38	58.00	66.11	74.73	83.10	92.56	102.64
3.6410	43.03	50.10	57.58	65.23	73.63	82.48	91.77	101.63
4.3703	42.67	49.60	56.58	64.47	72.76	81.60	90.85	100.62

^aUnits; m , $\text{mol} \cdot \text{kg}^{-1}$; Λ , $\text{S} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$.

salt (propylparaben sodium salt, PrPBONa, Fluka, Germany, PhEur, $M = 202.18 \text{ g/mol}$), and butyl-4-hydroxybenzoate sodium salt (butylparaben sodium salt, BuPBONa, Chemo GmbH, Germany, PhEur, $M = 216.21 \text{ g/mol}$) were used in the experiment. MePBONa and EtPBONa were dried for 24 h at $T \approx 400 \text{ K}$ with a vacuum line ($p < 0.01 \text{ Pa}$) and stored in a desiccator over P_2O_5 before use. Due to relatively low melting points, PrPBONa and BuPBONa were not dried before use, but the humidity of the samples was analyzed through Karl Fischer

titration and taken into account in calculating the concentrations.

Stock solutions were prepared by mass from pure compounds and demineralized distilled water. Demineralized water was distilled two times in a quartz bidistillation apparatus (Destamat Bi 18E, Heraeus). The final product with specific conductivity $< 6 \times 10^{-7} \text{ S} \cdot \text{cm}^{-1}$ was distilled into a flask permitting storage and transfer of water into the measuring cell under an atmosphere of nitrogen.

Table 2. Limiting Molar and Ionic Conductances of Parabens and Sodium Hydroxide, Λ^0 and λ^0 ; the Quint–Viallard Conductivity Equation Coefficients, S , E , J_1 , and J_2 ; the Standard Deviations of Conductivity Fitting, $\sigma(\Lambda)$; the Dissociation Constants of Parabens and Water, K and K_w ; the Standard Changes of Thermodynamic Functions, ΔG° , ΔH° , and $T\Delta S^\circ$, in the Dissociation Reaction; and Densities, Viscosities, and Dielectric Constants of Water, d , η , and D , in the Investigated Temperature Range^a

	278.15 K	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
Methylparaben Sodium Salt								
λ^{0b}	15.70	18.36	21.21	24.25	27.38	30.69	34.14	37.58
Λ^{0b}	46.00	53.24	60.93	69.06	77.53	86.41	95.67	104.92
S	45.35	52.86	60.89	69.42	78.43	87.93	97.90	108.28
E	−0.068	−0.068	−0.052	−0.002	0.060	0.162	0.306	0.401
J_1	79.54	92.95	107.42	123.01	139.57	157.28	176.12	195.58
J_2	113.33	132.70	153.67	176.33	200.52	226.47	254.18	282.97
10^9K	3.80	4.50	5.20	5.95	6.70	7.55	8.65	9.30
ΔG°	44.84	45.25	45.70	46.16	46.66	47.14	47.57	48.15
ΔH°	21.22	20.44	19.69	18.92	18.15	17.34	16.46	15.70
$T\Delta S^\circ$	−23.62	−24.80	−26.01	−27.25	−28.51	−29.79	−31.11	−32.45
$\sigma(\Lambda)$	0.12	0.12	0.15	0.17	0.17	0.14	0.13	0.17
Ethylparaben Sodium Salt								
Λ^{0b}	14.80	17.38	20.15	23.15	26.21	29.52	32.91	36.43
Λ^{0b}	45.10	52.26	59.87	67.96	76.36	85.24	94.44	103.77
S	45.15	52.64	60.65	69.17	78.16	87.65	97.61	108.00
E	−0.260	−0.284	−0.287	−0.251	−0.210	−0.114	0.012	0.118
J_1	78.33	91.60	105.95	121.46	137.90	155.57	174.31	193.84
J_2	111.63	130.80	151.60	174.15	198.16	224.06	251.63	280.52
10^9K	3.65	4.45	5.15	6.05	6.80	7.90	8.85	9.45
ΔG°	44.93	45.27	45.72	46.12	46.62	47.02	47.51	48.11
ΔH°	24.78	23.33	21.95	20.46	19.02	17.44	15.89	14.41
$T\Delta S^\circ$	−20.16	−21.94	−23.78	−25.66	−27.60	−29.58	−31.62	−33.70
$\sigma(\Lambda)$	0.06	0.07	0.11	0.12	0.16	0.21	0.24	0.31
Propylparaben Sodium Salt								
λ^{0b}	13.99	16.45	19.12	22.00	24.89	28.00	31.14	34.46
Λ^{0b}	44.29	51.33	58.84	66.81	75.04	83.72	92.67	101.80
S	44.97	52.43	60.42	68.91	77.86	87.30	97.20	107.54
E	−0.436	−0.487	−0.517	−0.512	−0.515	−0.471	−0.412	−0.362
J_1	77.23	90.33	104.52	119.83	136.01	153.37	171.69	190.90
J_2	110.08	129.01	149.58	171.86	195.50	220.95	247.95	276.37
10^9K	2.95	3.70	4.50	5.35	6.10	6.95	7.80	8.50
ΔG°	45.42	45.71	46.05	46.42	46.89	47.35	47.83	48.38
ΔH°	29.79	27.46	25.10	22.70	20.31	17.82	15.28	12.72
$T\Delta S^\circ$	−15.63	−18.24	−20.94	−23.72	−26.58	−29.53	−32.56	−35.67
$\sigma(\Lambda)$	0.04	0.03	0.03	0.03	0.06	0.04	0.05	0.14
Butylparaben Sodium Salt								
λ^{0b}	13.36	15.79	18.27	20.92	23.81	26.86	30.08	33.54
Λ^{0b}	43.66	50.67	57.99	65.73	73.96	82.58	91.61	100.88
S	44.83	52.28	60.22	68.66	77.61	87.04	96.95	107.32
E	−0.5714	−0.6321	−0.7067	−0.7560	−0.7640	−0.7380	−0.6680	−0.5890
J_1	76.38	89.43	103.33	118.32	134.47	151.71	170.12	189.50
J_2	108.88	127.74	147.91	169.72	193.32	218.62	245.73	274.40
10^9K	2.40	3.15	3.70	4.40	5.20	6.35	7.45	8.30
ΔG°	45.90	46.09	46.51	46.90	47.29	47.57	47.95	48.45
ΔH°	28.54	27.55	26.77	25.92	25.04	24.03	23.07	22.21
$T\Delta S^\circ$	−17.36	−18.54	−19.74	−20.98	−22.25	−23.55	−24.88	−26.24
$\sigma(\Lambda)$	0.07	0.10	0.17	0.18	0.21	0.23	0.23	0.29
Sodium Hydroxide and Water Parameters								
λ_+^{0b}	30.30	34.88	39.72	44.81	50.15	55.72	61.53	67.34
λ_-^{0b}	123.4	142.0	160.6	179.2	198.3	216.4	235.0	251.5
Λ^0	153.70	176.88	200.32	224.01	248.45	272.12	296.53	318.83
S	69.27	80.54	92.35	104.70	117.70	131.00	144.95	158.90
E	48.03	55.81	63.91	72.33	81.19	90.14	99.54	108.73
J_1	150.98	175.77	201.42	228.00	316.96	284.27	314.11	342.29
J_2	219.42	255.87	293.90	333.63	375.83	418.51	463.88	507.89
d_0	0.99997	0.99970	0.99910	0.99821	0.99705	0.99565	0.99404	0.99222

Table 2. continued

	278.15 K	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
Sodium Hydroxide and Water Parameters								
η	1.5192	1.3069	1.1382	1.002	0.8903	0.7975	0.7195	0.6531
D	85.897	83.943	82.039	80.176	78.358	76.581	74.846	73.151
$10^{14}K_w$	0.1846	0.2918	0.4506	0.6813	1.008	1.466	2.089	2.917

^aUnits: λ^0 , Λ^0 , $S \cdot c^{1/2}$; E_c , J_1c , $J_2c^{3/2}$, $\sigma(\Lambda)$, $S \cdot cm^2 \cdot mol^{-1}$; K , K_w , $mol \cdot dm^{-3}$; d_0 , $kg \cdot dm^{-3}$; η , $mPa \cdot s$; ΔG° , ΔH° , $T\Delta S^\circ$, $kJ \cdot mol^{-1}$. ^b $\Lambda^0 = \Lambda^0(RPBO\text{Na})$, $\lambda^0 = \lambda^0(RPBO^-)$, $\lambda_+^0 = \lambda^0(Na^+)$, $\lambda_-^0 = \lambda^0(OH^-)$.

Conductivity Measurement. The conductivities of the solutions were determined with the help of a three-electrode measuring cell, described elsewhere.²² The cell was calibrated with dilute potassium chloride solutions²³ and immersed in the high-precision thermostat described previously.²⁴ The temperature dependence of the cell constant was taken into account.²³ The water bath can be set to each temperature using a temperature program with a reproducibility of 0.005 K. The temperature in the precision thermostat bath was additionally checked with calibrated Pt100 resistance thermometer (MPMI 1004/300 Merz) in connection with a Multimeter HP 3458 A. The resistance measurements of the solutions in the cell were performed using a precision LCR Meter Agilent 4284 A.

At the beginning of every measuring cycle, the cell was filled with a known mass of water (~ 660 g). After the measurement of water conductivity at all temperatures of the temperature program, the stepwise concentration was carried out by successive additions of known masses of stock solution with a gastight syringe. After every addition, the temperature program was run by the computer and all the measured data (frequency-dependent resistance and temperature) were stored and also partially shown on display to track the measuring process. A home-developed software package was used for temperature control and acquisition of conductivity data. The measuring procedure, including corrections and extrapolation of the sample conductivity, κ , to infinite frequency, has been previously described.²⁴

The densities, d , of the stock solutions and the final solutions in the conductivity cell, collected in Table 1, were determined at 298.15 ± 0.01 K by the method of Kratky et al.²⁵ using Anton Paar density meter DMA 5000 (Anton Paar, Graz, Austria) with a declared reproducibility $\sim 1 \times 10^{-3} kg \cdot m^{-3}$. A linear change of density at temperature T , $d(T)$ with increasing salt content for diluted solutions was assumed, $d(T) = d_0(T) + bm$, where $d_0(T)$ is the density of water at given temperature, taken from the literature²⁶ and listed in Table 2. From these data the density gradients b for all the examined electrolytes were determined. As usual, they are considered to be independent of temperature and are reported in Table 1 together with molar conductivities, $\Lambda = \kappa/c$, of all investigated systems. Molar conductivities are given as a function of electrolyte molality, m , which relates to the corresponding (temperature-dependent) molar concentration $c(T)$, via $c(T) = md(T)/(1 + M_2m)$, where M_2 is the molar mass of the solute and $d(T)$ is the density of the solution at temperature T . The estimated uncertainty for d is within $\pm 0.05 kg \cdot m^{-3}$. Considering the sources of error (calibration, measurements, impurities), the specific conductivities are estimated to be accurate within 0.3%.

pH Measurement. The pH values of final solutions in the conductivity cell were checked at 298.15 ± 0.02 K with a glass electrode (Mettler Toledo, InLab 423). The pH meter (Iskra MA 5740, Slovenia) was calibrated using borate buffer of pH = 9.180 at 298.15 K.

RESULTS AND DISCUSSION

Determined molar conductivities of paraben sodium salts, Λ , as a function of molality, m , and temperature, T , are presented in Table 1 and illustrated in Figure 1 at 298.15 K. Molar

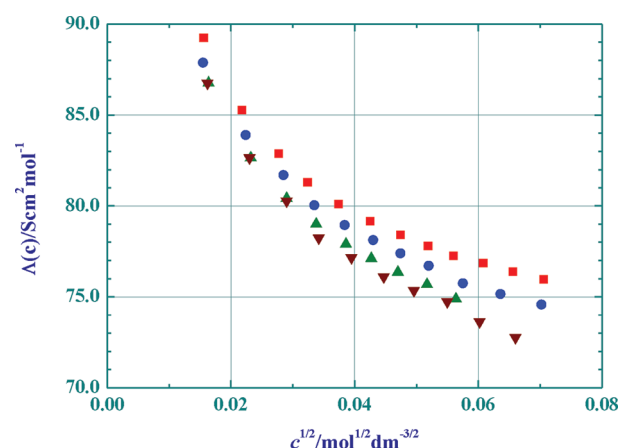


Figure 1. Molar conductivity, $\Lambda(c)$, of paraben sodium salts at 298.15 K: (■) methylparaben sodium salt; (●) ethylparaben sodium salt; (▲) propylparaben sodium salt; and (▼) butylparaben sodium salt.

conductivities can be represented as a sum of ionic contributions

$$\Lambda = \frac{\kappa}{c} = \sum_{j=1}^n \frac{|z_j|c_j\lambda_j}{c} \quad (1)$$

where κ is the measured specific conductance, λ_j are the ionic conductances, c_j and z_j are the concentrations and charges of the individual ions present in the solution, and c denotes the analytical concentration of the electrolyte. The ionic conductances, λ_j , in this work are represented by the Quint–Viallard conductivity equations^{27–29}

$$\lambda_j = \lambda_j^0 - S_j\sqrt{I} + E_jI \ln I + J_{1j}I - J_{2j}I^{3/2} \quad (2)$$

where λ_j^0 is the limiting conductance of the j th ion and I is the ionic strength of the solution. The coefficients S_j , E_j , J_{1j} , and J_{2j} are rather complex functions of the viscosity, η , the dielectric constant of pure water, D , and the average cation–anion distances of closest approach, a_j . Equation 1 can be arranged as a sum of contributions from pairs of ions, where the conductivity equation for each pair has the form

$$\Lambda = \Lambda^0 - S\sqrt{I} + EI \ln I + J_1I - J_2I^{3/2} \quad (3)$$

and the coefficients in eq 3 are the sum of the coefficients of the corresponding cation and anion.

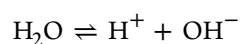
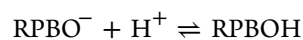
From the form of conductivity curves it is clear that paraben sodium salts deviate from the expected behavior of a strong 1:1

Table 3. Fractions of the Paraben Ions, α ; Calculated and Experimental pH Values of the Solutions; Contributions to the Conductivity from the $(\text{Na}^+ + \text{RPBO}^-)$ and $(\text{Na}^+ + \text{OH}^-)$ Pairs of Ions, Λ_1 and Λ_2 ; and Calculated and Experimental Conductances of Paraben Solutions as a Function of Concentration, c , at 298.15 K^a

$10^3 c^b$	α	pH _{calcd}	pH _{expt}	Λ_1	Λ_2	Λ_{calcd}	Λ_{expt}
Methylparaben Sodium Salt							
0.2441	0.9245	9.25		70.57	18.62	89.20	89.25
0.4752	0.9453	9.39		71.73	13.46	85.19	85.27
0.7653	0.9566	9.49		72.19	10.65	82.83	82.87
1.0510	0.9628	9.56		72.33	9.11	81.44	81.29
1.3963	0.9675	9.62		72.36	7.92	80.28	80.11
1.8073	0.9713	9.67		72.30	6.99	79.29	79.16
2.2484	0.9741	9.72		72.18	6.31	78.49	78.41
2.6977	0.9761	9.75		72.04	5.80	77.84	77.80
3.1322	0.9776	9.79		71.90	5.42	77.32	77.25
3.6936	0.9791	9.82		71.70	5.05	76.75	76.84
4.3091	0.9804	9.86		71.49	4.73	76.23	76.38
4.9875	0.9814	9.89	9.72 ± 0.05	71.27	4.47	75.73	75.95
Ethylparaben Sodium Salt							
0.2393	0.9243	9.24		69.49	18.67	88.16	87.88
0.5012	0.9470	9.40		70.72	13.02	83.74	83.90
0.8115	0.9581	9.50		71.13	10.27	81.40	81.70
1.1205	0.9642	9.57		71.25	8.76	80.00	80.03
1.4750	0.9686	9.62		71.24	7.66	78.90	78.94
1.8484	0.9718	9.67		71.18	6.87	78.04	78.12
2.2464	0.9742	9.71		71.07	6.26	77.33	77.39
2.7050	0.9763	9.75		70.92	5.75	76.67	76.70
3.3063	0.9783	9.80		70.72	5.26	75.97	75.74
4.0437	0.9800	9.84		70.46	4.82	75.29	75.15
4.9217	0.9814	9.89	9.68 ± 0.05	70.17	4.46	74.62	74.57
Propylparaben Sodium Salt							
0.2691	0.9266	9.28		67.42	18.09	85.51	85.45
0.5374	0.9475	9.43		68.46	12.91	81.37	81.40
0.8425	0.9578	9.52		68.81	10.34	79.15	79.21
1.1400	0.9636	9.59		68.91	8.89	77.80	77.82
1.4900	0.9679	9.64		68.90	7.83	76.73	76.73
1.8200	0.9708	9.68		68.84	7.10	75.94	75.95
2.2100	0.9734	9.73		68.73	6.46	75.19	75.22
2.6700	0.9756	9.77		68.59	5.92	74.51	74.55
3.1800	0.9774	9.80	9.60 ± 0.05	68.42	5.47	73.89	73.76
Butylparaben Sodium Salt							
0.2631	0.9178	9.32		66.76	20.28	87.04	86.75
0.5286	0.9412	9.47		68.00	14.45	82.45	82.65
0.8408	0.9531	9.56		68.45	11.50	79.95	80.27
1.1667	0.9600	9.63		68.61	9.78	78.39	78.24
1.5614	0.9652	9.69		68.63	8.48	77.11	77.16
2.0022	0.9691	9.74		68.57	7.51	76.07	76.10
2.4555	0.9720	9.78		68.46	6.80	75.26	75.35
3.0232	0.9745	9.83		68.30	6.17	74.47	74.73
3.6282	0.9765	9.87		68.11	5.67	73.78	73.63
4.3544	0.9783	9.91	9.83 ± 0.05	67.88	5.23	73.11	72.76

^aUnits; c , mol·dm⁻³; Λ , S·cm²·mol⁻¹. ^bConcentrations c at 298.15 K.

electrolyte (Figure 1). Considering that the paraben salts (RPBONa) come from weak organic acids and when dissolved in water they partially hydrolyze, we can assume the following set of reactions:³⁰



(4)

The mass-action equations for these reactions can be written as

$$K = \frac{a_{\text{H}^+} a_{\text{RPBO}^-}}{a_{\text{RPBOH}}} = \frac{[\text{H}^+][\text{RPBO}^-] f_{\text{H}^+} f_{\text{RPBO}^-}}{[\text{RPBOH}] f_{\text{RPBOH}}}$$

$$= \frac{[\text{H}^+][\text{RPBO}^-]}{[\text{RPBOH}]} F_1$$

$$F_1 = f_{\text{H}^+} f_{\text{RPB}^-}; \quad f_{\text{RPBOH}} = 1 \quad (5)$$

and

$$\begin{aligned} K_w &= a_{\text{H}^+}a_{\text{OH}^-} \\ &= [\text{H}^+][\text{OH}^-]f_{\text{H}^+}f_{\text{OH}^-} \\ &= [\text{H}^+][\text{OH}^-]F_2 \\ F_2 &= f_{\text{H}^+}f_{\text{OH}^-} \end{aligned} \quad (6)$$

The material and charge balance equations are

$$\begin{aligned} [\text{RPBONa}] &= [\text{RPBO}^-] + [\text{RPBOH}] \\ [\text{Na}^+] + [\text{H}^+] &= [\text{OH}^-] + [\text{RPBO}^-] \end{aligned} \quad (7)$$

Introducing

$$\begin{aligned} [\text{Na}^+] &= c \\ [\text{RPBO}^-] &= c\alpha_{\text{RPBO}^-} = c\alpha \\ [\text{H}^+] &= c\alpha_{\text{H}^+} = c\beta \\ [\text{OH}^-] &= c\alpha_{\text{OH}^-} \\ [\text{RPBOH}] &= c\alpha_{\text{RPBOH}} \end{aligned} \quad (8)$$

into the equations in (7) we get

$$\begin{aligned} \alpha_{\text{RPBOH}} &= 1 - \alpha \\ \alpha_{\text{OH}^-} &= 1 + \beta - \alpha \end{aligned} \quad (9)$$

and the mass-action equations become

$$\begin{aligned} K &= \frac{c\alpha\beta}{1 - \alpha}F_1 \\ K_w &= c^2\beta(1 + \beta - \alpha)F_2 \end{aligned} \quad (10)$$

The individual activity coefficients of ions in dilute solutions f_j , which appear in the products F_1 and F_2 , can be approximated by the Debye–Hückel equations

$$\begin{aligned} \log[f_j(T)] &= -\frac{z_j^2 A(T)\sqrt{I}}{1 + a_j B(T)\sqrt{I}} \\ A(T) &= \frac{1.8246 \times 10^6}{[D(T)T]^{3/2}}; \\ B(T) &= \frac{50.29 \times 10^8}{[D(T)T]^{1/2}} \end{aligned} \quad (11)$$

where $D(T)$ is the dielectric constant of water at T , a_j are the ion size parameters, and I denotes the ionic strength of the solution, which in our case is $I = c(1 + \beta)$. In calculations, the values of the size parameters ($a(\text{Na}^+) = 4.0 \text{ \AA}$, $a(\text{OH}^-) = 3.5 \text{ \AA}$, and $a(\text{RPBO}^-) = 5.0 \text{ \AA}$) were prescribed and they are assumed to be independent of temperature.³¹ Thus, if the dissociation constants K and K_w are known, the simultaneous algebraic equations in (10) can be solved by an iterative procedure to give the fractions of ions α and β . In terms of these fractions, the conductivity eq 1 can be written as

$$\begin{aligned} \Lambda &= \lambda(\text{Na}^+) + \beta\lambda(\text{H}^+) + \alpha\lambda(\text{RPBO}^-) \\ &\quad + (1 + \beta - \alpha)\lambda(\text{OH}^-) \end{aligned} \quad (12)$$

or in the form of three ion-pair contributions

$$\begin{aligned} \Lambda &= \alpha\Lambda_1 + (1 - \alpha)\Lambda_2 + \beta\Lambda_3 \\ \Lambda_1 &= [\lambda(\text{Na}^+) + \lambda(\text{RPBO}^-)] \\ \Lambda_2 &= [\lambda(\text{Na}^+) + \lambda(\text{OH}^-)] \\ \Lambda_3 &= [\lambda(\text{H}^+) + \lambda(\text{OH}^-)] \end{aligned} \quad (13)$$

However, the third term in the equations in (13) is negligible because values of β , the fractions of hydrogen ions, are very small.

Since at a given temperature, T , physical properties of pure water and limiting ionic conductances, $\lambda^0(\text{Na}^+)$ and $\lambda^0(\text{OH}^-)$, are known from the literature^{32,33} (Table 2) and the distances of closest approach in the Quint–Villard conductivity equations can be taken as the average value of the ion size parameters in the ion pairs, the representation of conductivities (Λ , c) reduces to the two-parameter optimization problem (unknown K and $\lambda^0(\text{RPBO}^-)$ values). In the iterative procedure, the calculations were carried out to achieve the best agreement between the measured and the calculated conductivities, i.e., to obtain the minimal value of the mean value of standard deviation

$$\sigma(\Lambda) = \sqrt{\frac{\sum_{j=1}^N (\Lambda_{j,\text{expt}} - \Lambda_{j,\text{calcd}})^2}{N - 1}} \quad (14)$$

where N is the number of experimental points in the paraben sodium salt–water system.

Final results of computations are presented in Table 2 and they include the limiting conductances of paraben ions, the Quint–Villard coefficients, the dissociation constants, and the thermodynamic functions associated with them, and the mean values of standard deviations of fitting conductivities. They also contain the properties of water and the limiting ionic conductances of Na^+ and OH^- ions. Detailed calculations are reported only at 298.15 K (Table 3), in order to illustrate the contributions of $(\text{Na}^+ + \text{RPBO}^-)$ and $(\text{Na}^+ + \text{OH}^-)$ pairs of ions to $\Lambda(c)$ and the corresponding pH value of the solutions, $\text{pH} = -\log(c\beta)$, calculated using the fractions of hydrogen ions β from equations in (10). For comparison, the experimental pH values of the final solutions in the conductivity cell are also presented in Table 3 and are in reasonable agreement with the calculated ones. As can be also observed in Table 3 and Figure 2, the contribution to the measured conductivity $\Lambda(c)$ from the $(\text{RPBO}^- + \text{Na}^+)$ pair of ions, $\Lambda_1(c)$, is nearly constant. This results from the fact that the fraction of paraben ions α increases with the concentration of sodium salt. On the contrary, the effect of hydrolysis becomes important in very dilute solution and therefore the contribution from the $(\text{Na}^+ + \text{OH}^-)$ pair of ions, $\Lambda_2(c)$, becomes more essential. As can be seen for $c \sim 0.0026 \text{ mol-dm}^{-3}$, the limiting conductance of methylparaben sodium salt, $\lambda^0(\text{MePBONa}, 298.15 \text{ K})$, is already lower than $\Lambda(c)$. This is the consequence of a large contribution coming from the OH^- ions. The limiting conductances of paraben ions, $\lambda^0(\text{RPBO}^-, T)$, decrease with increasing alkyl group of the molecule and they decrease nearly linearly with the molecular mass of paraben sodium salt. Their values are similar to those of typical organic acid anions.³⁴

The temperature dependence of limiting conductances of paraben ions, $\lambda^0(\text{RPBO}^-, T)$, can be expressed in terms of the Walden product,³² $\eta(T)\lambda^0(\text{RPBO}^-, T)$, or the partial molar

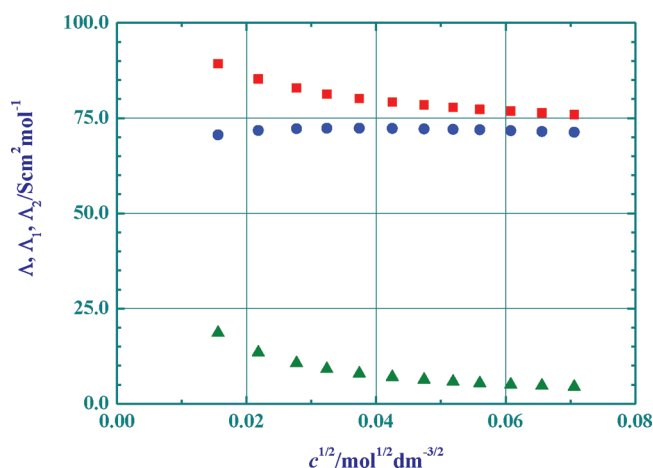


Figure 2. Experimental molar conductivity, $\Lambda(c)$, of methylparaben sodium salt at 298.15 K and the corresponding contributions to it: $\Lambda_1(c)$ from the $(\text{MeBPO}^- + \text{Na}^+)$ pair of ions and $\Lambda_2(c)$ from the $(\text{Na}^+ + \text{OH}^-)$ pair of ions: (■) $\Lambda(c)$; (●) $\Lambda_1(c)$; (▲) $\Lambda_2(c)$.

enthalpy associated with the ion movement, $\Delta H_\lambda(T)^{35}$

$$\left(\frac{\partial \ln[\lambda^0(\text{RPBO}^-, T)d_0^{2/3}(T)]}{\partial T} \right)_P = \frac{\Delta H_\lambda(T)}{RT^2} \quad (15)$$

where $d_0(T)$ is the density of pure water. If the enthalpy $\Delta H_\lambda(T)$ is independent of temperature, it follows from eq 15 that

$$\ln[\lambda^0(\text{RPBO}^-, T)d_0^{2/3}(T)] = -\frac{\Delta H_\lambda}{RT} + \text{const} \quad (16)$$

and such a behavior can be actually observed in Figure 3.

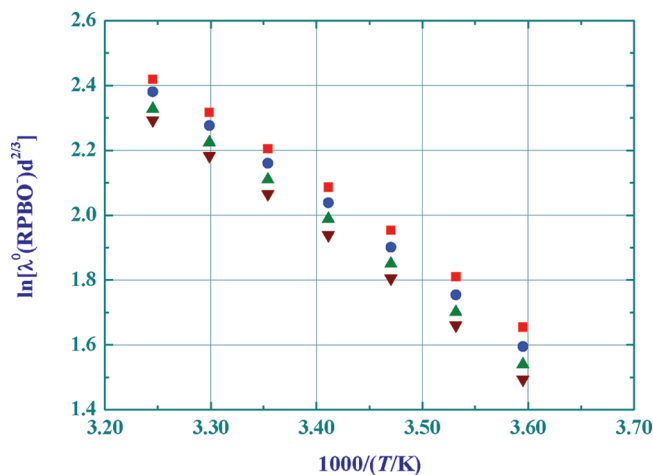


Figure 3. Values of $\ln[\lambda^0(\text{RPBO}^-)d^{2/3}]$ as a function of $1/T$: (■) methylparaben sodium salt; (●) ethylparaben sodium salt; (▲) propylparaben sodium salt; (▼) butylparaben sodium salt.

The corresponding partial molar enthalpies associated with the ion movement are $\Delta H_\lambda(\text{MePBO}^-) = 17.7 \text{ kJ} \cdot \text{mol}^{-1}$, $\Delta H_\lambda(\text{EtPBO}^-) = 18.3 \text{ kJ} \cdot \text{mol}^{-1}$, $\Delta H_\lambda(\text{PrPBO}^-) = 18.3 \text{ kJ} \cdot \text{mol}^{-1}$, and $\Delta H_\lambda(\text{BuPBO}^-) = 18.6 \text{ kJ} \cdot \text{mol}^{-1}$, determined from eq 16.

The Walden products in the investigated temperature range are practically temperature independent, $\eta(T)\lambda^0(\text{MePBO}^-, T) = 0.243 \pm 0.003 \text{ S} \cdot \text{cm}^2 \cdot \text{equiv}^{-1} \cdot \text{Pa} \cdot \text{s}$, $\eta(T)\lambda^0(\text{EtPBO}^-, T) = 0.232 \pm 0.005 \text{ S} \cdot \text{cm}^2 \cdot \text{equiv}^{-1} \cdot \text{Pa} \cdot \text{s}$, $\eta(T)\lambda^0(\text{PrPBO}^-, T) = 0.220 \pm 0.005$

$\text{S} \cdot \text{cm}^2 \cdot \text{equiv}^{-1} \cdot \text{Pa} \cdot \text{s}$, and $\eta(T)\lambda^0(\text{BuPBO}^-, T) = 0.211 \pm 0.005 \text{ S} \cdot \text{cm}^2 \cdot \text{equiv}^{-1} \cdot \text{Pa} \cdot \text{s}$.

The dissociation constants of investigated parabens can be expressed as a function of temperature

$$\begin{aligned} \ln K(\text{MePBOH}) &= 115.59 - \frac{7836.1}{(T/\text{K})} - 18.977 \ln(T/\text{K}) \\ R^2 &= 0.9991 \end{aligned}$$

$$\begin{aligned} \ln K(\text{EtPBOH}) &= 225.05 - \frac{12794}{(T/\text{K})} - 35.265 \ln(T/\text{K}) \\ R^2 &= 0.9986 \end{aligned}$$

$$\begin{aligned} \ln K(\text{PrPBOH}) &= 384.15 - \frac{20011}{(T/\text{K})} - 58.962 \ln(T/\text{K}) \\ R^2 &= 0.9998 \end{aligned}$$

$$\begin{aligned} \ln K(\text{BuPBOH}) &= 137.49 - \frac{9524.4}{(T/\text{K})} - 21.869 \ln(T/\text{K}) \\ R^2 &= 0.9974 \end{aligned} \quad (17)$$

The only known values for dissociation constants of parabens in the literature are those at 298.15 K^{15,20} and they are smaller by about a factor of 1.5 of that reported here (Table 2). However, they were determined by potentiometric measurements in solutions of 0.1 M ionic strength (concentration of Na^+ ions), not in pure water, and were also supported by pH-buffer components.²⁰

Temperature dependence of dissociation constants, $K(T)$, permits to evaluate the standard thermodynamic functions associated with the dissociation process of parabens

$$\begin{aligned} \Delta G^\circ(T) &= -RT \ln K(T) \\ \Delta G^\circ(T) &= \Delta H^\circ(T) - T\Delta S^\circ(T) \\ \Delta S^\circ(T) &= - \left(\frac{\partial \Delta G^\circ(T)}{\partial T} \right)_P \end{aligned} \quad (18)$$

The determined thermodynamic functions (Table 2) indicate that both the enthalpic and entropic terms are of nearly equal importance ($\Delta G^\circ > T\Delta S^\circ \approx \Delta H^\circ$, $\partial \Delta G^\circ / \partial T > 0$, $\partial \Delta H^\circ / \partial T < 0$, and $\partial \Delta S^\circ / \partial T < 0$). Similar behavior is observed for many substituted phenols.^{36,37}

CONCLUSIONS

Systematic determination of conductivity data for four paraben sodium salts was performed in dilute aqueous solutions from 278.15 to 313.15 K. The limiting conductances of paraben anions were evaluated by considering the hydrolysis effect after salts are dissolved in water. It was observed that the Walden products of paraben anions are almost independent of temperature. The conductivity measurements also permitted to determine the dissociation constants of parabens in water and the thermodynamic functions associated with the dissociation process.

At all the temperatures, the values obtained for the limiting conductivities of methylparaben anion (MePBO^-) are very close to the values reported for the anion of 4-hydroxybenzoic acid sodium salt (p -salicylate anion, Sal-p^-) recently, for example, $\lambda^0(\text{MePBO}^-, 298.15 \text{ K}) = 27.38 \text{ S}\cdot\text{cm}^2\cdot\text{mol}^{-1}$ (Table 2) and $\lambda^0(\text{Sal-p}^-, 298.15 \text{ K}) = 26.93 \text{ S}\cdot\text{cm}^2\cdot\text{mol}^{-1}$.³⁸ The same goes for the values of the corresponding partial molar enthalpies associated with the ion movement ($\Delta H_i(\text{MePBO}^-) = 17.7 \text{ kJ}\cdot\text{mol}^{-1}$ and $\Delta H_i(\text{Sal-p}^-) = 17.5 \text{ kJ}\cdot\text{mol}^{-1}$). Thus, it can be assumed that the methyl group does not hinder ionic movement distinctly in this case. On the other hand, the mobility of the paraben anion is decreasing with the alkyl chain length (27.38, 26.21, 24.98, and 23.81 $\text{S}\cdot\text{cm}^2\cdot\text{mol}^{-1}$ for methyl-, ethyl-, propyl-, and butylparaben at 298.15 K, respectively) and the corresponding partial molar enthalpies are becoming slightly higher.

Finally, it can be concluded that the main difference between parabens and their analogue sodium p -salicylate is the pronounced hydrolysis effect. Namely, whereas sodium p -salicylate shows typical behavior of a strong 1:1 electrolyte in water, aqueous solutions of parabens have a very high pH values.

AUTHOR INFORMATION

Corresponding Author

*E-mail: apelblat@bgu.ac.il (A.A.); marija.bester@fkkt.uni-lj.si (M.B.-R.). Tel: +386 1 2419 410 (M.B.-R.). Fax: +386 1 2419 425 (M.B.-R.).

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REFERENCES

- (1) Aalto, T. R.; Firman, M. C.; Rigler, N. E. *J. Am. Pharm. A.* **1953**, *42*, 449–457.
- (2) Bocobo, F. C.; Mopper, C.; Harrell, E. R.; Curtis, A. C. *J. Invest. Dermat.* **1956**, *26*, 239–242.
- (3) Soni, M. G.; Burdock, G. A.; Taylor, S. L.; Greenberg, N. A. *Food Chem. Toxicol.* **2001**, *39*, 513–532.
- (4) Soni, M. G.; Taylor, S. L.; Greenberg, N. A.; Burdock, G. A. *Food Chem. Toxicol.* **2002**, *40*, 1335–1373.
- (5) Routledge, E. J.; Parker, J.; Odum, J.; Ashby, J.; Sumpter, J. P. *Toxicol. Appl. Pharmacol.* **1998**, *153*, 12–19.
- (6) Oishi, S. *Toxicol. Ind. Health* **2001**, *17*, 31–39.
- (7) Oishi, S. *Arch. Toxicol.* **2002**, *76*, 423–429.
- (8) Oishi, S. *Food Chem. Toxicol.* **2002**, *40*, 1807–1813.
- (9) Darbre, P. D.; Aljarrah, A.; Miller, W. R.; Coldham, N. G.; Sauer, M. J. *J. Appl. Toxicol.* **2004**, *24*, 5–13.
- (10) Harvey, P. W.; Everett, D. J. *J. Appl. Toxicol.* **2004**, *24*, 1–4.
- (11) Soni, M. G.; Carabin, I. G.; Burdock, G. A. *Food Chem. Toxicol.* **2005**, *43*, 985–1015.
- (12) Andersen, F. A. *Int. J. Toxicol.* **2008**, *27*, 1–82.
- (13) Shanmugam, G.; Ramaswamy, B. R.; Radhakrishnan, V.; Tao, H. *Microchem. J.* **2010**, *96*, 391–396.
- (14) Valkova, N.; Lépine, F.; Văleanu, L.; Dupont, M.; Labrie, L.; Biscillon, J. G.; Beaudet, R.; Shareck, F.; Villemur, R. *Appl. Environ. Microbiol.* **2001**, *67*, 2404–2409.
- (15) Freese, E.; Levin, B. C.; Pearce, R.; Sreevalsan, T.; Kaufman, J. J. *Tetralogy* **1979**, *20*, 413–440.
- (16) Pekkarinen, L.; Tommila, E. *Acta Chem. Scand.* **1959**, *13*, 1019–1030.
- (17) Raval, N. N.; Parrott, E. L. *J. Pharm. Sci.* **1967**, *56*, 274–276.
- (18) Blaug, S. M.; Grant, D. E. *J. Soc. Cosmet. Chem.* **1974**, *25*, 495–506.
- (19) Loh, W.; Volpe, P. L. O. *J. Colloid Interface Sci.* **1992**, *154*, 369–377.
- (20) Vlasenko, A. S.; Loginova, L. P.; Iwashchenko, E. L. *J. Mol. Liq.* **2009**, *145*, 182–187.
- (21) O'Neill, M. A. A.; Beezer, A. E.; Labetaulle, C.; Nicolaides, L.; Mitchell, J. C.; Orchard, J. A.; Conor, J. A.; Kemp, R. B.; Olomolaiye, D. *Thermochim. Acta* **2003**, *399*, 63–71.
- (22) Barthel, J.; Wachter, R.; Gores, H.-J. Temperature Dependence of Conductance of Electrolyte in Nonaqueous Solutions. In *Modern Aspects of Electrochemistry*; Conway, B. E., Bockris, J. O'M., Eds.; Plenum Press: New York, 1979.
- (23) Barthel, J.; Feuerlein, F.; Neueder, R.; Wachter, R. *J. Solution Chem.* **1980**, *9*, 209–219.
- (24) Bešter-Rogač, M.; Habe, D. *Acta Chim. Slov.* **2006**, *53*, 391–395.
- (25) Kratky, O.; Leopold, H.; Stabinger, H. N. *Z. Angew. Phys.* **1969**, *27*, 273–277.
- (26) Herington, E. F. G. *Pure Appl. Chem.* **1976**, *48*, 1–9.
- (27) Quint, J.; Viallard, A. *J. Solution Chem.* **1978**, *7*, 137–153.
- (28) Quint, J.; Viallard, A. *J. Solution Chem.* **1978**, *7*, 525–531.
- (29) Quint, J.; Viallard, A. *J. Solution Chem.* **1978**, *7*, 533–548.
- (30) Bešter-Rogač, M.; Bončina, M.; Apelblat, Y.; Apelblat, A. *J. Phys. Chem. B* **2007**, *111*, 11957–11967.
- (31) Kielland, J. *J. Am. Chem. Soc.* **1937**, *59*, 1675–1678.
- (32) Robinson, R. A.; Stokes, R. H. *Electrolyte Solutions*; Butterworths: London, 1959.
- (33) Light, T. S.; Licht, S.; Bevilacqua, A. C. *Electrochem. Solid-State Lett.* **2005**, *8*, E16–E19.
- (34) Apelblat, A. *J. Mol. Liq.* **2002**, *95*, 99–145.
- (35) Brummer, S. B.; Hills, G. J. *Trans. Faraday Soc.* **1961**, *57*, 1816–1822.
- (36) Hepler, L. G.; O'Hara, W. F. *J. Phys. Chem.* **1961**, *65*, 811–814.
- (37) Rosés, M.; Rived, F.; Bosch, E. *J. Chromatogr. A* **2000**, *867*, 45–56.
- (38) Bešter-Rogač, M. *J. Chem. Eng. Data* **2011**, *56*, 4965–4971.