



Ionic strength effect on the deprotonation of *para*-sulfonatocalix[4]arene

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Abstract: The deprotonation of *para*-sulfonatocalix[4]arene was studied by a combination of spectrophotometric and potentiometric methods at 25 °C. The ionic strength of the solutions was kept constant by sodium perchlorate as a background electrolyte at 0.10–4.0 mol dm⁻³. The spectral changes evidenced proton dissociation of only one hydroxyl group of calixarene in the studied pH range of 2–10. The p*K*_a values were calculated using the STAR program by multivariate curve resolution of the absorbance data. The results indicated that the acid–base behavior of *para*-sulfonatocalix[4]arene varied strongly with increasing ionic strength of the solution. The dependence of the deprotonation constant on ionic strength was explained by means of the Specific Ion Interaction Theory (SIT). The activity coefficients of the species were modeled using a modified SIT approach. The extracted specific ion interaction parameters were associated with the thermodynamic deprotonation constant of *para*-sulfonatocalix[4]arene.

Keywords: deprotonation; sulfonatocalix[4]arene; ionic strength; SIT.

INTRODUCTION

Calix[*n*]arenes are a class of macrocyclic receptors synthesized by the base-induced condensation of formaldehyde with *para*-alkylphenols. The parent structure of calix[*n*]arenes is assembled from several phenolic rings interconnected by methylene bridges, resulting in an electron-rich, hydrophobic cavity. This particular architecture and also the simple derivatization of calixarenes by modification at both the upper and lower rims makes them potential candidates in various fields, such as biological, analytical and supramolecular chemistry.^{1–4} *para*-Sulfonatocalix[*n*]arenes, in which the upper rims are functionalized by SO₃⁻ groups, are a water-soluble type of calixarenes with diverse biochemical functions, including enzyme inhibition, antiviral, antibacterial and antithrombotic activities.^{4–6}

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Most of the beneficial effects of these cyclic oligomers arises from their ability as a suitable host molecule to interact with neutral and ionic species through hydrophobic, π - π , cation- π and hydrogen bonding interactions, especially by their lower rim hydroxyl groups.^{2,7}

The chemistry of calixarenes is closely related to the nature of their hydroxyl groups at the lower rim. Hydroxyl groups play a major role in conformational flexibility, cavity size and selective binding behavior of calixarenes.⁸⁻¹⁰ In addition, lower rim functionalization is one of the most common methodologies applied in the routine synthesis of numerous calixarene derivatives, which is followed by an initial dissociation of hydroxyl groups.¹⁰ Therefore to gain profound insight into the nature of the phenolic hydroxyl groups of *para*-sulfonatocalix[*n*]arenes, an accurate thermodynamics analysis of their acid-base properties seemed necessary. However, the determination of the pK_a values of *para*-sulfonatocalix[*n*]arenes is accompanied by some limitations, such as the complication of proton dissociations and the interference of acidic sulfonato groups. As an initial attempt, the acid-base behavior of *para*-sulfonatocalix[4]arene (SC4), Fig. 1, was studied by Shinkai *et al.*¹¹ From this study, the first phenolic hydroxyl group of SC4 was found to be extremely acidic ($pK_a < 1$). Although later studies confirmed that the first deprotonation of SC4 occurs at relatively high acidic pH value, a much larger pK_a value was determined when the strong acid dissociation of sulfonic acid groups were considered in the calculation.¹²⁻¹⁴

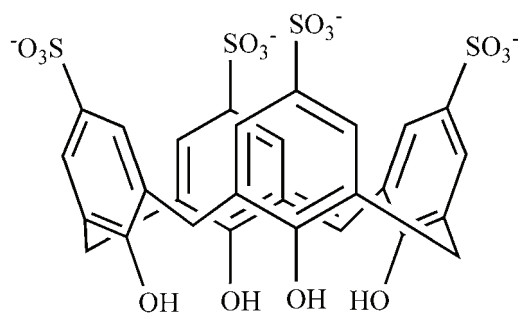


Fig. 1. Chemical structure of *para*-sulfonatocalix[4]arene.

Unfortunately, not only are there a few data for the pK_a value of SC4 in the literature, but also their determinations were performed under different experimental conditions (ionic media and ionic strength), which makes the prediction and modeling of the chemical speciation of SC4 in aqueous solutions difficult.¹²⁻¹⁴ With the aim of extracting the thermodynamics standard state for pK_a , the deprotonation of SC4 was studied in the present work by a combination of spectroscopic and potentiometric methods over a wide range of ionic strengths, $0.10 \leq I$ (mol dm⁻³) ≤ 4.0 , in a NaClO₄ electrolyte at 25 °C. The dependence of deprotonation constant on ionic strength and ionic interaction parameters were evaluated by the Specific Ion Interaction Theory (SIT).¹⁵⁻¹⁹

EXPERIMENTAL

The *para*-sulfonatocalix[4]arene sodium salt was obtained from Sigma-Aldrich. NaOH and HClO₄ were purchased from Merck. Double-distilled water with a conductivity of 1.3±0.1 μΩ⁻¹ cm⁻¹ was used. Sodium perchlorate was supplied by Merck as an analytical reagent grade material and was used without further purification.

Potentiometric measurements were performed in a double-walled thermostated reaction vessel at 25 °C. A model 3520 Jenway research potentiometer with a combined pH electrode was used for the *emf* measurement in the potentiometric titrations of the acidic mixture solutions.

The spectrophotometric measurements were performed on a Shimadzu 2100 UV-Vis spectrophotometer with a Pentium 4 computer and using thermostated matched 10 mm quartz cells. A flow measurement cell was used. A peristaltic pump allowed the circulation of the solution under study from the potentiometric cell to the spectrophotometric cell, so the absorbance and the *emf* of the solution could be measured simultaneously. To exclude carbon dioxide from the system, a stream of purified nitrogen was passed through a sodium hydroxide solution and then bubbled slowly through the reaction solution.

Prior to each spectrophotometric titration, the potentiometric cell was calibrated to obtain formal electrode potential E°_{cell} at each ionic strength.²⁰⁻²² Approximately 20 mL of solutions of HClO₄ in constant ionic strength of NaClO₄ were titrated by the stepwise addition of NaOH solution. The equilibrium *emf* values of the cell were recorded after allowing potential stabilization. The E°_{cell} values were computed from the Nernst equation knowing the exact concentration of H⁺ in all titration points. In the next section, 25 mL of an acidic solution of SC4 was titrated with a sodium hydroxide solution (0.1 mol dm⁻³). The absorbance data were recorded in the interval of 200–400 nm after reading the *emf* values of the potentiometric cell. Then spectroscopic titration data were introduced into the STAR program²³ to calculate the pK_a values of SC4.

RESULTS AND DISCUSSION

Calibration of potentiometric cell for each ionic strength

According to the Nernst equation, the potential of a potentiometric cell equipped by a glass electrode can be presented as:

$$E_{\text{cell}} = E^{\circ}_{\text{cell}} + k \log [\text{H}^+] + k \log \gamma_{\text{H}^+} + E_{\text{LJ}} \quad (1)$$

where E_{LJ} is the liquid junction potential, $k = 2.303RT/F$ in which R , T and F have their usual meaning and γ_{H^+} is the activity coefficient of hydrogen ion. As the ionic strength of the solution was kept constant for each experiment, the activity coefficient of hydrogen ion was also constant. The non-ideality of solutions is then included in k_a (the specific constant of the potentiometric cell in acidic region), and thus:

$$E_{\text{cell}} = k_a + k \log [\text{H}^+] \quad (2)$$

with k_a being $E^{\circ}_{\text{cell}} + k \log \gamma_{\text{H}^+} + E_{\text{LJ}}$. The hydrogen ion concentration can be easily calculated by:

$$[\text{H}^+] = (M_{\text{H}}V_0 - M_{\text{OH}}V_1) / (V_0 + V_1) \quad (3)$$

where M_H and M_{OH} are the molarities of acid and base, respectively, and V_0 and V_1 are the initial volume of acid and the added volume of sodium hydroxide solution, respectively. The k_a values were calculated from measured *emf* and known concentration of solvated proton in every titration point by linear regression analysis. For each experiment at constant ionic strength, the slopes obtained from least squares analysis were close to the theoretical Nernst value (59.167 mV at 25 °C) with correlation coefficients of nearly $r^2 = 0.99$. Accordingly, the pH values could be properly measured at each constant ionic strength by:

$$p_cH = (k_a - E_{cell}) / k \quad (4)$$

Computing the protonation constants

Typical spectral changes of SC4 at a constant ionic strength of 3 mol dm⁻³ NaClO₄ are shown in Fig. 2.

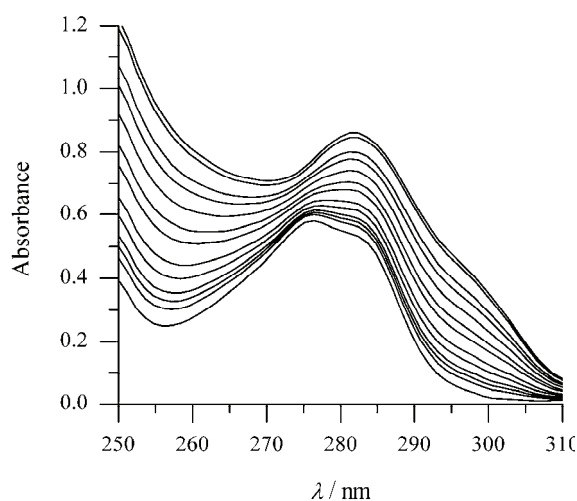


Fig. 2. Spectral change of *para*-sulfonatocalix[4]arene (1.45×10^{-4} mol dm⁻³) with increasing pH at an ionic strength of 3 mol dm⁻³ NaClO₄.

To analyze mathematically the deprotonation equilibria, the absorbance data gathered from solutions of different pH values were used to construct a matrix **R** of size $m \times n$ where m is the number of different pH values in which absorbance was determined in n wavelengths at one nm intervals. According to the Beer law, a least squares analysis was performed in STAR program environment to decompose the data matrix **R** into a matrix of pure concentration, **C**, and a matrix of pure spectral profiles, **S**, with the optimal residual error matrix **E**.

$$\mathbf{R} = \mathbf{CS} + \mathbf{E} \quad (5)$$

In iterative cycles, those matrices **C** and **S** were determined which best represent the original matrix **R**. The matrix of pure concentration profiles is related to protonation constant and total concentration of the compounds. Under suitable constraints, the nonlinear least-squares fitting continues until best set of

parameters (pK_a and molar absorptivities of the species) that result in a minimum of \mathbf{E} is found.

The optimal fitting between theoretical and experimental absorbance data was achieved when only one of four possible deprotonation equilibria of SC4 was considered in the calculation. Therefore, the gradual spectral shift of SC4 to longer wavelength in the studied pH range is attributed to the first deprotonation of its phenolic hydroxyl groups that can be represented by:



It seems that further proton dissociation may be observed at $\text{pH} > 11$. This explanation is in good qualitative agreement with previous studies by other groups.^{12–14} The pK_a values of SC4 calculated by the STAR program in different ionic strengths are reported in Table I in the molar and molal concentration scale.

Ionic strength effect

According to Eq. (6), the first deprotonation constant of SC4 can be given by:

$$K_a^T = \frac{[\text{H}^+][\text{H}_3\text{L}^{5-}]}{[\text{H}_4\text{L}^{4-}]} \frac{\gamma_{\text{H}^+} \gamma_{\text{H}_3\text{L}^{5-}}}{\gamma_{\text{H}_4\text{L}^{4-}}} = K_a \frac{\gamma_{\text{H}^+} \gamma_{\text{H}_3\text{L}^{5-}}}{\gamma_{\text{H}_4\text{L}^{4-}}} \quad (7)$$

where γ_i is activity coefficient of species i ; K_a^T represents thermodynamic deprotonation constant of SC4, and K_a stands for stoichiometric constant determined at each ionic strength. By taking the negative logarithm on Eq. (7):

$$\text{p}K_a = \text{p}K_a^T + \log \gamma_{\text{H}^+} + \log \gamma_{\text{H}_3\text{L}^{5-}} - \log \gamma_{\text{H}_4\text{L}^{4-}} \quad (8)$$

The dependence of the pK_a values on ionic strength may be analyzed by considering the well-known Specific Ion Interaction Theory (SIT).^{15–19} In the original SIT model, the activity coefficient of ion i with charge z_i in a solution of ionic strength I (on the molal scale) at 25 °C can be expressed by the equation:

$$\log \gamma_i = -z_i^2 \frac{0.51\sqrt{I}}{1+1.5\sqrt{I}} + \sum_j \varepsilon_{ij} m_j \quad (9)$$

The ion interaction coefficient, ε_{ij} , usually called the SIT parameter, interprets the specific short-range interactions of ion i with ion j in its molal concentration m_j . The SIT model assumes that interaction coefficient is zero for two electrically like sign ions or neutral species. Although SIT parameters are considered to be approximately constant for some ionic media in the range $0.50 \leq I$ (mol kg^{-1}) ≤ 3.50 , literature data indicate that they are function of I at lower and higher ionic strengths.²⁴ An expertise group in Italy modified the SIT model and introduced the concentration dependency of ε by the term:^{25,26}

$$\varepsilon = \varepsilon_{\infty} + \frac{\varepsilon_0 - \varepsilon_{\infty}}{1 + I} \quad (10)$$

By considering the modified SIT model for the calculation of activity coefficients of species, Eq. (8) can be reformulated as follows:

$$\text{p}K_{\text{a}} = \text{p}K_{\text{a}}^T - z^* \frac{0.51\sqrt{I}}{1 + \sqrt{I}} + \Delta\varepsilon I \quad (11)$$

where

$$z^* = \sum (\text{charges})_{\text{products}}^2 - \sum (\text{charges})_{\text{reactants}}^2 \quad (12)$$

$$\Delta\varepsilon = \varepsilon_{\text{H}_3\text{L}^{5-}, \text{Na}^+} + \varepsilon_{\text{H}^+, \text{ClO}_4^-} - \varepsilon_{\text{H}_4\text{L}^{4-}, \text{Na}^+} \quad (13)$$

It should be noted that the $\text{p}K_{\text{a}}$ and I values are in the molal concentration scale; in addition, all SIT parameters were defined concentration-dependent by the use of Eq. (10).

The experimental $\text{p}K_{\text{a}}$ values from Table I were fitted into Eq. (11) as a function of ionic strength by least squares regression analysis. The results were $\text{p}K_{\text{a}}^T = 4.13 \pm 0.05$, $\Delta\varepsilon_0 = 1.79 \pm 0.13$ and $\Delta\varepsilon_{\infty} = 0.20 \pm 0.02$. The goodness of fit of the SIT model was judged by the excellent square correlation coefficient $R^2 = 0.97$, associated with low values of the standard deviation obtained for each of regression coefficients. This is illustrated better in Fig. 3, where the experimental $\text{p}K_{\text{a}}$ values together with modeled values from SIT approach, Eq. (11), are depicted as a function of the square root of the molal ionic strength.

TABLE I. The $\text{p}K_{\text{a}}$ values of SC4 in different ionic strength of NaClO_4 at 25 °C

I		$\text{p}K_{\text{a}}$	
mol kg^{-1}	mol kg^{-1}	mol dm^{-3}	mol kg^{-1}
0.10	0.10	3.24 ± 0.02	3.24
0.25	0.25	3.05 ± 0.01	3.05
0.50	0.51	2.93 ± 0.03	2.92
0.75	0.78	3.01 ± 0.01	2.99
1.00	1.05	3.14 ± 0.02	3.12
1.50	1.62	3.26 ± 0.05	3.23
2.00	2.21	3.39 ± 0.02	3.35
3.00	3.50	3.65 ± 0.02	3.58
4.00	4.95	3.90 ± 0.04	3.81

CONCLUSIONS

The acid–base properties of SC4 were investigated at 25 °C by an accurate spectroscopic method over a wide range of ionic strengths, supplied by sodium perchlorate. Spectral analysis indicates that only one of the four hydroxyl groups of SC4 dissociates in pH range 2–10. The $\text{p}K_{\text{a}}$ values assigned for first depro-

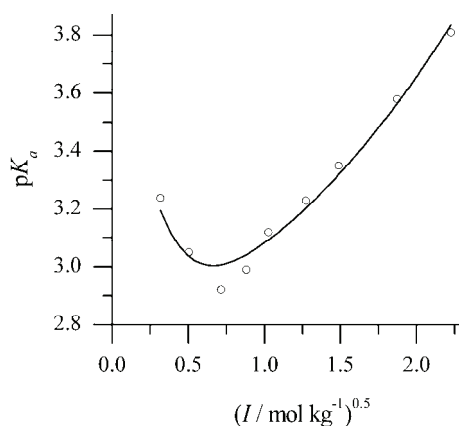


Fig. 3. pK_a values of *para*-sulfonatocalix-[4]arene vs. the square root of the ionic strength of the solution. Symbols refer to experimental data, while the solid line represents the value calculated according to the SIT model.

tonation equilibrium were calculated by multivariate curve fitting implemented in the STAR program. The results showed that, as a regular trend, the pK_a of SC4 first decreased sharply to its minimum value at an ionic strength of around 0.5 mol kg⁻¹ and then increased in a relatively linear manner. The SIT theory was applied successfully to describe the ionic strength dependency of the pK_a values. The thermodynamic deprotonation constant at infinite ionic strength was calculated together with the overall specific ion interaction coefficients.

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ИЗВОД

УТИЦАЈ ЈОНСКЕ ЈАЧИНЕ НА ДЕПРОТОНАЦИЈУ *para*-СУЛФОНАТОКАЛИКС[4]АРЕНА

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Депротонација *para*-сулфонатокаликс[4]арена је проучавана комбиновањем спектрофотометријских и потенциометријских метода на 25 °С. Јонска јачина раствора је одржавана константном помоћу натријум-перхлората на 0,10 до 4,0 mol dm⁻³. Спектралне промене показују да долази до дисоцијације протона са само једне хидроксилне групе каликсарена у испитиваном опсегу рН од 2–10. pK_a вредности су израчунате коришћењем STAR софтвера за мултиваријантну анализу апсорпционих података. Резултати указују да кисело–базно понашање *para*-сулфонатокаликс[4]арена јако варира са порастом јонске јачине раствора. Зависност депротонационих константи од јонске јачине је објашњена коришћењем теорије специфичних јонских интеракција (SIT). Коefицијенти активности испитиваних врста су моделовани модификованим SIT приступом. Параметри специфичне јонске интеракције су добијени са термодинамичком депротонационом константом за *para*-сулфонатокаликс[4]арен.

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