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Ionization of some derivatives of benzamide, oxamide and malonamide in DMF–water mixture

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Abstract

The ionization of six compounds of bis-phenolic amides was studied spectrophotochemically in DMF–water mixture. The compounds showed two pK_a values in the range of 5.97–7.32 for pK_{a_1} and 7.61–8.44 for pK_{a_2}. The obtained values of K_a were normalized using the distribution diagrams of the different species and found to be in the range of 5.81–7.42 for pK_{a_1} and 7.48–8.27 for pK_{a2}.

Keywords: Bis-orthophenolicamides; DMF; Water; Ionization

1. Introduction

Recently, much interest has been directed to the synthesis and characterization of benzamide, oxamide and malonamide derivatives due to their interesting applications in diverse fields [1–4]. Most of these compounds have the ability to ligate alkali and alkaline-earth metal cations, thus representing excellent ionophores for the construction of alkali and alkaline-earth cations-selective electrodes [5,6]. However, the literature lacks sufficient information about the ionization behavior of bis(*o*-hydroxy benzamido) alkanes, *N*,*N*′-bis(*o*-hydroxyphenyl)oxamide, and *N*,*N*′-bis(*o*-hydroxyphenyl) malonamide. Investigation of such behavior is very important because it pave the way for understanding the mechanism of action of these compounds as complexing agents and/or ionophores. Furthermore the determination of the ionization constants of organic compounds, in general, is very valuable in applying separation techniques using these compounds. Spectrophotometric measurements for the determination of such constants have been reported in many publications [7,8]. In the present work pK_{a_1} and pK_{a_2} have been determined, spectrophotometrically, for bis(*o*-hydroxybenzamido)alkanes (BD-1 to BD-4), *N*,*N*′-bis(*o*-hydroxyphenyl)oxamide (BD-5), and *N*,*N*′-bis(*o*-hydroxyphenyl)malonamide (BD-6) compounds (Scheme 1).

The ionization equilibria of the compounds BD-1–BD-6 show the species, H_2R, HR^-, and R^{-2} where ε_{HR} has been found to be intermediate between ε_{H_2R} and ε_R at all wavelengths except at the isosbestic point of the spectra. In contrast to ε_{H_2R} and ε_R, the value of ε_{HR} was very difficult to be determined directly from the absorbance–pH curve.

A calculation method for pK_a has been previously suggested [7,8] depending on the absorbances of the fully protonated species (A_{H_2R}) and the deprotonated species (A_R) and supposing that the absorbance of the mono-protonated species (A_{HR}) is unknown. However, the method requires many calculation steps and application of sophisticated equations. In the present paper, a new approach has been applied successfully for the determination of (A_{HR}) from the spectral data and use it together with (A_{H_2R}) and (A_R) for the determination of the ionization constants of the investigated compounds. A method has been presented for normalization of the obtained constants.

2. Experimental

2.1. Chemicals and solutions

The following compounds have been prepared as previously described [1–4]:1,2-bis(2-hydroxybenzoylamino)-

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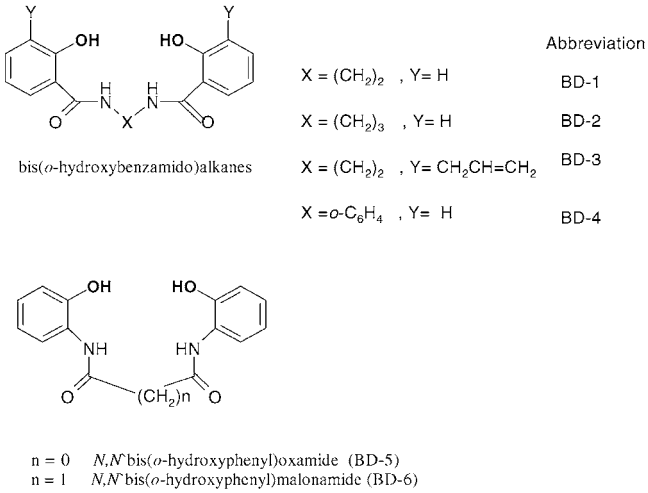

Scheme 1.

ethane (BD-1); 1,3-bis(2-hydroxybenzoylamino) propane (BD-2); 3-allyl-1,2-bis(2-hydroxybenzoylamino)ethane (BD-3); 1,2-bis(2-hydroxybenzoylamino)benzene (BD-4); *N*,*N*′ bis(2-hydroxyphenyl)oxamide (BD-5) and *N*,*N*′ bis(*o*-hydroxyphenyl) malonamide (BD-6). All the prepared compounds were characterized after crystallization with the appropriate solvent by microanalysis for C, H, N, by ^{1}H NMR and by ^{13}C NMR spectrometry. Analytical grade reagents were used for the preparation of the solutions. Because of the very low solubility of the investigated compounds, determination of their ionization constants was carried out in 50% (v/v) DMF–water solvent.

2.2. Measurements

The absorption spectra of the solutions were recorded on a Cary-5/Varian UV–vis spectrophotometer in the range of 250–380 nm.

The values of pH were measured with an Orion Model 710-A pH meter. The pH meter was calibrated regularly before use with standard 0.05 M potassium hydrogen phthalate buffer solution in 50% (v/v) DMF–water mixture [9].

2.3. Spectrophotometric determination of the ionization constants

The method is based on studying the absorption spectra of the investigated compounds in 50% aqueous-DMF medium at different pH values. From the spectra obtained, absorbance values at selected wavelengths are plotted as a function of pH. The pH values were corrected for the presence of the non-aqueous part of the solvent. For this purpose, the combined glass electrode was calibrated using 0.05 M potassium hydrogen phthalate buffer solution made in 50% (v/v) DMF–water solvent [9].

2.4. Procedure

To a 50 mL volumetric flask containing 5.0 mL of BD-1 (1.0×10^{-3} mol L^{-1}), BD-2 (1.0×10^{-3} mol L^{-1}), BD-3 (2.0×10^{-3} mol L^{-1}), BD-4 (1.0×10^{-3} mol L^{-1}), BD-5 (2.0×10^{-3} mol L^{-1}) or BD-6 (2.0×10^{-3} mol L^{-1}) solution in DMF, 25.0 mL of 0.2 mol L^{-1} tetramethylammonium chloride (TMAC) aqueous solution were transferred. The volume was completed to the mark with DMF. After thoroughly mixing, the solution was transferred into a 100 mL conical flask and its pH value is measured after calibrating the pH meter with the potassium hydrogen phthalate buffer in 50% (v/v) DMF–water mixture. The absorption spectrum of the solution is scanned over the range of 250–380 nm using dry clean quartz cuvette of 1.0 cm path length. After scaning the spectrum, the content of the cell was returned to the conical flask containing the mother solution. The pH value of the solution was then raised by adding very small aliquot portions ($\sim$ 5 μL) of 0.1 mol L^{-1} NaOH solution and the spectrum at the new pH is scanned again as above. The process is repeated at different pH values till obtaining constant absorbance values which means a nearly complete ionization. The average total volume of NaOH added is about $\sim$0.5 mL which represents minor effect on accuracy as the systematic errors due to dilution will not exceed 1.0%. Representative spectra at different pH values for BD-1, are shown in Fig. 1. All spectral measurements were made in presence of 0.1 mol L^{-1} tetramethylammonium chloride to provide nearly constant ionic strength of 0.1.

The absorbance values at different wavelengths in the range between λ_{max} of the non-ionized species H_2R and that of the ionized one R^{-2} (Table 1) are plotted versus pH of the solution and used to calculate K_a. Fig. 2. shows representatives of such plots for BD-1.

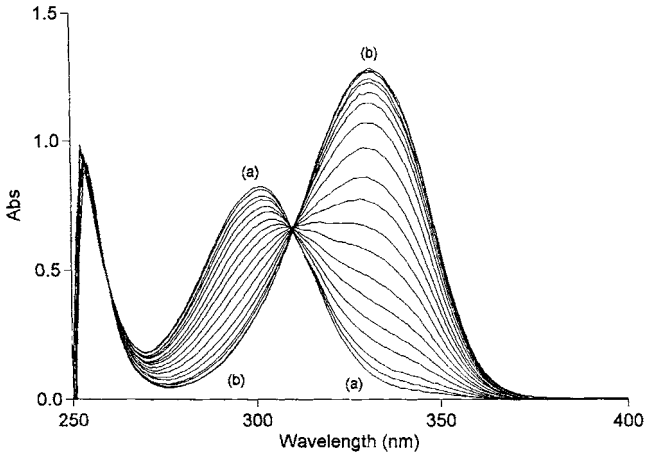

Fig. 1. Absorption spectra of 1.0×10^{-4} mol L^{-1} solutions of BD-1 in 50% (v/v) DMF–water mixture at different pH values between 5.52 (spectrum a) and 9.47 (spectrum b).

Table 1
Spectral data and ionization constants of the bis(*o*-hydroxybenzamido)-alkanes (BD-1 to BD-4), *N*,*N*′ bis(*o*-hydroxyphenyl)oxamide (BD-5), and *N*,*N*′ bis(*o*-hydroxyphenyl)malonamide (BD-6)

Compound	λ_{max} nm (H_2R)	ε (H_2R) (mol^{-1} L cm^{-1})	λ_{max} nm (R^{-2})	ε (R^{-2}) (mol^{-1} L cm^{-1})	λ (nm) isospestic	pK_{a_1}	S_{R_2}[a] (%)	pK_{a_2}	S_{R_2}[a] (%)
BD-1	300.6	466.9	330.9	1178.0	309.7	6.15	2.08	7.66	0.60
BD-2	300.9	412.3	330.4	1076.5	309.5	6.31	2.52	7.61	0.71
BD-3	308.0	427.2	334.3	1082.7	316.2	6.82	1.33	8.13	0.12
BD-4	308.0	832.0	338.0	1280.0	316.3	5.97	1.55	8.05	0.81
BD-5	311.0	850.0	367.4	1098.0	336.2	7.29	1.68	8.24	0.56
BD-6	286.0	641.0	315.5	1488.5	295.4	7.32	1.18	8.44	0.31

[a] S_R (%): coefficient of variation.

2.5. Ionization behaviour in presence of different salts

The above procedure has been applied in presence of LiCl, NaCl and KCl to study the effect of the presence of different alkali metals on the ionization of the compounds.

3. Results and discussion

The solutions of the investigated compounds BD-1, BD-2, BD-3, BD-4, BD-5 and BD-6, in 50% (v/v DMF–water solvent mixture), exhibited broad bands at λ_{max} of about 300.6, 300.9, 308.0, 308.0, 311.0, and 286.0 nm with corresponding pH values of 5.52, 5.40, 5.77, 5.12, 5.29 and 5.26, respectively. These bands are assigned to π–π* transitions in the non-ionized H_2R species. Generally, in all cases it was clear that as the pH value of the solution increases, the intensity of the H_2R band decreases and the band is gradually changed to a shoulder, the change is associated with a gradual shift to longer wavelengths.

Concurrent with this gradual vanishing of the H_2R band a new band is observed at wavelength of about 340.0 nm as a weak shoulder. The absorbance at this shoulder increases gradually with the increase in pH value and the shoulder changes to a strong band at about 330.6 nm as the pH approaches the value of 9.47 for BD-1, Fig. 1. For the other derivatives BD-2, BD-3, BD-4, BD-5 and BD-6 the new band appears at $\lambda_{max:}$ 330.6, 334.3, 338.2, 367.4, and 315.5 nm, respectively.

It is evident that the band at ∼300.0 nm for all the investigated compounds is attributed to the H_2R species and as the pH increases, the concentration of this species decreases and the concentration of HR^- species, increases. This change is associated with a net decrease in absorbance which reveal

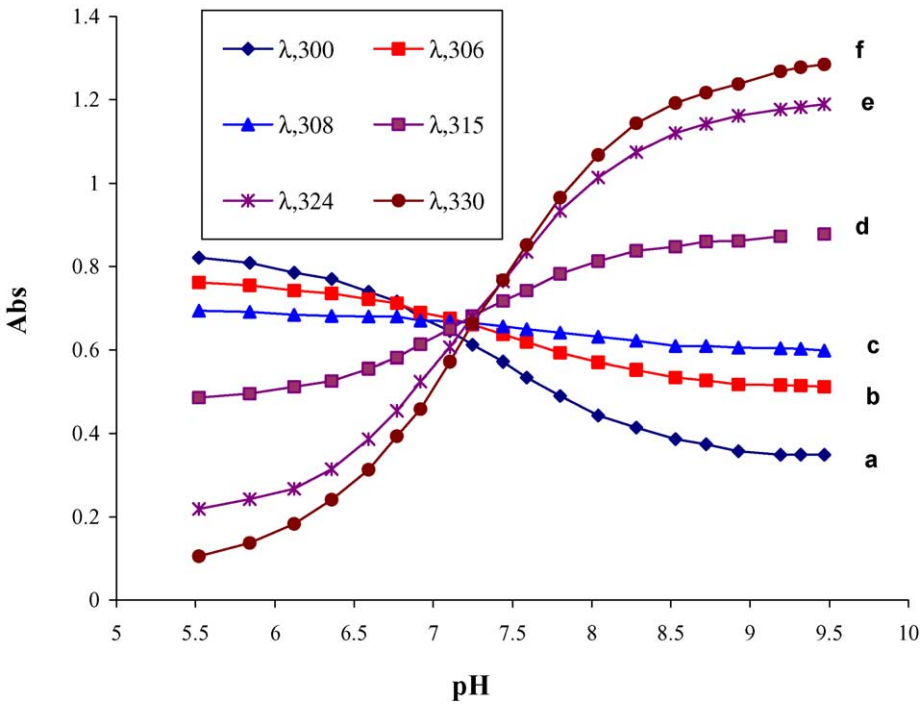

Fig. 2. Absorbance/pH curves, for BD-1, at different wavelengths ranging between λ_{max} of the non-ionized species, H_2R (300 nm) and that of ionized species, R^{-2} (330 nm).

that HR^- has lower absorbitivity than H_2R. Also, this change in proportionality causes the shift in λ_{max} of H_2R, and the appearance of the shoulder band. Continuing increasing the pH value results in conversion of HR^- to the ionized species R^{-2} which have higher molar absorptivity at its characteristic λ_{max}. Therefore, at λ_{max} of H_2R, $\varepsilon_{H_2R} > \varepsilon_{HR} > \varepsilon_R$ while the reverse order is observed at λ_{max} of R^{-2}. This leads to the conclusion that two absorbance–pH curves plotted at two wavelengths on the two sides of the isospestic point would intercept at pH value where HR^- predominates.

3.1. Determination of the ionization constants

The ionization constants are given by

$$K_{a_1} = \frac{[HR^-][H^+]}{[H_2R]} \quad (1)$$

$$K_{a_2} = \frac{[R^{-2}][H^+]}{[HR^-]} \quad (2)$$

The species concentrations have been used instead of activities as the measurements were made in very dilute solutions; moreover the solvent is partially aqueous which decreases to a large extent the effect of ionic spheres.

The relative changes of the equilibrium concentrations of H_2R, HR^-, and R^{-2} as the pH of the medium vary can be followed by plotting the absorbance–pH value (Fig. 2). At wavelengths shorter than that of the isosbestic point and longer than λ_{max} of H_2R, descending absorbance values were obtained as the pH increases (Fig. 2, at $\lambda = 300$, 306 and 308 nm) indicating gradual conversion of H_2R to R^{-2} passing by HR^-. At wavelengths longer than that of the isosbestic point and shorter than λ_{max} of the ionized species R^{-2}, ascending absorbance is obtained as the pH value increases (Fig. 2, at λ =315, 324 and 330 nm). The magnitude of variation in absorbance–pH depends on the relative molar absorptivites of the absorbing species H_2R, HR^- and R^{-2} at the concerned wavelengths. The values of the molar absorptivities of the three species come close as we approach λ of the isosbestic point, and consequently, less sharp *S*-curve is obtained. However all curves met at a point with certain pH value and the absorbance at this point, is mainly attributed to the the species HR^-.

The ionization constants K_{a_1} and K_{a_2} of each of the benzamide compounds can be calculated from any of the absorbance–pH curves shown in Fig. 2. However, in the present work, the calculations have been applied to data obtained at λ_{max} of the ionized species R^{-2} (Fig. 2, λ =330 nm) because the magnitude of change at this wavelength is maximum.

At any point on the absorbance–pH curve, the absorbance of the solution is a result of contribution of the three equilibrating species H_2R, HR^- and R^{-2} with different percentages depending on the pH value. At pH values sufficiently lower than pK_{a_1}, the H_2R species can be considered the only existing species with absorbance (A_{H_2R}) while on the other hand at pH values sufficiently higher than pK_{a_2}, the absorbance recorded (A_R) can be totally attributed to the ionized species (R^{-2}). At pH value where the absorbance–pH curves at different wavelengths meet, the absorbance value (A_{HR}) is mainly due to presence of HR^- species Fig. 2. For equilibrium mixture of the three species of the diprotic acid, the absorbance value is given by the following equation [7,8]

$$A = \frac{(A_R + A_{HR}[H]/K_{a_2} + A_{H_2R}[H]^2/K_{a_1}K_{a_2})}{(1 + [H]/K_{a_2} + [H]^2/K_{a_1}K_{a_2})} \quad (3)$$

For simplicity charges are omitted. Dividing both numerator and denomerator by $[H]^2$, Eq. (3) can be modified to

$$A = \frac{(A_R/[H]^2 + A_{HR}/[H]M + A_{H_2R}/N)}{(1/[H]^2 + 1/[H]M + 1/N)} \quad (4)$$

where $M = K_{a_2}$ and $N = K_{a_1}$ K_{a2}Then,

$$\frac{A}{[H]^2} + \frac{A}{[H]M} + \frac{A}{N} = \frac{A_R}{[H]^2} + \frac{A_{HR}}{[H]M} + \frac{A_{H_2R}}{N} \quad (5)$$

By rearrangement

$$\frac{A}{[H]^2} - \frac{A_R}{[H]^2} = \left(\frac{1}{M}\right)\left(\frac{A_{HR^-}}{[H]}\right)\frac{A}{[H]} + \left(\frac{1}{N}\right)(A_{H_2R} - A) \quad (6)$$

Dividing both sides by (A_{H_2R}−A), the following equation is obtained.

$$\frac{A/[H]^2 - A_R/[H]^2}{A_{H_2R} - A} = \frac{(1/M)(A_{HR}/[H] - A/[H])}{(A_{H_2R} - A)} + 1/N \quad (7)$$

Eq. (7) is a linear relation-ship of the type ($y = ax + b$) where $a = 1/M$ and $b = 1/N$ that can be solved algebrically or graphically to obtain the values of K_{a_1} and K_{a_2}. In the present work Eq. (7) was solved algebrically for two different absorbance values and K_{a_1} and K_{a_2} values were obtained. Three replicate calculations were made for three different pairs of absorbance and the mean values together with the corresponding coefficients of variation (S_R) are given (Table 1). The method of calculation proved high degree of precision as indicated by the very low values of the obtained (S_R) every time.

4. Calculation of the normalized ionization constants

For a polybasic acids, the distribution diagram [10] illustrates how the relative amounts of the different species vary as a function of pH. For the investigated compounds, the distribution diagrams have been constructed based on their ionization constants given in (Table 1). From the representative diagrams shown in Fig. 3, it is clear that at pH 4.00, H_2R exists nearly alone and as the pH increases, the fraction of it decreases as a result of the gradual formation of HR^- in addition to the appearance and growing of R^{-2}

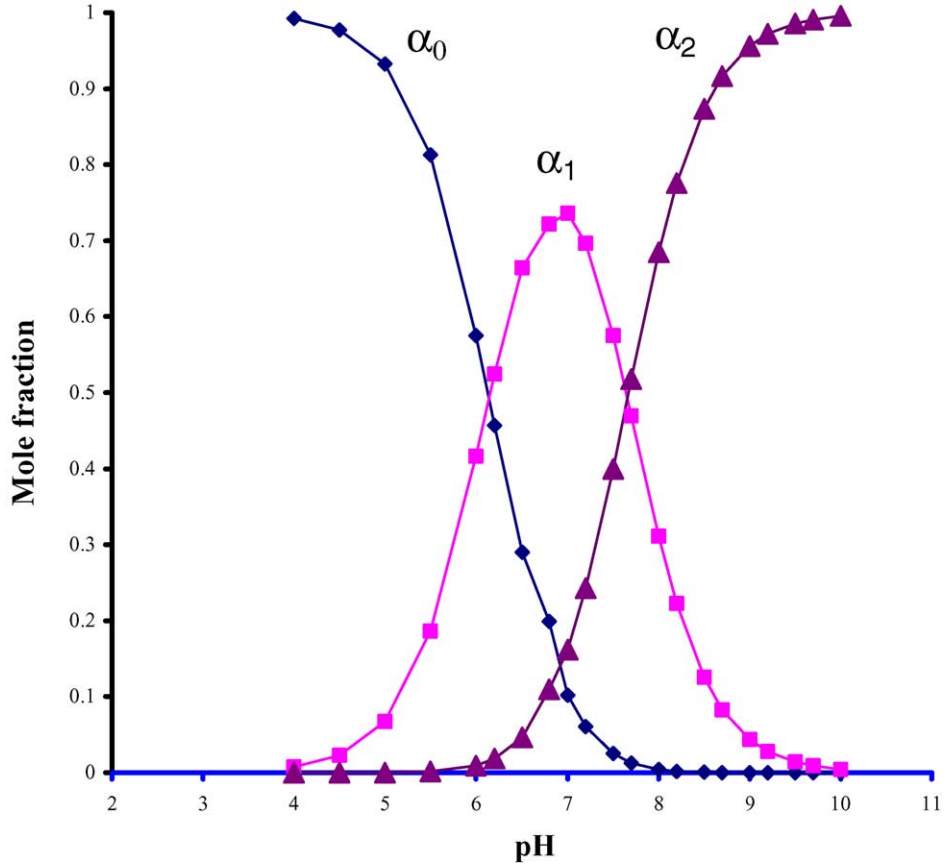

Fig. 3. Distribution diagram for BD-1 as a function of pH. (α_0, α_1 and α_2 are the fractions existing of H_2R, HR^- and R^{-2}, respectively).

species starting from pH ~ 5.50. The species HR^- reaches maximum formation at pH equal to 6.84, then its mole fraction (α_1) decreases again while the mole fraction (α_2) of the species R^{-2} continue to increase reaching the value of 1.0 at pH ~10.00. Similar trends were found for the other derivatives with slight changes in the pH values corresponding to maximum existence of the different species (Table 2).

The values of α_1, at pH values where maximum percentage of HR^- exists, were found to range between 0.59778 for BD-5 and 0.84593 for BD-4. Since the absorbances (A) at these pH values were taken as A_{HR}, it was necessary to normalize the obtained pK_a values by calculating $(A_{HR})_{norm}$ as follows

$$(A_{HR})_{norm} = A\alpha_1 \quad (8)$$

Substituting in Eq. (7) with $(A_{HR})_{norm}$ instead of A_{HR}, normalized ionization constants for the investigated compounds are obtained (Table 2).

Comparing the obtained values of pK_a for the benzamide derivatives BD-1 to BD-4, it is clear that BD-3 has pK_{a_1} higher than those for BD-1, BD-2 and BD-4. This is most probably due to the presence of the allyl constituent in the position *Y*- instead of H in the other compounds (Scheme 1). The allyl group with its π-bond contributes to the conjugate system of the molecule as a whole rendering the adjacent (–OH) group weaker as an acid. On the other hand BD-6 exhibited pK_{a_1} and pK_{a_2} slightly higher than the corresponding values for BD-5, this is due to the effect of presence of ($–CH_2–$) group between the two amide groups in BD-6 where this group is absent in case of BD-5. Consequently in

Table 2
Normalized ionization constants of bis(*o*-hydroxybenzamido)alkanes (BD-1 to BD-4), *N*,*N*′ bis(*o*-hydroxyphenyl)oxamide (BD-5), and *N*,*N*′ bis(*o*-hydroxyphenyl)-malonamide (BD-6)

Compound	pH of maximum HR^-	α_1	pK_{a_1}	$(pK_{a_1})_{norm}$	pK_{a_2}	$(pK_{a_2})_{norm}$
BD-1	6.84	0.73647	6.15	6.14	7.66	7.55
BD-2	6.94	0.69440	6.31	6.27	7.61	7.48
BD-3	7.50	0.69439	6.82	6.81	8.13	7.95
BD-4	7.00	0.84593	5.97	5.81	8.05	7.84
BD-5	7.70	0.59778	7.29	7.31	8.24	7.98
BD-6	7.96	0.60775	7.32	7.42	8.44	8.27

BD-5, the mutual effect of the two symmetrical halves on each other is greater and slightly stronger acidity is expected.

4.1. Effect of alkali metal cations

The ionization of BD-1 has been investigated by following the proposed method in presence of 0.2 mol L^{-1} LiCl, NaCl, and KCl. It was found that such cations are chelated very weakly with the concerned compound as indicated by a slight change in the absorbance–pH curves obtained for the compound either in the H_2R or R^{-2} regions of spectra.

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