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Determination of the Dissociation Constant of Some Substituted Phenols by Potentiometric Method in Acetonitrile-Water Mixtures

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Abstract: The dissociation constants of phenol, 2–methylphenol, 3–methylphenol, 4–methylphenol, and 4–ethylphenol have been determined by potentiometric titration in a electrochemical cell with glass electrode at 25 °C in water and in the mixtures of acetonitrile and water where the following volume fractions (before mixing) of acetonitrile were used: 0.10, 0.20, and 0.30. The ionic strength of the solutions was adjusted to be 0.1 mol dm^{-3} using KCl. The dissociation constants were calculated by using the commercial Hyperquad 2008 program. The obtained results are in good concordance withliterature values.

Key words: Phenols, acid dissociation constant, potentiometric method.

Bazı Substitue Fenollerin Ayrışma Sabitlerinin Asetonitril-Su Karışımlarında Potansiyometrik Metotla Tayini

Özet: Fenol, 2-metilfenol, 3-metilfenol, 4-metilfenol ve 4-etilfenol'ün ayrışma sabitleri %10-20-30 oranlarında hazırlanan asetonitril –su karışımında 25 °C potansiyometrik olarak elektrokimyasal hücrede elektrot ile tayin edilmiştir.Titrasyon çözeltilerinde iyonik şiddet KCl kullanılarak 0.1 mol dm^{-3} olarak ayarlanmıştır. Ayrışma sabitleri ticari bir program olan Hyperquad 2008 ile hesaplanmıştır. Elde edilen sonuçlar literatürdeki değerlerle uyumluluk göstermektedir.

Anahtar kelimeler: Fenol, asidik ayrışma sabiti, potansiyometrik yöntem.

1. Introduction

Acid dissociation constants (pKa) are important parameters to indicate the extent of ionization of molecules in solution at different pH values. The acidity constants of organic reagents play a basic role in many analytical procedures. It has been shown that the acid-base properties affect the toxicity, chromatographic retention behaviour and pharmaceutical properties of organic acid and bases [1].

The pKa value is a key parameter to predict the ionization state of a molecule with respect to pH. Knowledge of this parameter is essential in the estimation of ADME (absorption, distribution, metabolism, and excretion) properties since absorption and distribution are highly affected by the ionization of compound. It is also necessary for the measurements of pH-dependent moleculer properties, for example solubility and lipophilicity of [2].

Solvent mixtures are interesting, because two solvents mixed together produce a solvent with quite different properties, both physically (electric permittivity, density, viscosity) and chemically (acid-base and accepter-donor properties) [3].

Acetonitrile (MeCN) is one of the most important dipolar aprotic solvent, it is used extensively as a reaction medium for mechanistic studies, in electrochemistry and in high performance liquid chromatography and it is also employed as a solvent for non aqueous titrations [4].

MeCN is as a weaker base and as a much weaker acid than water. It has a relatively high dielectric constant (ε:36) and a small autoprotolysis constant (pKs: 33,6). Accordingly, MeCN acts as a strogly differentiating solvent with a modest solvating power for many polar ionic solutes [5].

Phenols are used extensively in the production or manufacture of a large variety of aromatic compounds including explosives, fertilizers, coke, illuminating gas, rubber, textiles,drug preparations and other plastics [6].

In this study, potentiometric titration was used to determine the pKa's of some phenols. The phenols were 2- methylphenol, 3-methylphenol, 4-methylphenol, 4-ethylphenol and phenol. We have proposed models that relate the pKa values with the solvent composition. The results are thought as necessary for the separation of compounds. The compounds were compared according to the nature of the substituent and its ring position, ortho, meta and para.

2. Material and Method

2.1. Chemicals and Reagents

Analytical reagent grade chemicals were used, unless otherwise indicated. Phenolic acids studied are shown in Table 1. 2- methylphenol, 3-methylphenol, 4-methylphenol, 4-ethylphenol and phenol were purchased from Merck KGaA, Darmstadt, Germany; Sigma, America and used without further purification.

Water, with conductivity lower than the unit of 0.05 S cm^{-1}, was obtained with a Milli-Q water purification system (Millipore Corp.). MeCN (HPLC grade), potassium hydroxide, potassium chloride, hydrochloric acid was supplied by Merck. All the solutions were prepared in 0.1mol L^{-1} potassium chloride to keep the ionic strength constant. The calibration of the electrode system was done potentiometrically by Gran's method.

2.2. Apparatus

The cell was thermostated externally at 25 ^{0}C ± 0.1 with a cooler system water bath (Heto CBN 8-30 and temperature control unit Heto HMT 200, Thermostat with external circul., Heto, Denmark) and the test solution was stirred magnetically under a continuous stream of purified nitrogen. The e.m.f measurements to evaluate the pH of the solution were performed with a model ORION 5 STAR pH/ion analyzer with Ag/AgCl combined pH electrode system (±0.1 mV).

3. Procedures

3.1. Potentiometric Measurements

The pKa values of phenols were determinated by titration of the appropriate solution of phenols in 10,20,30 % (v/v) MeCN in water mixtures, using KOH solution as titrant, according to the criteria endorsed by IUPAC [7,8].

The standardisation of the electrode system was carried out, each time in MeCN- water mixtures studied by Gran's method [9].

For this purpose, on estimated amount of solution, at the same conditions as temperature, ionic strength and solvent composition (hereafter will be called background solution), was placed in a double-walled, thermostated vessel. The potential was allowed to stabilize after each addition of acid or base and then value was used to obtain the standart potential of the cell, E^o. The electrode was immersed in background solution and it was titrated with a strong base in the same experimental conditions of ionic strength and solvent composition. In all experiments, chromatographic pure nitrogen gas was used in titration cell. Usually, about 10 or 12 additions is enough for verify E^o to be accurately determined. pH of the background solution from 2 which is a value about two units lower than the pKa of the compound studied.

In second step, a suitable amount af phenol compound was added to the pre-titrated background solution. From the pair of potential values and volume added, pKa values were calculated using HYPERQUAD 2008 program (written by Peter Gans, Protonic Software, [10].This program can be used to derive acid dissociation constants from potentiometric data. The stability constant program is performed by means of a compiled Fortran program. The program takes its data from files and outputs its results to a file. Once the calculation is finished the results appear in the output viewer.

4. Results and Discussions

4.1. Theoretical Background

4.1.1. Analysis Methods

The analysis methods commonly used to derive pKa's from titration curves include Gran's plot and least-square non-linear regression. When a monoprotic weak acid is titrated by strong base, the Gran's plot expressed by the following equation [11].

$$[H^+]\, V_B = K_a\, (V_E - V_B) \qquad (1)$$

Where V_E and V_B are the volume of base added at equivalence point and at any point, respectively, K_a is the acid dissociation constant. Thus, a plot of $[H^+]$ V_B , *vs* V_E $-V_B$ will yield a linear curve with a slope of $K_{a.}$ This method presumes that the weak acid mainly exists in the protonated form (HA), thus only a portion of data, which is well before the equivalence point, is suitable for this point. Plot of calibration values of phenol in 10% (v/v) MeCN is Fig. 1. The Gran function is showed Vtot*10^E/g. The correlation coefficient (R) can range between +1 and -1. We got R as 0,99996 form Figure 1.

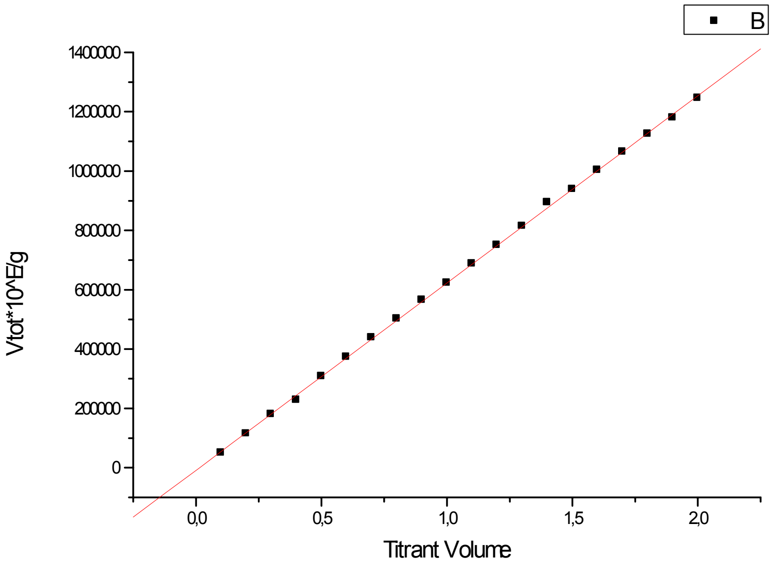

Figure 1 . Plot of calibration values of phenol in 10% (v/v) MeCN.

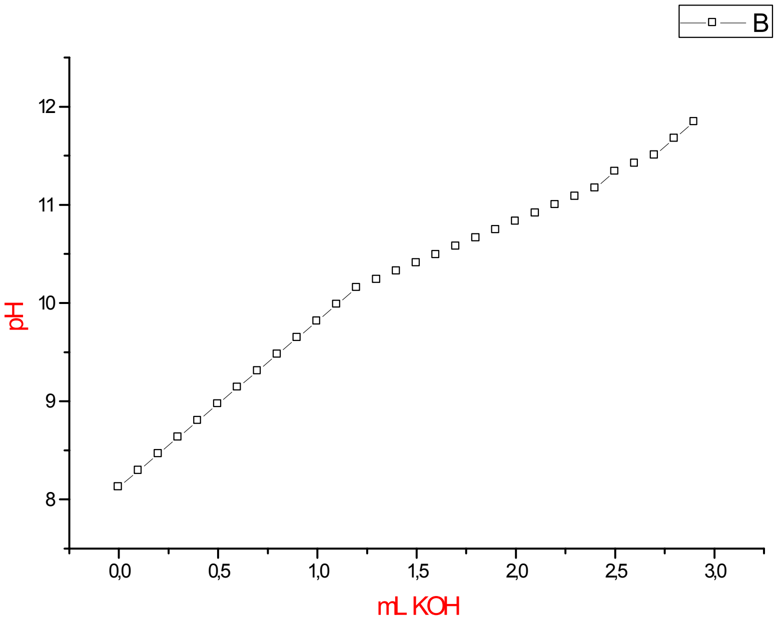

Figure 2. Potentiometric titration curves of phenol.

Figure 2 shows a typical potentiometric titration curveof phenol in 10 % (v/v) MeCN in water.

Potentiometric pK_a values were obtained from several series of independent measurements. As an example, one series of measurements for the titration of phenol in 10 % (v/v) MeCN and water using KOH as a titrant is shown in Figure2, in which the symbols indicate experimental values and solid line indicates the theorical titration curves.

4.1.2. Behaviour of Electrode Assembly in Aqueous MeCN and pH Determination*

The glass electrode is highly responsive in MeCN- water solution. The hydrogen ion activity in the MeCN water mixtures calculated as:

$$-\log a_H = pH^* = -\log[H^+]\, f^* \qquad (2)$$

Where $[H^+]$ is the stoichiometric hydrogen ion concentration and f* is the activity coefficient for a monovalent ion in the MeCN-water mixture. When the electromotive force measured in mV (E) is plotted versus the pH*, a straight line $E = E^o - b.\ pH^*$ where E^o is the cell constant.

The pH* of a given MeCN-water solution can be evaluated from the E measurement. The values for the intercept E^o and the slope b in mixtures. Slope were very close to the Nernstian value (59,16 mV pH^{-1})

Table 1. The pK_a values of phenolic compounds obtained by potentiometric method in water and 10%-20%-30% (v/v) acetonitrile-water mixture

Phenolic compounds	H_2O pK_a	%10 MeCN pK_a	%20 MeCN pK_a	%30 MeCN pK_a
2-methylphenol (o-kresol)	9.94±0.07	10.12±0.05 9.98[b]	10.19±0.01	10.65±0.05
3-methylphenol (m-kresol)	9.99±0.01 10.00[a]	10.19±0.05 10.15[b]	10.82±0.03 11.06[a]	11.09±0.04 11.35[a]
4-methylphenol (p-kresol)	9.39±0.03	9.90±0.04 9.44[b]	10.04±0.06	10.49±0.05
4-ethylphenol	9.99±0.12	10.09±0.33 10.04[b]	10,11±0.002	10.14±0.07
phenol	9.92±0.07 9.98[a]	10.08±0.05 10.03[b]	10.53±0.34 10.80[a]	10.99±0.45 11.13[a]

a :. Ref 12
b: Ref 6

Table 1 shows the dissociation constants of substituted phenols studied obtained by potentiometric methods using the Hyperquad 2006 program in different MeCN-water mixtures up to 30 % (v/v) MeCN and the respective standard deviation.

From Table 1, it is deduced that the variations of pK_a values with the percentage of MeCN were different for each substance. The pK_a values increased for all phenols as the MeCN content increased. The pK_a values of phenols varied even when the percentage of MeCN was low, by the increasing of MeCN content up to 30 % (v/v) MeCN, the pK_a values showed regular increasing. This can be explained by structural features of MeCN-water mixtures because the dissociation of uncharged acids in MeCN-water, as in other aqueous-organic mixtures, is ruled by electrostatic interactions as well as specific solute-solvent interactions. .The obtained results are in good concordance with literature values [6,12].

5. Conclusions

In this investigation, the determination of dissociation constants of 2- methylphenol, 3-methylphenol, 4-methylphenol, 4-ethylphenol and phenol compounds by potentiometric method has been performed. Acid–base constants in acetonitrile–water solution can be determined through calibration of the electrode system with pH standards prepared in the same working acetonitrile–water mixtures or with the common aqueous pH standards. The variation of the pKa values of bases with solvent composition in any of the two pH scales is different than the variation of the pKa values of acids.The pKa values of acids increase when the contents of acetonitrile in the mixture increase, whereas, pKa values of bases decrease, reach a minimum and then increase. The pK_a values of phenols varied even when the percentage of MeCN was low, by the increasing of MeCN content up to 30 % (v/v) MeCN, the pK_a values showed regular increasing.

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