

Spectrometric Determination of pK_a Values for some Phenolic Compounds in Acetonitrile – Water Mixture

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Abstract

The pK_a values of ten phenolic compounds (phenol, 4-fluorophenol, 4-iodophenol, 3-bromophenol, 4-methylphenol, 4-nitrophenol, 4-ethylphenol, 2-methylphenol, 3-nitrophenol, and 3-methylphenol) in 10% (v/v) acetonitrile-water mixture using spectrometric measurements have been determined. The electronic absorption spectra of phenolic compounds at various pH values (pH 2.0 -11.0) at 200-500 nm intervals were recorded. The calibration of the electrode system was done potentiometrically by Gran's method. Data were processed using the programme STAR (Stability Constants by Absorbance Readings). The obtained results are in good concordance with literature values.

Key words: phenolic compounds, dissociation constants, spectrometry.

Introduction

Acid dissociation constants 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.^{1,2}

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 titrations³. MeCN behaves as a weaker base and as a much weaker acid than water. It has a relatively high dielectric constant ($\epsilon = 36$) and a small autoprotolysis constant ($pK_s=33.6$). Accordingly, MeCN acts as a strongly differentiating solvent with a modest solvating power for many polar ionic solutes.⁴

The spectrometric method depends upon the direct determination of the ratio of molecular species (neutral molecule) to ionized species. In this respect, the data are no different from those obtained by potentiometric titration; the thermodynamics of ionic and nonionic interactions do not depend on the experimental method used to determine them. For this

purpose, the spectrum of the non-ionized species is obtained, using a buffer solution whose pH is so chosen that the compound to be measured is present wholly as this species. This spectrum is compared with that of pure ionized species similarly isolated at another suitable pH. A wavelength is chosen at which the greatest difference between the absorbances of the two species is observed. This is termed the “analytical wavelength”. By using this at various pH values, intermediate between those at which the spectra of the two species were obtained, the ratio of ionized to non-ionized species is calculated. This is possible because a series of two component mixture is formed in which the ratio of the two species depends solely upon the pH at which the solution is optically measured.

Beer's law has been tested extensively and, absent chemical complications, usually holds for concentrations below 10^{-2} M. At higher concentrations, the absorbance-concentrations relation may be nonlinear but the concentration can still be determined with the help of a calibration curve. A wide range of concentrations can be determined through appropriate choice of the optical path length and the measurement wavelength.⁵

The spectroscopic instrumentation used today, however, almost invariably has the capacity to collect data in a full spectral range. Using a single or a few wavelengths discards most of the information in the collected spectra and requires both the presence of

the knowledge of such suitable wavelengths. However, in many cases, the spectral responses of components overlap and analysis is no longer straightforward.^{6,7}

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.^{8,9} The dissociation constant of phenols are important physicochemical parameters for a thorough understanding of certain chemical phenomena such as activity and reacting rates, biological uptake and receptor binding of substances at the molecular level. Traditionally, water has been considered the solvent which best represents the biological conditions. However, hydro-organic mixtures, such as MeCN - water, have been found especially suitable because they show simultaneously a low polar character and a partially aqueous content, as do all biological systems.

Dissociation constants of substances can be determined by several different methods. The potentiometric, chromatographic, electrophoretic methods also have been used widely. But a method based on spectrometry has been still used widely by the help of improving computer programs.¹⁰⁻¹² In most of these methods a physical property of the analyte is measured as a function of the pH of the solution and the resulting data are used for the determination of dissociation constant. The use of MeCN-water mixtures requires the correct measurement of pH in these media. Measurements are performed in a similar way to those performed in water using IUPAC standardization rules.¹³⁻¹⁵

In this work, we have determined the pK_a values of selected phenol substances in 10% (v/v) MeCN-water mixtures using spectrometric measurements. We studied at the media of %10 since phenols have not been determined as spectrometric in this media so far. The results are thought as necessary for the separation of compounds at the methods of chromatographic and electrophoretic.

Experimental

Chemicals and reagents

Analytical reagent grade chemicals were used, unless otherwise indicated. Polyphenolic acids studied are shown in Fig. 1. phenol, 4-fluorophenol, 4-iodophenol, 3-bromophenol, 4-methylphenol, 4-nitrophenol, 4-ethylphenol, 2-methylphenol, 3-nitrophenol, and 3-methylphenol were purchased from Merck, Sigma and used without further purification. Water, with conductivity lower than 0.05 S cm^{-1} , was obtained with a Milli-Q water purification system (Millipore Corp.). MeCN (HPLC grade), was supplied by Merck. Potassium hydroxide (Merck), potassium chloride

(Merck), hydrochloric acid (Merck) was used. While spectrometric measurements were done, solutions of individual phenolic compounds were prepared at a concentration of approximately $5.10^{-4} \text{ mol L}^{-1}$. All the solutions were prepared in 0.1 mol L^{-1} potassium chloride to adjust the ionic strength. The calibration of the electrode system was done potentiometrically by Gran's method.^{16,17}

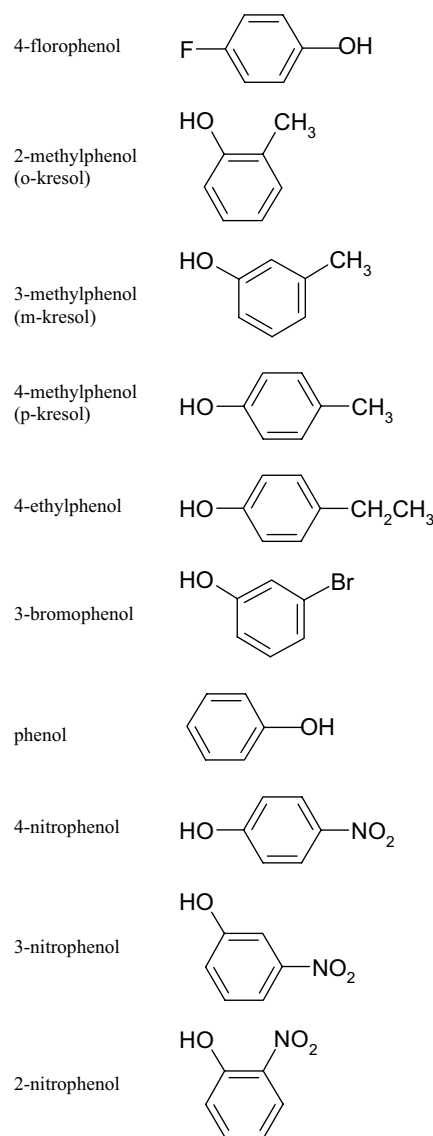


Figure 1. Structural formulae of studied phenolic compounds

Apparatus

The UV-Vis spectra, obtained to determine absorptiometric pK_a values, were recorded at each pH using a Perkin-Elmer LAMBDA 20 spectrophotometer, equipped with 1 cm path length cell, controlled by personal computer. A peristaltic pump equipped with

the spectrometer was used to circulate the solution from the titration vessel to the spectrophotometer cell, and vice versa, through Teflon or Tygon tubes in a closed loop circuit with continuous flow. The cell was thermostated externally at $25\text{ }^{\circ}\text{C} \pm 0.1$ with a cooler system water bath (Heto CBN 8-30 and temperature control unit Heto HMT 200) 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 Mettler-Toledo MA 235 pH/ion analyzer with Hanna HI 1332 Ag/AgCl combined pH electrode system (± 0.1 mv).

Procedures

Spectrometric measurements

The pK_a values of the different substances were determined by means of the data obtained from spectrometric titrations in 10% (v/v) acetonitrile–water mixture at $25\text{ }^{\circ}\text{C} \pm 0.1$ and in 0.1 mol L^{-1} ionic strength (KCl). For each phenolic compound various series of measurements were performed in studied media. In the first step, the electrodic system was calibrated by Gran's method as in the case of potentiometric measurements in order to obtain E° value. Previously, a suitable amount of a solution containing the compound to be analyzed at the required conditions of temperature, ionic strength and solvent composition, was added to the pre-titrated background solution and small amounts of sodium hydroxide or hydrochloric acid solutions were then added. The spectral data were obtained by adding small amounts of acid or base to change the pH in the range of 2.0–11.0. These amounts should be high enough to provoke a measurable change in the pH of the test solution, but also small enough to allow the increase of volume to be neglected. At each pH, UV-Vis spectra were recorded with 1 nm resolution in order to obtain different spectra around the maximum λ for each polyphenolic acids. After each addition, the potential was allowed to stabilize and the potential value was used to calculate the pH of the solution using the value of E° calculated in the calibration step. In the UV-Vis spectrometric titrations, the test solution was pumped to a spectrometric flow-cell by means of a peristaltic pump. After each addition of titrant, and after waiting for the potential reading to be stable, a spectrum was recorded, all relevant data were stored, and a new volume of titrant was added to restart the cycle. Data were processed using the programme STAR (Stability Constants by Absorbance Readings)¹⁸ which calculate stability constants and molar absorbances of the pure species by multi linear regression. It can work with up to 50 different spectra with 50 different points each. This programme allows to handling of systems with up to five components, which form up to 25 species.

The STAR program requires a previous model of the chemical equilibria, based upon the existence of certain chemical species, to be postulated. From this model and from additional chemical information, such as the total concentration of the components, the pH of the solutions and the experimental spectral data, the refined equilibrium constant and the corresponding pure spectra of each species can be obtained taking into account the activity coefficients. The optimization is performed by means of a non-linear least-squares procedure.

Results and Discussion

The electronic absorption spectra of phenolic compounds in 10% (v/v) MeCN–water mixtures at various pH values at 200–500 nm intervals were recorded. Sample spectra of phenol and 2-methylphenol at different pH values in studied media are shown in Fig. 2 and Fig.3.

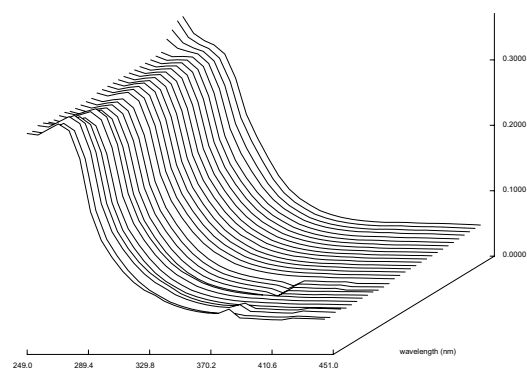


Figure 2. Plot of experimental absorbance values of phenol wavelength as a function of pH in 10% (v/v) MeCN.

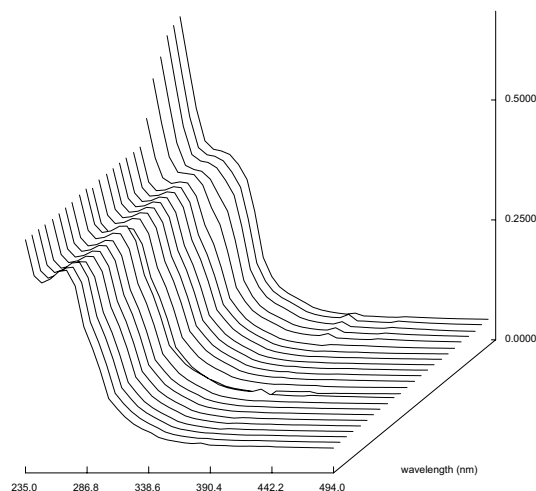


Figure 3. Plot of experimental absorbance values of 2-methylphenol wavelength as a function of pH in 10% (v/v) MeCN

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 acceptor–donor properties). As far as the acid–base properties are concerned, an important feature is that the nature of the solvent is crucial for the strength of acids and bases. In particular, important is the proton affinity or, in other words, the proton-donating and proton-accepting properties of solvent, as well as its polarity. Also the ionization degree of solute depends on the dielectric constant of solvent. Media of high dielectric constants are strongly ionizing, whereas those of low dielectric constants ionize to a lesser extent. By mixing solvents of different polarity in proper ratios, dielectric constant of the medium can be varied and, at the same time, the strength of dissolved acids and bases. It should also be emphasized that solvent mixtures can be more convenient than individual solvents owing to enhanced solubilising capacity and more manageable shape of acid–base titration curves.

The standards used for the determination of the pK_a values have successfully been utilized in hydro organic media and employed in particular for spectroscopy as an experimental technique. On the other hand, increasing interest in acid–base interactions taking place in solvent mixtures raised the need for the development of a method for the determination of the pK_a values for standards in such media. For this reason, the primary objective of this contribution was to develop a spectroscopic method for the determination of acid dissociation constants (commonly expressed as pK_a) of phenolic compounds in solvent mixtures.

Table 1. The pK_a values of phenolic compounds obtained by spectrometric method in MeCN–water media.

Compounds	H ₂ O pK_a	10% (v/v) MeCN pK_a
4-florophenol	9.95 ^a	9.79 (0.03)*
2-methylphenol	10.28 ^a	9.98 (0.02)
(o-kresol)	10.28 ^b	
3-methylphenol	10.08 ^a	10.15 (0.03)
(m-kresol)	10.00 ^b	
4-methylphenol	10.19 ^a	9.44 (0.02)
(p-kresol)	10.25 ^b	
4-ethylphenol	-	10.04 (0.02)
3-bromophenol	9.11 ^a	10.22 (0.09)
	8.87 ^b	
Phenol	9.95 ^a	9.92 (0.04)
	9.98 ^b	
3-nitrophenol	8.39 ^b	9.38 (0.07)
2-nitrophenol	7.24 ^b	8.23 (0.08)
4-nitrophenol	7.16 ^b	8.45 (0.04)

* Standard deviations are in parenthesis.

^a pK_a values are obtained from Ref. (23)

^b pK_a values are obtained from Ref. (24)

From Table 1, it is deduced that the variations of the pK_a values with the percentage of MeCN were different for each substance. If it is compared the strengths of a series of phenolic compounds with each other, it is saw there are significant variations according to nature of the substituent and its ring position ortho, meta or para. Because of methyl group's electron transmitter property in 10% MeCN media pK_a values of all three methylphenols are usually decreased according to pK_a values in water media, nitro group is electron attractive. pK_a values of all nitrophenols are increased according to pK_a values in water media. The pK_a values of halogenated phenols are changed according to electronegative of halogen.

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 (solvation effects).^{19–22}

Conclusion

In this investigation, the determination of dissociation constants of phenol, 4-fluorophenol, 4-iodophenol, 3-bromophenol, 4-methylphenol, 4-nitrophenol, 4-ethylphenol, 2-methylphenol, 3-nitrophenol, and 3-methylphenol compounds by spectrometric method has been performed. Although spectrometric method requires a relatively high pure substance, at least one of species (acid or basic) must contain an absorbing group and the time and effort to calibrate the electrodic system, it provides excellent precision in the measurements, the true dissociation constants can be measured directly without inter ionic effects having to be considered, the optical properties of the ions are virtually constant up to relatively high concentrations.

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Povzetek

Spektrometrično smo določili pK_a vrednosti derivatov fenola (fenol, 4-fluorofenol, 4-jodofenol, 3-bromofenol, 4-metilfenol, 4-nitrofenol, 4-etilfenol, 2-metilfenol, 3-nitrofenol, and 3-metilfenol) v 10% (v/v) raztopinah acetonitril-voda. Elektronske absorpcijske spektre smo posneli pri pH 2.0–11.0 v območju 200–500 nm. Elektrode smo kalibrirali potenciometrično po Granovi metodi. Podatke smo obdelali s programom STAR (Stability Constants by Absorbance Readings). Dobljeni rezultati se dobro ujemajo z vrednostmi iz literature.