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Spectrophotometric Determination of pK_a Values for Some Benzoic Acid Compounds in Acetonitrile-Water Mixtures

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The dissociation pK_a values of benzoic acid and substituted benzoic acids have been determined in water and acetonitrile-water mixtures (10%, 20%, 30%) by spectrophotometric measurements. The results obtained show that the solvents affect the acid equilibrium. Acetonitrile acts as a strongly differentiating solvent with a modest solvating power for many polar ionic solutes. Linear relationships between pK_a values in acetonitrile-water mixtures and pK_a values in pure water have been established for fourteen benzoic acids. The pHab is a computer program using the calculation dissociation constants from spectrophotometric data obtained from solutions at known pH.

Key Words: pK_a, **Substituted benzoic acid, Acetonitrile-water mixtures, Acid equilibrium.**

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 solvents; it is used extensively as a reaction medium for mechanistic studies, in electrochemistry, and in high performance liquid chromatography and also employed as a solvent for non-aqueous titrations[3]. MeCN behaves as a weaker base and as a much weaker acid than water. It has a relatively high dielectric constant ($\varepsilon = 36$) and a small autoprotolysis constant ($pK_w = 33.6$). Accordingly, MeCN acts as a strongly differentiating solvent with a modest solvating power for many polar ionic solutes[4].

Beer's law has been tested extensively and in the absence of chemical complications, usually holds for concentrations below 10^{-2} M. At higher concentrations, the absorbance-concentrations relation may be non-linear 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 of 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 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].

The dissociation constants of benzoic acids 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 spectrophotometry has been still used widely by the help of improving computer programs[8–10]. 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[11–13].

In this work, the pK_a values of selected benzoic acid substances in water and 10%, 20%, 30% (v/v) MeCN-water mixtures using spectrophotometric measurements is determined. The results are thought as necessary for the separation of compounds by chromatographic and electrophoretic methods.

EXPERIMENTAL

Absorbance measurements were carried out by using a Perkin-Elmer Lambda 20 double beam UV-Vis spectrophotometer interfaced to an IBM SX-486 microcomputer for the spectral acquisition provided with a UV-Win Lab software and subsequent manipulation of experimental data. The absorbance measurements were carried out in two matching quartz 1.0 cm cells with a 1 mm path length. The emf measurements to evaluate the pH of the solution were performed with a model Metleer-Toledo MA 235 pH/ion analyzer with Hanna HI 1332 Ag/AgCl combined pH electrode system (± 0.1 mv).

Analytical reagent grade chemicals were used, unless otherwise indicated. Benzoic acid and substituted benzoic acids were purchased from Merck (Darmstadt, Germany), Aldrich (Milwaukee, USA) and Fluka (Milwaukee, USA). Water, with conductivity lower than 0.05 S cm^{-1}, was obtained with a Milli-Q water purification system (Millipore Corp.). MeCN (HPLC grade), NaOH, NaCl, HCl were purchased from Merck (Darmstadt, Germany). Solutions of individual benzoic acid compounds were prepared at a concentration of *ca.* 5×10^{-4} 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 Grans method[14].

Spectrophotometric measurements: The pK_a values of the different substances were determined by means of the data obtained from spectrophotometric titrations in water and different acetonitrile-water mixtures at 25°C ± 0.1 and in

0.1 mol L^{-1} ionic strength (NaCl). In the first step, the electrodic system was calibrated by Gran's method[14] 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 hydrochloric acid solutions were then added. The spectral data were obtained by adding small amounts of 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 benzoic 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 spectrophotometric 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 pHab.

Computer Programme

The programme pHab, which has been written for the determination of equilibrium constants from spectrophotometric data obtained from solutions at known pH. It can work with up to 100 different spectra with 100 different points each. pHab 2000 is a fully integrated Windows program, which performs almost all the functions previously performed by the three programs pHabedit, pHab and pHabout. In addition there are now better facilities for preliminary analysis of data, including manual fitting and principal component analysis. The model is specified by giving the log β values together with the coefficients, which define the stoichiometry of the species formed. For example, in the following sample data the formation constant for the species AH and AH_2 are defined as follows: $[AH] = b_{11}[A][H]$; $[AH_2] = b_{12}[A][H]^2$. Formally these are cumulative association constants. In pHab, it is assumed that the reagent H^+ is always present and is the last of the reagents listed.

The traditional argument for wavelength selection is that choosing the wavelength corresponding to an absorbance maximum in a species spectrum gives the most information concerning the concentration of that species. Other wavelengths give less information and each implies the existence of another set of unknown molar absorbance. Therefore, the purpose of doing multi-wavelength calculation is to ameliorate a little the effects of experimental noise, but its value is not as great as might be expected since the ratio of the number of observations to the number of unknown quantities does not increase by a large amount. Furthermore, the truth is that molar absorbance and equilibrium constant are multiplied together in Beer's law so that there is a correlation between these quantities that is masked by the method of calculation. The optimization is performed by means of a non-linear least-squares procedure[15].

RESULTS AND DISCUSSION

The absorption spectra of benzoic acid compounds in water and (10%, 20%, 30%) (v/v) MeCN-water mixtures at various pH values at 200–500 nm intervals were recorded (Figs. 1–4).

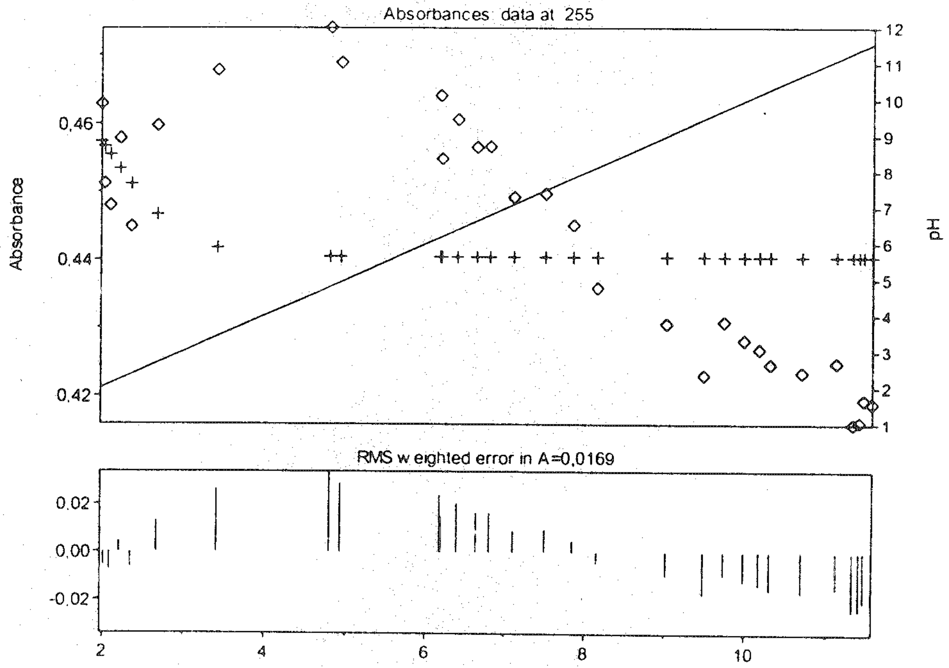

Fig. 1. (a) Plot of experimental absorbance values of 3,5-dinitrobenzoic acid wavelength as a function of pH in water

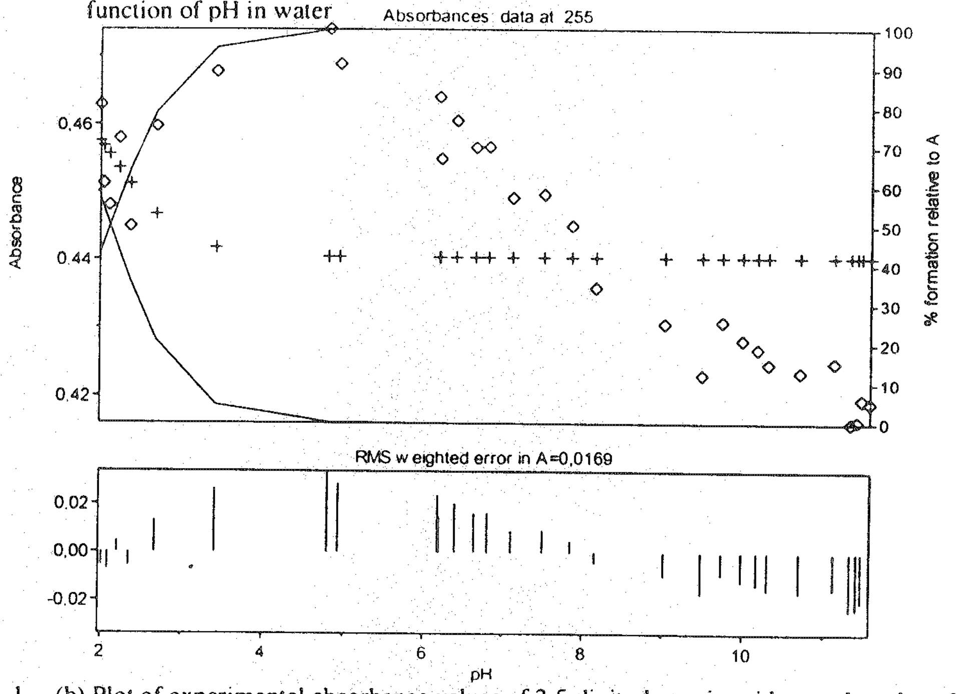

Fig. 1. (b) Plot of experimental absorbance values of 3,5-dinitrobenzoic acid wave length as % formation relative to ion in water

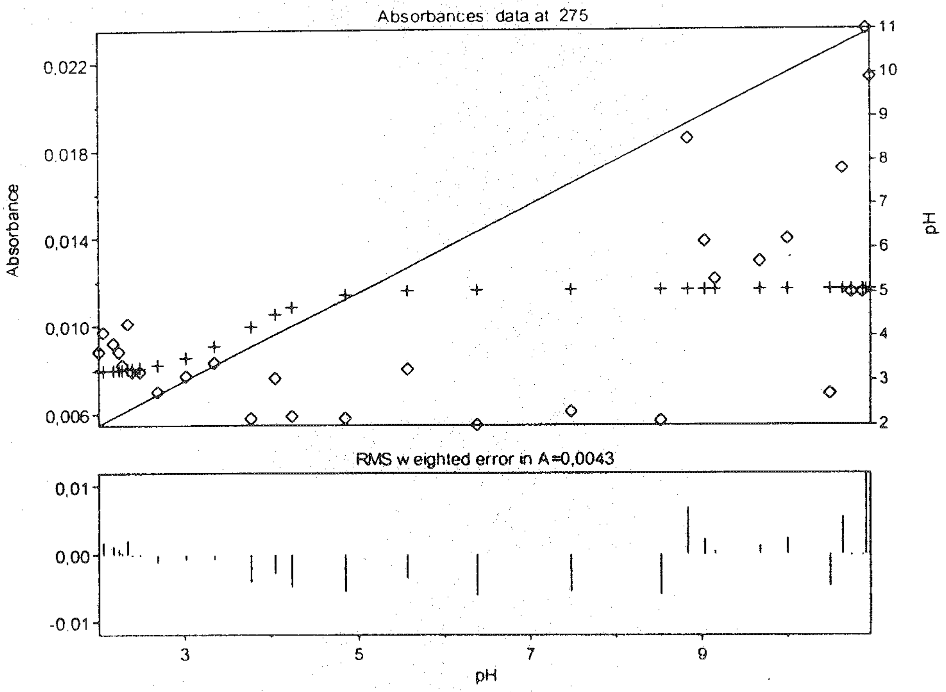

Fig. 2. (a) Plot of experimental absorbance values of 3,5-dinitrobenzoic acid wavelength as a function of pH in 10% (v/v) MeCN

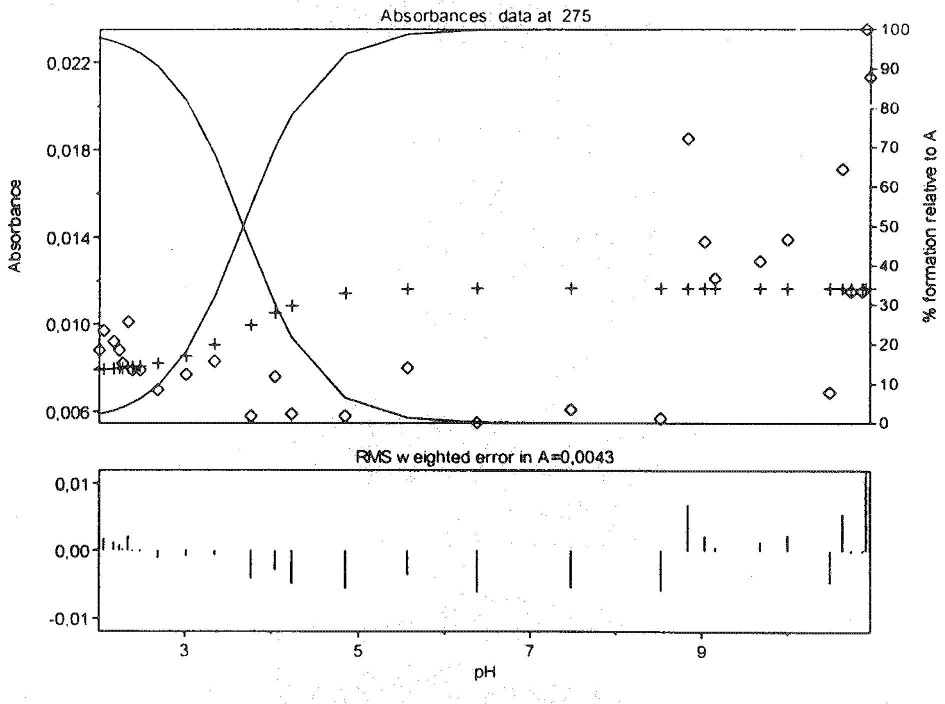

Fig. 2. (b) Plot of experimental absorbance values of 3,5-dinitrobenzoic acid wave length as % formation relative to ion in 10% (v/v) MeCN

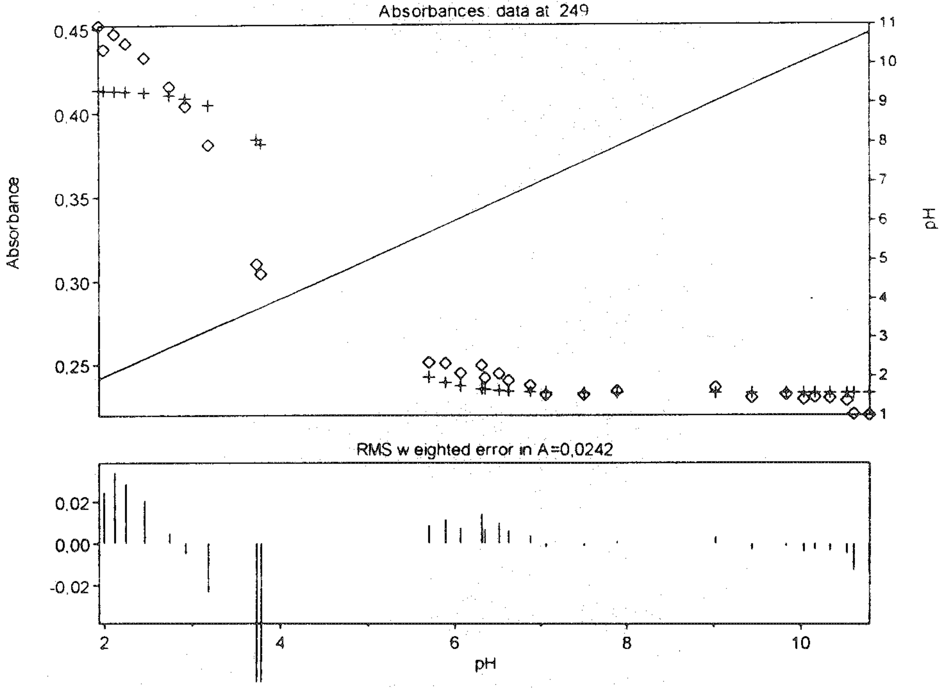

Fig. 3. (a) Plot of experimental absorbance values of 4-bromobenzoic acid wavelength as a function of pH in water

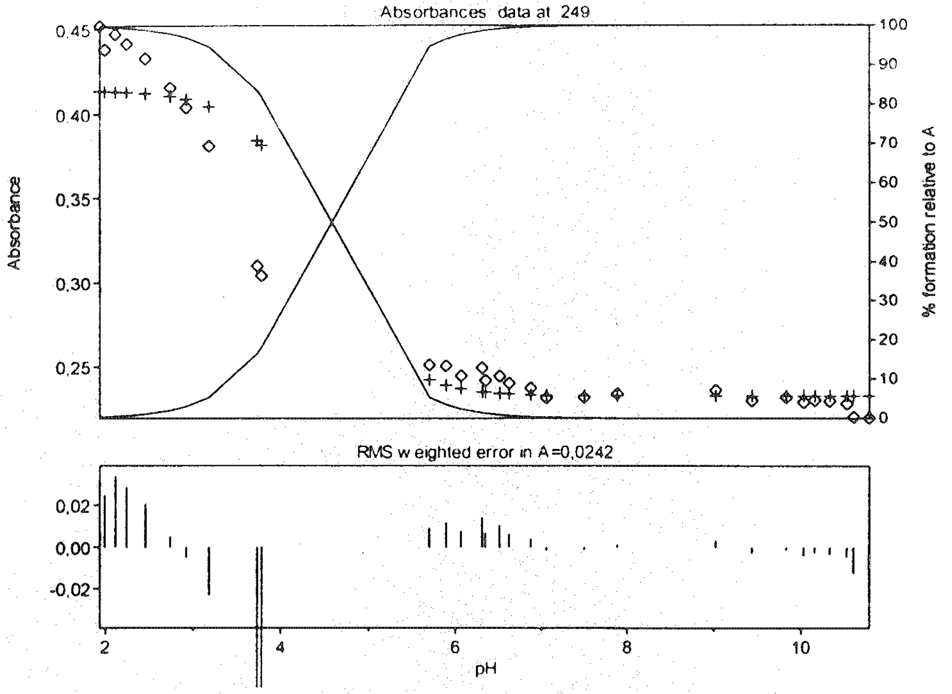

Fig. 3. (b) Plot of experimental absorbance values of 4-bromobenzoic acid wave length as % formation relative to ion in water

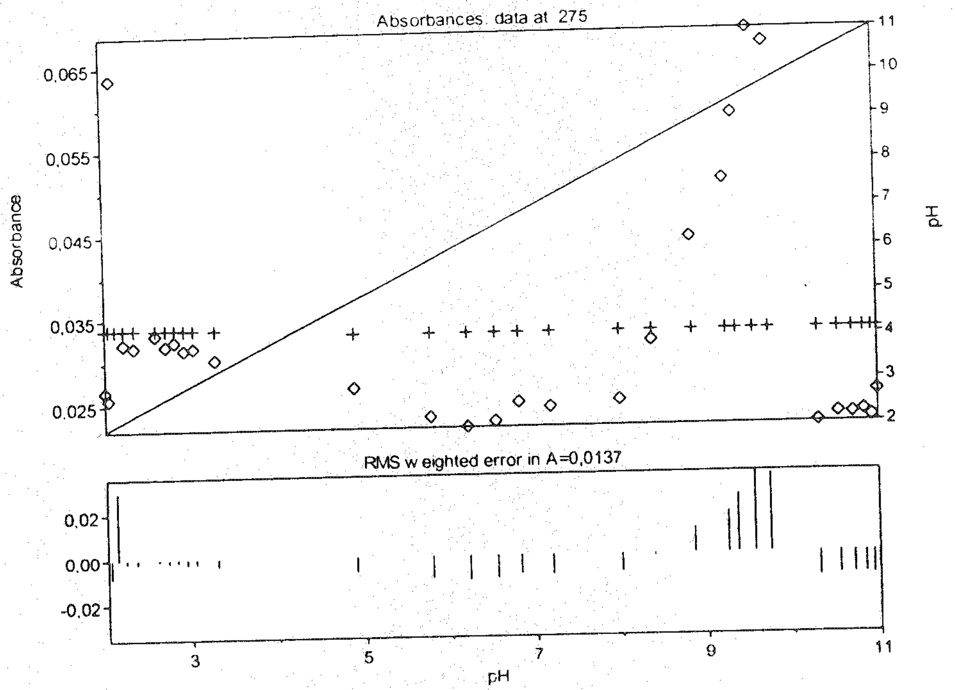

Fig. 4. (a) Plot of experimental absorbance values of 4-bromobenzoic acid wavelength as a function of pH in 20% (v/v) MeCN

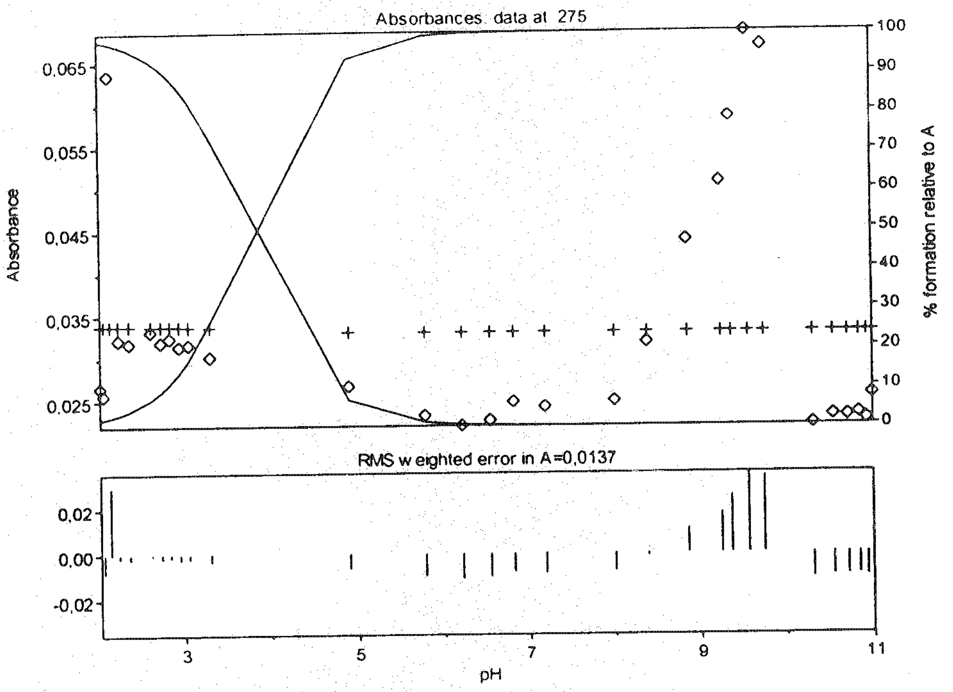

Fig. 4. (b) Plot of experimental absorbance values of 4-bromobenzoic acid wave length as % formation relative to ion in 10% (v/v) MeCN

At (a) part of all figures, there is plot of experimental absorbance values of benzoic acids wavelength as a function of pH in acetonitrile-water mixtures. pH is increased by adding small amounts of base to change the pH in the range of 2.0–11.0. It is seen that pH changing is regularly.

At (b) part of all figures, there is plot of experimental absorbance values of benzoic acids wavelength as % formation relative to ion in acetonitrile-water mixtures. Ion is formed by adding small amounts of base.

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 solubilizing 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 (pK_a) of compounds in solvent mixtures.

From Table-1 and Table-2, it is deduced that the variations of the pK_a values with the percentage of MeCN were different for each substance. However, the pK_a values increased for all benzoic acids as the MeCN content increased as expected. 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)[16–19].

If it is compared the strengths of a series of substituted benzoic acids with the strength of benzoic acid itself, it is saw that there are significant variations according to the nature of the substituent and its ring position, ortho, meta or para. Thus, all three nitro benzoic acids are appreciably stronger than benzoic acid in the order 4-nitrobenzoic acid > 3-nitrobenzoic acid > 2-nitrobenzoic acid > benzoic acid.

TABLE-1
THEORICAL pK_a VALUES OF BENZOIC ACID COMPOUNDS

Compounds	H_2O pK_a	10% MeCN pK_a	20% MeCN pK_a	30% MeCN pK_a
4-Nitrobenzoic acid	3.43[17] 3.44[18] 3.43[19]	3.50[17]	3.82[17]	4.10[17]
3-Nitrobenzoic acid	3.49[17] 3.49[18] 3.46[19]	3.54[17]	3.75[17]	4.01[17]
2-Nitrobenzoic acid	2.22[17] 2.17[18] 2.17[19]	2.58[17]	2.95[17]	3.29[17]
2,4-Nitrobenzoic acid	1.42[17] 1.43[18] 1.43[19]	—	—	—
3,5-Nitrobenzoic acid	2.82[17] 2.82[18]	—	—	—
3-Bromobenzoic acid	3.82[17] 3.81[18] 3.81[19]	—	—	—
4-Bromobenzoic acid	3.97[17] 4.00[18]	—	—	—
2-Chlorobenzoic acid	2.94[17] 2.94[18] 2.90[19]	—	—	—
2,4-Dichlorobenzoic acid	2.72[17]	—	—	—
3,4-Dichlorobenzoic acid	3.60[17]	—	—	—
4-Hydroxybenzoic acid	4.58[17] 4.58[18] pka2 : 9.23[18] 2.98[19]	—	—	—
Benzoic acid	4.21[17] 4.21[18] 4.204[19] 4.231[20]	4.49[17]	4.77[17]	5.05[17]
2,4,6-Trimethyl benzoic acid	3.44[17] 3.44[18]	—	—	—

TABLE-2

pK_a VALUES OF BENZOIC ACID COMPOUNDS OBTAINED BY SPECTROPHOTOMETRIC METHOD IN WATER AND IN WATER AND ACETONITRILE-WATER MEDIA (10, 20, AND 30%)

Compounds	H_2O pK_a	10% MeCN pK_a	20% MeCN pK_a	30% MeCN pK_a
4-Nitrobenzoic acid	3.4400 ± 0.0105	3.4800 ± 0.0452	3.8194 ± 0.0328	4.1138 ± 0.0934
3-Nitrobenzoic acid	3.4532 ± 0.0110	3.5155 ± 0.1119	3.7254 ± 0.0489	4.0469 ± 0.0202
2-Nitrobenzoic acid	2.3586 ± 0.0217	2.4374 ± 0.0116	2.9309 ± 0.0110	3.2875 ± 0.0205
2,4-Dinitrobenzoic acid	2.3493 ± 0.0105	2.6534 ± 0.1344	2.7489 ± 0.0174	2.9090 ± 0.0090
3,5-Dinitrobenzoic acid	2.8109 ± 0.0137	2.9766 ± 0.0248	3.3500 ± 0.0740	3.8000 ± 0.0256
3-Bromobenzoic acid	3.8124 ± 0.0190	3.9500 ± 0.0280	4.2832 ± 0.0173	4.5000 ± 0.0373
4-Bromobenzoic acid	3.9705 ± 0.0806	4.1475 ± 0.0536	4.4620 ± 0.0723	4.5300 ± 0.0118
2-Chlorobenzoic acid	2.9418 ± 0.0105	3.1400 ± 0.0930	3.5333 ± 0.0815	3.8000 ± 0.0739
2,4-Dichlorobenzoic acid	2.7132 ± 0.1193	3.0162 ± 0.1263	3.1142 ± 0.0615	3.4811 ± 0.0486
3,4-Dichlorobenzoic acid	3.5780 ± 0.0480	3.7821 ± 0.0763	4.1964 ± 0.0087	4.4848 ± 0.0607
4-Hydroxybenzoic acid	4.5331 ± 0.0272 9.2166 ± 0.0001	4.8593 ± 0.0108 9.4985 ± 0.0106	5.0027 ± 0.0480 9.5669 ± 0.0001	5.2806 ± 0.0147 9.9074 ± 0.0142
2-Hydroxybenzoic acid	3.0022 ± 0.0510 12.284 ± 0.0495	3.2257 ± 0.0285 12.556 ± 0.0127	3.6338 ± 0.0335 12.762 ± 0.0781	3.8000 ± 0.0544 13.246 ± 0.0558
Benzoic acid	4.2031 ± 0.0720	4.4832 ± 0.0416	4.4771 ± 0.0379	4.9697 ± 0.0300
2,4,6-Trimethyl benzoic acid	3.4042 ± 0.0753	3.5500 ± 0.0854	3.9716 ± 0.0407	4.3320 ± 0.0397

Conclusion

In this investigation, the determination of dissociation constants of benzoic acid compounds by spectrophotometric method has been performed. Although spectrophotometric method requires a relatively high pure substance, at least one of the 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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