



J. Chem. Pharm. Res., 2010, 2(3):551-558

ISSN No: 0975-7384
CODEN(USA): JCPRC5

Determination of the protonation constant of some new 3-alkyl(aryl)-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivative compounds with spectrophotometric method

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ABSTRACT

The protonation constant values of different four triazole derivatives have been determined in ethanol %50 – water %50 mixtures by spectrophotometric methods. The electronic absorption spectra of different four triazole derivatives at various pH values at 190-400 nm intervals were recorded. The calibration of the electrode system was done potentiometrically by Gran's method. Data were calculated using the linearization method with Henderson-Hasselbach equation. The obtained results are in good accordance with potentiometric values.

Key words: Protonation constant, triazole, spectrophotometric method.

INTRODUCTION

Acidity measurements of organic compounds have a long history dating back to the end of the 19th century, when the first pKa was measured. Since then a vast body of data on acidities in various solvents has been collected (1-4). The measurements have mostly been limited to polar solvents, however, with water being by far the most exploited medium, followed by alcohols and dipolar aprotic solvents. Several studies, involving the formation and investigation of biological activities of some 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives, have been reported (5-16). It is known that these derivatives have weak acidic properties.

A number of studies have been reported on the protonation constants of these derivatives in different media (17–20) however, very little information on the protonation constants of these derivatives in water and organic solvent-water mixtures has been published so far (21-23). In addition, 1,2,4-triazole and 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives are reported to show a broad spectrum of biological activities such as antifungal, antimicrobial, hypoglycemic,

antihypertensive, analgesic, antiparasitic, hypocholesteremic, antiviral, anti-inflammatory, antioxidant, antitumor and anti-HIV properties (24-29).

Lambert 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 (30). Protonation constant of weak acidic compounds can be determined by several different methods. The potentiometric, chromatographic, electrophoretic methods also have been used widely (31).

In this work, the pKa values of some new 3-alkyl(aryl)-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivatives in ethanol %50 – water %50 mixtures using spectrophotometric measurements in determined. New 3-alkyl(aryl)-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivatives were synthesized according to the reported reference 32. It is observed that the obtained results are in good accordance with potentiometric values.

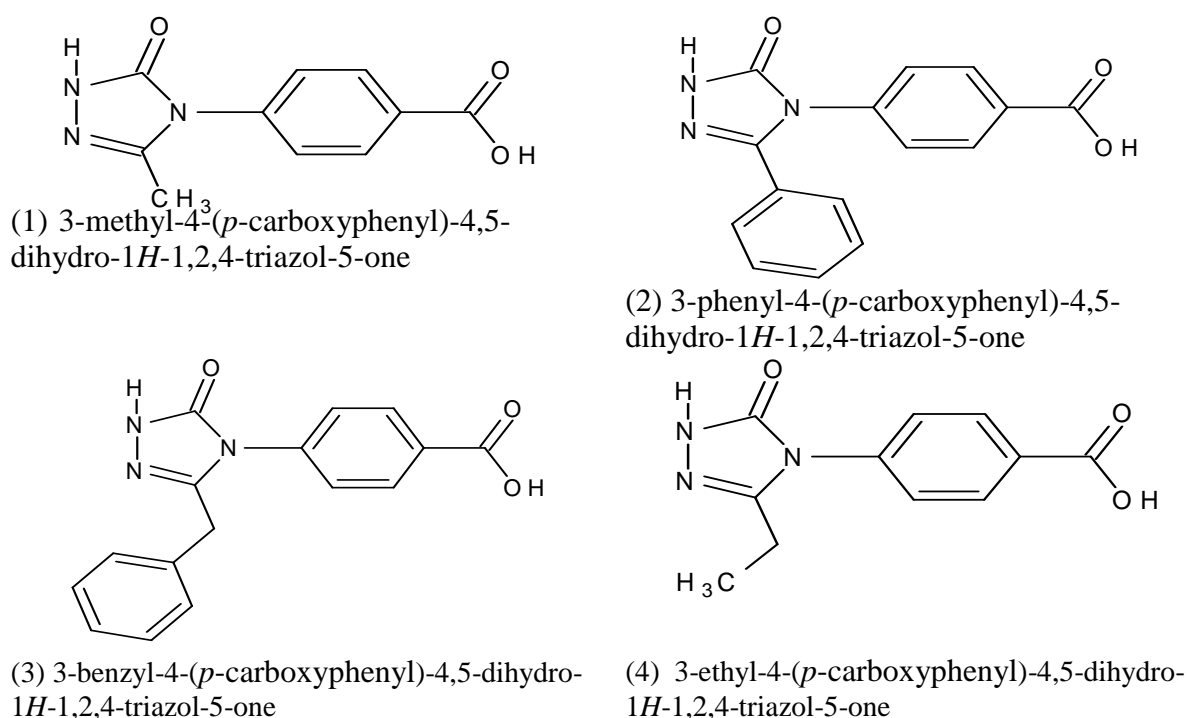


Fig: 1 Structural formulae of studied triazole derivatives

EXPERIMENTAL SECTION

In this study, four different triazole derivatives [(1) 3-methyl-4-(*p*-carboxy phenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one, (2) 3-phenyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one, (3) 3-benzyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one and (4) 3-ethyl-4-(*p*-carboxy phenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one] were synthesized according to new method of microwave-assisted synthesis in Rize University Organic Chemistry Research Laboratory. These triazole derivatives studied are shown in Fig. 1. Doubly distilled conductivity water was used as aqueous medium as well as for the preparation of ethanol %50 – water %50 mixtures. All other chemicals used in this investigation were reagent grade purity. Water conductivity lower than 0.05 S cm^{-1} . Ethanol was supplied by Merck. Potassium hydroxide

(Merck), potassium chloride (Merck), hydrochloric acid (Merck) was used. While spectrophotometric measurements were done, solutions of individual triazole derivatives were prepared at a concentration of approximately 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 Gran's method (33-34).

Absorbance measurements were carried out by using a Shimadzu 2450 UV/Vis spectrophotometer. 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 HANNA 4521 meter with Ag/AgCl combined pH electrode system (± 0.1 mV). The pK_a values of the different triazole derivatives were determined by means of the data obtained from spectrophotometric titrations in ethanol %50 – water %50 mixtures at $25^{\circ}\text{C} \pm 0.1$ and in 0.1 mol L⁻¹ ionic strength (NaCl). 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 0.05 mL NaOH change the pH in the range of 3.0-10.0. These amounts should be high enough to provoke a measurable change in the pH of the test solution. At each pH, UV/Vis spectra were recorder with 1 nm resolution in order to obtain different spectra around the maximum λ for each triazole derivatives. 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^o calculated in the calibration step. 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 new volume of titrant was added to restart the cycle. All data were calculated using the linearization method with Henderson-Hasselbach equation.

$$\log \left(\frac{A_{\lambda} - A_{\lambda\text{HA}}}{A_{\lambda\text{A}} - A_{\lambda}} \right) = \text{pH} - \text{pK}_a$$

Fig: 2 Henderson-Hasselbach equation

RESULTS AND DISCUSSION

The absorption spectra of four different triazole derivatives in ethanol %50 – water %50 mixtures at various pH values 190 – 400 nm intervals were recorded. Spectra of all triazole derivatives at different pH values in studied media are shown in Fig. 3-6.

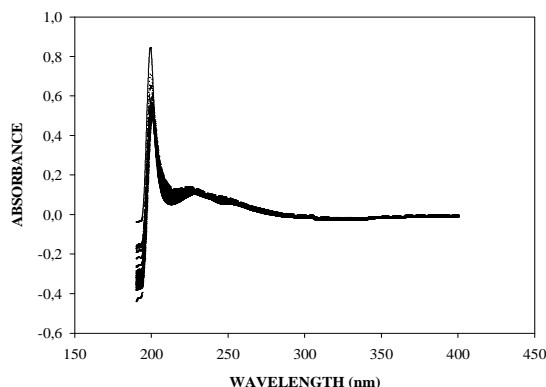


Fig: 3 Plot of experimental absorbance values of 3-methyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one wavelength as a function of pH in ethanol %50 – water %50 mixtures

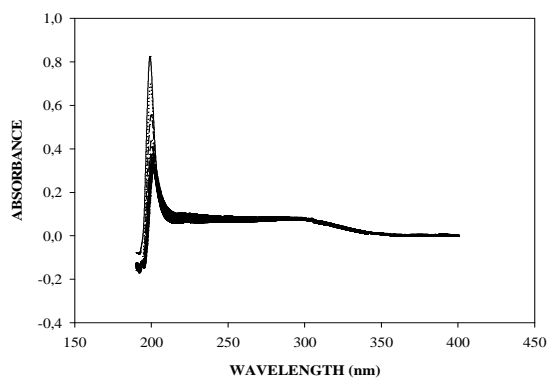


Fig: 4 Plot of experimental absorbance values of 3- phenyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one wavelength as a function of pH in ethanol %50 – water %50 mixtures

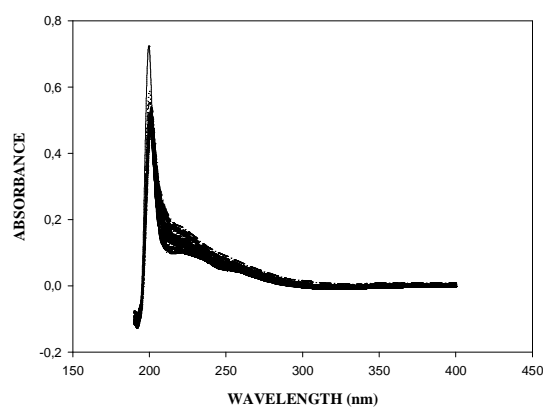


Fig: 5 Plot of experimental absorbance values of 3-benzyl-4-(*p*-carboxyphenyl)-4,5 dihydro-1*H*-1,2,4-triazol-5-one wavelength as a function of pH in ethanol %50 – water %50 mixtures

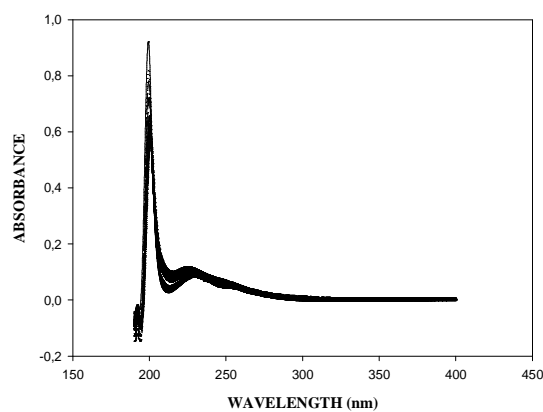


Fig: 6 Plot of experimental absorbance values of 3-ethyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one wavelength as a function of pH in ethanol %50 – water %50 mixtures

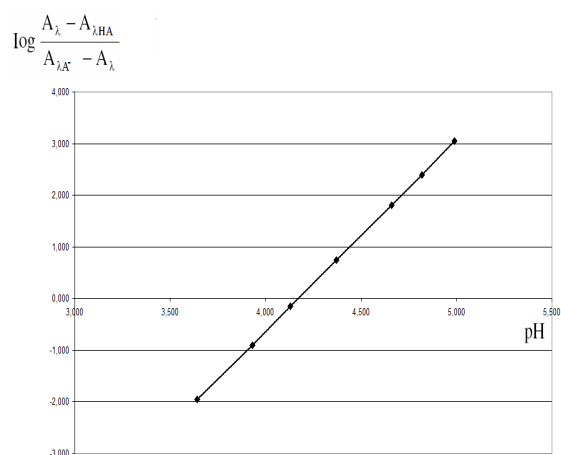


Fig: 7 Plot of calculated $\log \left(\frac{A_{\lambda} - A_{\lambda HA}}{A_{\lambda A} - A_{\lambda}} \right)$ of 3-methyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one as a function of pH in studied ethanol %50 – water %50 mixtures

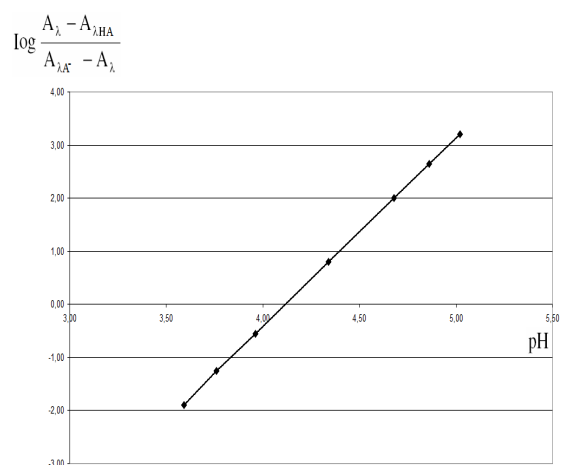


Fig: 8 Plot of calculated $\log \left(\frac{A_{\lambda} - A_{\lambda HA}}{A_{\lambda A} - A_{\lambda}} \right)$ of 3-phenyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one as a function of pH in studied ethanol %50 – water %50 mixtures

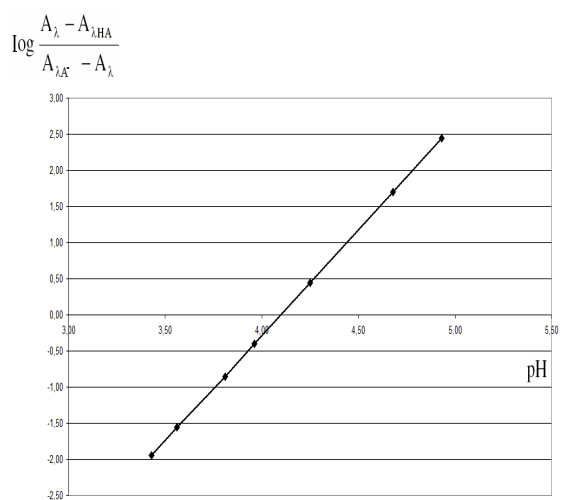


Fig: 9 Plot of calculated $\log\left(\frac{A_\lambda - A_{\lambda HA}}{A_{\lambda A} - A_\lambda}\right)$ of 3-benzyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one as a function of pH in studied ethanol %50 – water %50 mixtures

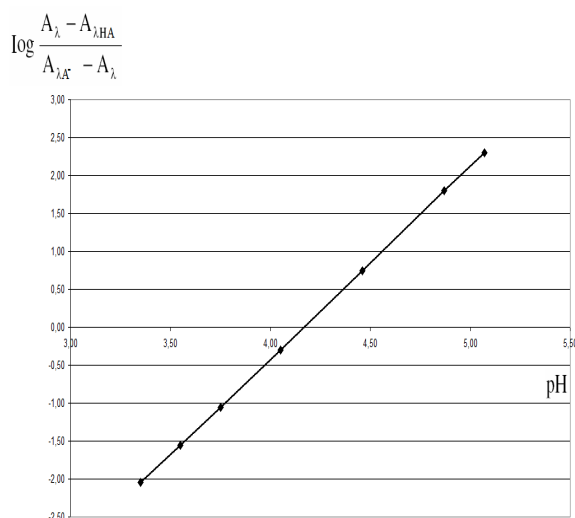


Fig: 10 Plot of calculated $\log\left(\frac{A_\lambda - A_{\lambda HA}}{A_{\lambda A} - A_\lambda}\right)$ of 3-ethyl-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one as a function of pH in studied ethanol %50 – water %50 mixtures

All data were calculated using the linearization method with Henderson-Hasselbach equation. And plot of $\log\left(\frac{A_\lambda - A_{\lambda HA}}{A_{\lambda A} - A_\lambda}\right)$ values of all triazole derivatives as a function of pH in ethanol %50 – water %50 mixtures. Plot of calculated $\log\left(\frac{A_\lambda - A_{\lambda HA}}{A_{\lambda A} - A_\lambda}\right)$ all triazole derivatives as a function of pH in studied media are shown in Fig. 7-10.

All the values presented are the average of at least 5 measurements and the standard deviations of each are listed. The corresponding pK_a values for all compounds, obtained from the spectrophotometric methods using the linearization method with Henderson-Hasselbach equation in ethanol %50 – water %50 mixtures are given in Table 1.

Table 1: Stoichiometric protonation constants of some 3-alkyl(aryl)- 4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives at 25°C in ethanol %50 – water %50 mixtures (μ = 0.1 M NaCl)

Compounds	pK _a
(1) 3-methyl-4-(<i>p</i> -carboxyphenyl)-4,5- dihydro-1 <i>H</i> -1,2,4-triazol-5-one	4.17±0.03
(2) 3-phenyl-4-(<i>p</i> -carboxyphenyl)-4,5-dihydro-1 <i>H</i> -1,2,4-triazol-5-one	4.12±0.02
(3) 3-benzyl-4-(<i>p</i> -carboxyphenyl)-4,5-dihydro-1 <i>H</i> -1,2,4-triazol-5-one	4.10±0.02
(4) 3-ethyl-4-(<i>p</i> -carboxyphenyl)-4,5-dihydro-1 <i>H</i> -1,2,4-triazol-5-one	4.17±0.04

This study is also concerned with the effect of solvent composition on the stoichiometric protonation constants. The literature data indicate that the equilibrium constants are directly related to the solvent composition (35-36). The data we obtained in our study also verify this. It is well known that the acidity of a compound depends on several factors. The two most important factors are the solvent effect and molecular structure. Table 1 shows that the corresponding pK_a values obtained from spectrophotometric titrations depend on the solvents

used and molecular structure of the compounds. As seen in Table 1, the acidic arrangement for compounds 1, 2, 3 and 4 (3-alkyl(aryl)-4-(*p*-carboxyphenyl)-4,5-dihydro-1*H*-1,2,4-triazole-5-one) is: $3 > 2 > 1 = 4$, Compound 3 shows the strongest acidic properties but compound 1 and 4 shows the weakest acidic properties within 3-alkyl(aryl)-4-(*p*-tbutylbenzyliden amino)-4,5-dihydro-1*H*-1, 2,4-triazole-5-one) in ethanol %50 – water %50 mixtures. This situation may be attributed to the hydrogen bonding between the negative ions formed and the solvent molecules in ethanol %50 – water %50 mixtures. As it is well known, the acidity of a compound depends on some factors. The two most important factors are the solvent effect and molecular structure.

CONCLUSION

In this investigation, the determination of dissociation constants of 3-alkyl(aryl)-4-(*p*-tbutylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivatives by spectrophotometric method has been performed. Although spectrophotometric method requires a relatively high pure substance, at least one of the species 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 constant 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.

Acknowledgements

The authors gratefully thank Rize University Scientific Research Project Unit for financial support of this project (project account number : 2008.102.02.3).

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