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Determination of protonation constants of some 3-alkyl(aryl)-4-(*p*-*tert*-butyl(benzyl/benzyliden)amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivatives with spectrophotometric method

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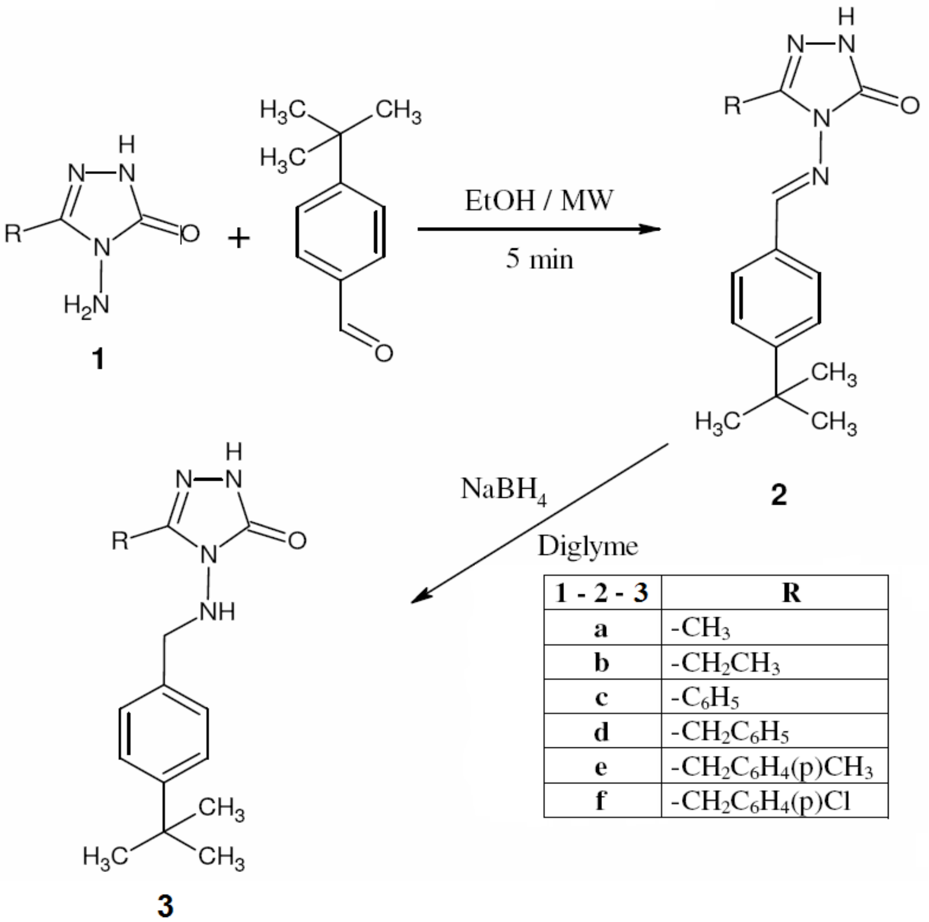
ABSTRACT

The protonation constant values of different twelve 3-alkyl(aryl)-4-(p-t-butyl(benzyl/ benzyliden)amino)-4,5-dihydro-1H-1,2,4-triazole-5-one derivatives have been determined in ethanol %50 – water %50 mixtures by spectrophotometric methods. The electronic absorption spectra of different twelve 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.

Keywords: 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].



1 - 2 - 3	R
a	$-CH_3$
b	$-CH_2CH_3$
c	$-C_6H_5$
d	$-CH_2C_6H_5$
e	$-CH_2C_6H_4(p)CH_3$
f	$-CH_2C_6H_4(p)Cl$

Scheme 1. Synthesis of some 3-alkyl(aryl)-4-(*p*-*t*-butyl(benzyl/benzyliden)amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one derivatives

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 different twelve 3-alkyl(aryl)-4-(p-*t*-butyl(benzyl/ benzyliden)amino)-4,5-dihydro-1H-1,2,4-triazole-5-one derivatives in ethanol %50 - water %50 mixtures using spectrophotometric measurements in determined. It is observed that the obtained results are in good accordance with potentiometric values. These twelve 3-alkyl(aryl)-4-(p-*t*-butyl (benzyl/ benzyliden)amino)-4,5- dihydro-1*H*-1,2,4-triazole-5-one derivatives were synthesized according to the reported reference [32]. And stoichiometric protonation constants of these triazole derivatives were determined potentiometrically in 50% (v/v) ethanol-water mixtures [33].

EXPERIMENTAL SECTION

In this study, twelve different 3-alkyl(aryl)-4-(*p-t*-butyl(benzyl/benzyliden)amino)-4,5- dihydro-1*H*-1,2,4-triazole-5-one derivatives [(2a) 3-methyl-4-(*p-t*-butylbenzylidenamino)-4,5 -dihydro-1*H*-1,2,4-triazole-5-one, (2b) 3-ethyl-4-(*p-t*-butylbenzyliden amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (2c) 3-phenyl-4-(*p-t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (2d) 3-benzyl-4-(*p-t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (2e) 3-(*p*-methyl benzyl)-4-(*p-t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (2f) 3-(*p*-chlorobenzyl)-4-(*p-t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3a) 3-methyl-4-(*p-t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3b) 3-ethyl-4-(*p-t*-butylbenzyl amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3c) 3-phenyl-4-(*p-t*-butylbenzylamino) -4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3d) 3-benzyl-4-(*p-t*-butylbenzyl amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3e) 3-(*p*-methylbenzyl)-4-(*p-t*-butylbenzyl amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one, (3f) 3-(*p*-chlorobenzyl)-4-(*p-t*-butylbenzyl amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one] have been determined in ethanol %50 – water %50 mixtures by spectrophotometric methods. These triazole derivatives studied are shown in Scheme 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 [34-35].

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 pKa values of the different triazole derivatives were determined by means of the data obtained from spectrophotometric titrations in ethanol %50 – water %50 mixtures at $25^{o}C\pm0.1$ 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 ($log\left(A_{\lambda} - A_{\lambda HA}/A^{-} - A_{\lambda}\right) = pH - pK_{a}$).

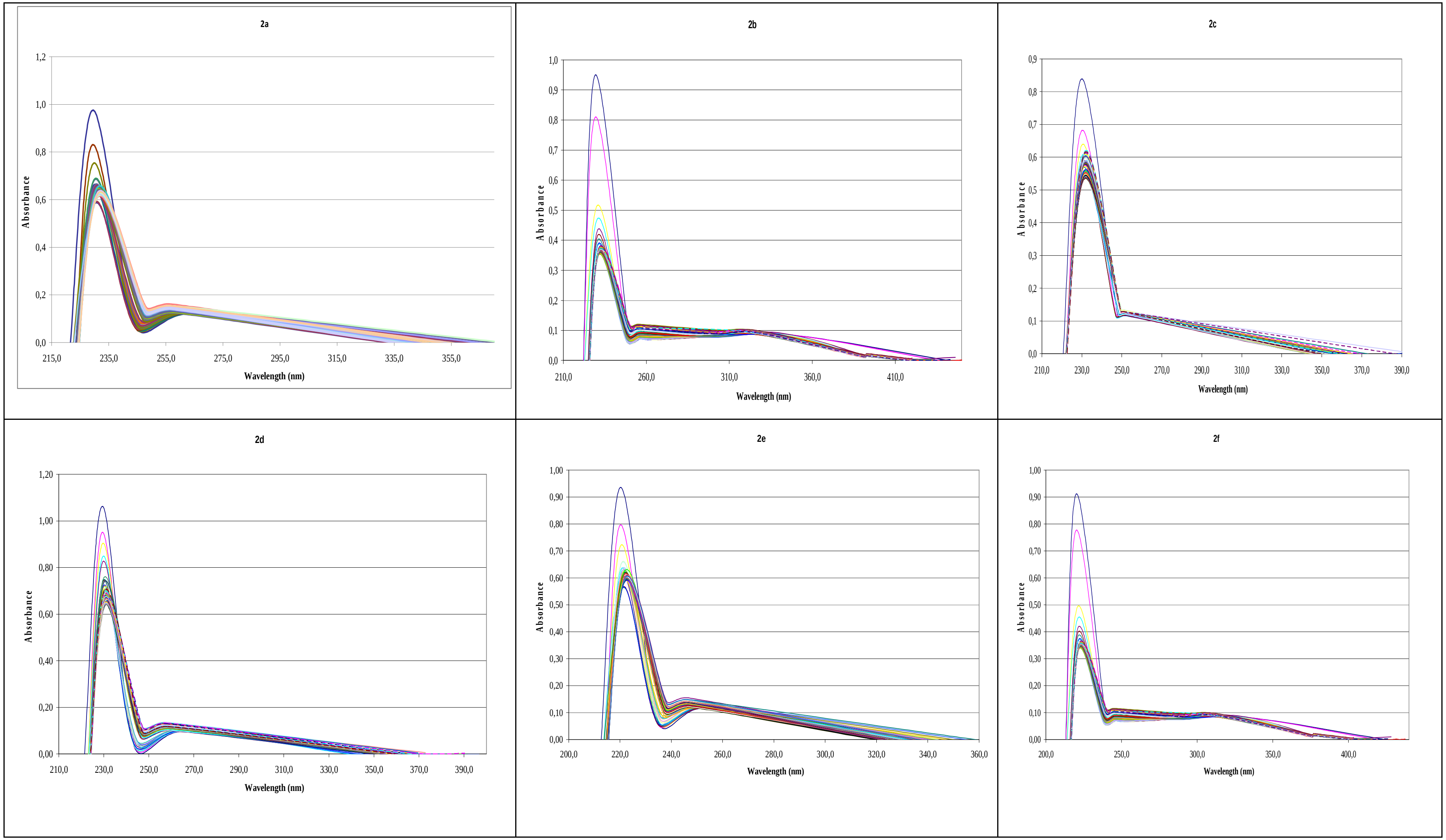


Figure 1. Plot of experimental absorbance values of 3-alkyl(aryl)-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one (2a-2f) wavelength as a function of pH in ethanol %50 – water %50 mixtures.

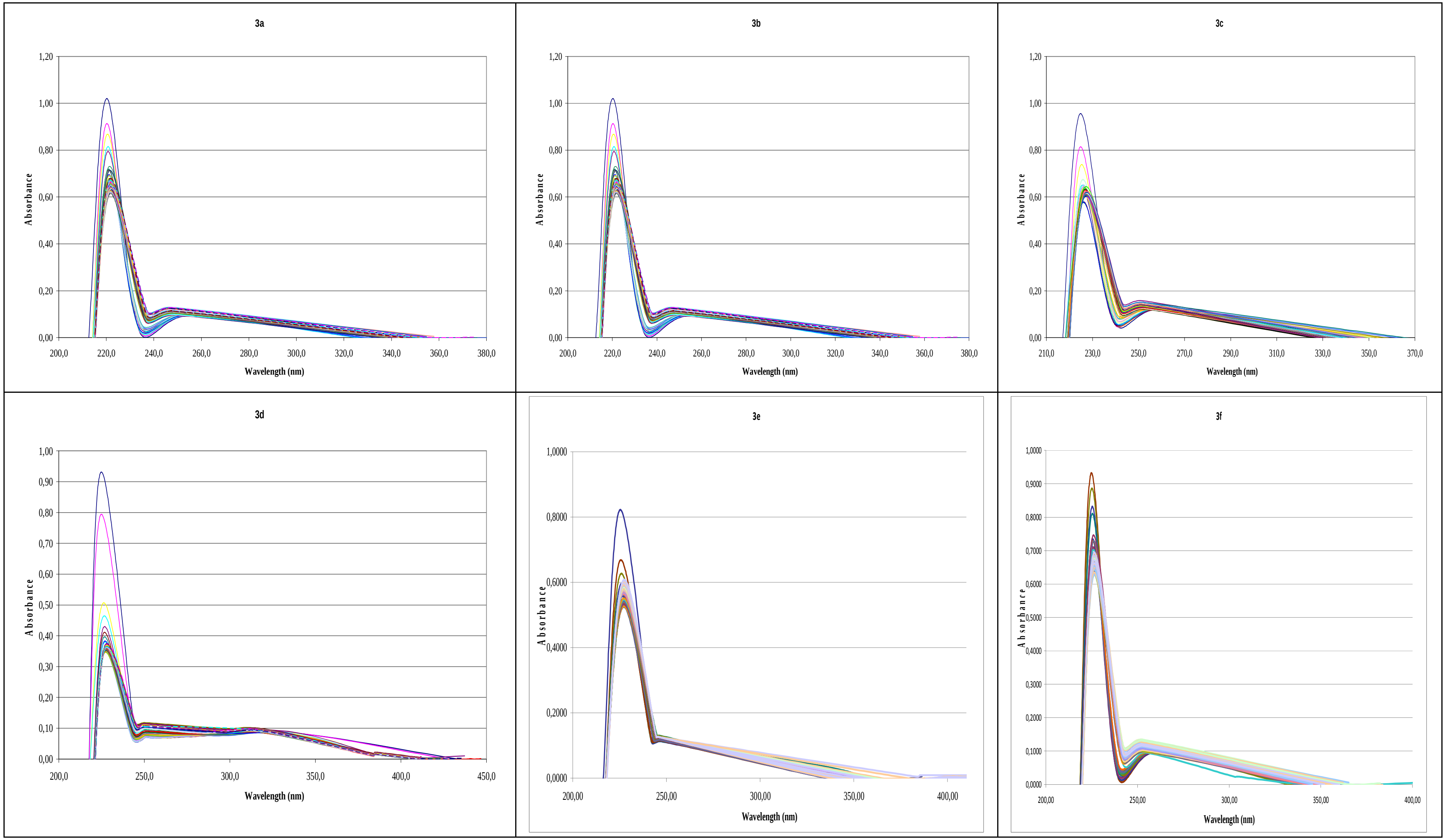


Figure 2. Plot of experimental absorbance values of 3-alkyl(aryl)-4-(*p*-*t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one (3a-3f) wavelength as a function of pH in ethanol %50 – water %50 mixtures.

RESULTS AND DISCUSSION

The absorption spectra of twelve 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 Figure 1-2. All data were calculated using the linearization method with Henderson-Hasselbach equation. And plot of $log = A - A_{HA} / A^{-} - A$ values of all triazole derivatives as a function of pH in ethanol %50 – water %50 mixtures. Plot of calculated $log = A - A_{HA} / A^{-} - A$ all triazole derivatives as a function of pH in studied media are shown in Figure 3-4. All the values presented are the average of at least 5 measurements and the standard deviations of each are listed. The corresponding pKa 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.

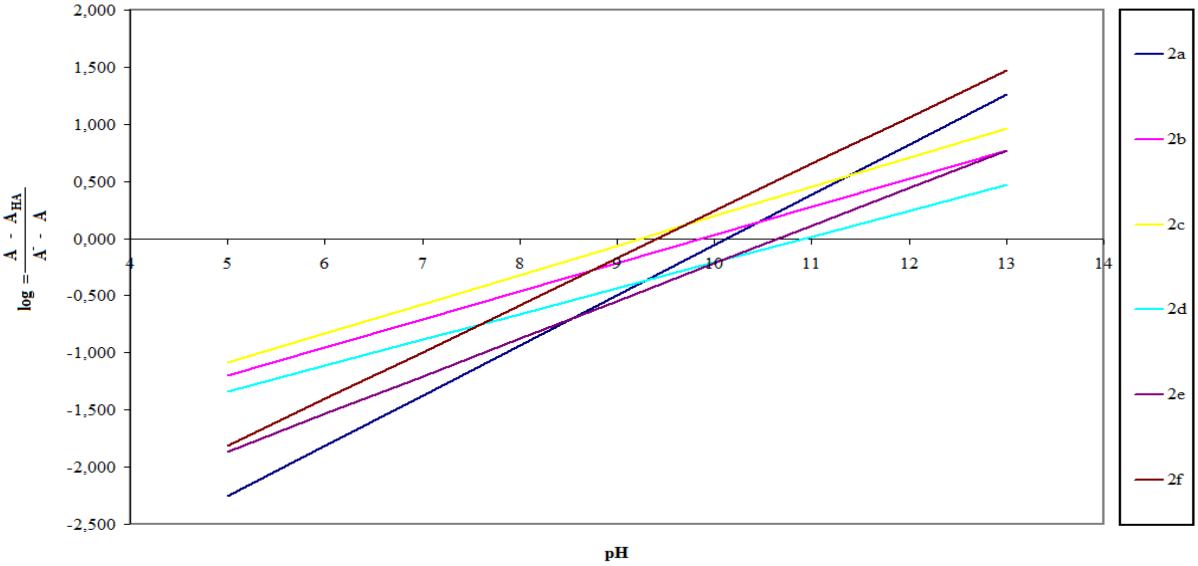


Figure 3. Plot of calculated $log = A - A_{HA} / A^{-} - A$ of 3-alkyl(aryl)-4-(*p*-*t*-butylbenzyliden amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one (2a-2f) as a function of pH in studied ethanol %50 – water %50 mixtures.

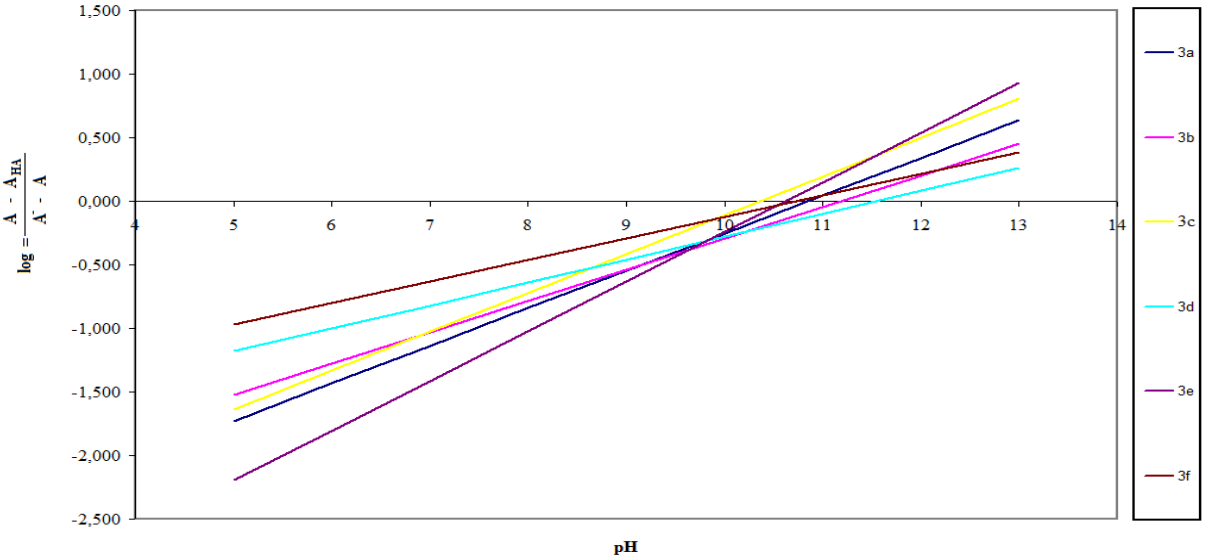


Figure 4. Plot of calculated $log = A - A_{HA} / A^{-} - A$ of 3-alkyl(aryl)-4-(*p*-*t*-butylbenzyl amino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one (3a-3f) as a function of pH in studied ethanol %50 – water %50 mixtures.

Table 1. Stoichiometric protonation constants of 3-alkyl(aryl)-4-(*p*-*t*-butyl(benzyl/benzyliden)amino)-4,5-dihydro-1H-1,2,4-triazole-5-one derivatives at 25^{o}C in ethanol %50 – water %50 mixtures (μ = 0.1 M NaCl).

Compound No	Compound name	pKa*	pKa**
2a	3-methyl-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.131±0.024	9.001 ± 0.018
2b	3-ethyl-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	9.874±0.017	8.180 ± 0.024
2c	3-phenyl-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	9.243±0.015	8.737 ± 0.013
2d	3-benzyl-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.936±0.013	10.132 ± 0.009
2e	3-(*p*-methylbenzyl)-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.662±0.016	9.259 ± 0.015
2f	3-(*p*-chlorobenzyl)-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	9.425±0.014	8.608 ± 0.022
3a	3-methyl-4-(*p*-*t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.853±0.013	9.993 ± 0.011
3b	3-ethyl-4-(*p*-*t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	11.174±0.015	10.297 ± 0.021
3c	3-phenyl-4-(*p*-*t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.361±0.018	9.421 ± 0.016
3d	3-benzyl-4-(*p*-*t*-butyl benzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	11.547±0.016	10.582 ± 0.022
3e	3-(*p*-methylbenzyl)-4-(*p*-*t*-butyl benzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.623±0.014	9.861 ± 0.020
3f	3-(*p*-chlorobenzyl)-4-(*p*-*t*-butyl benzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one	10.738±0.015	9.921 ± 0.014

** All compounds pKa were determined by spectrophotometric methods, ** All compounds pKa were determined by potentiometric methods and these values taken reference 33.*

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 [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 pKa values obtained from spectrophotometric titrations depend on the solvents used and molecular structure of the compounds. As seen in Table 3, the acidic arrangement for compounds 2a, 2b, 2c, 2d, 2e and 2f (3-alkyl(aryl)-4-(*p*-*t*-butylbenzylidenamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one) is : 2c > 2f > 2b > 2a > 2e > 2d. Compound 2c shows the strongest acidic properties but compound 2d shows the weakest acidic properties in this series. The acidic arrangement for compounds 3a, 3b, 3c, 3d, 3e and 3f (3-alkyl(aryl)-4-(*p*-*t*-butylbenzylamino)-4,5-dihydro-1*H*-1,2,4-triazole-5-one) is : 3c > 3e > 3f > 3a > 3b > 3d. Compound 3c shows the strongest acidic properties but compound 3d shows the weakest acidic properties in this series. Acidic arrangement for all compounds is 2c > 2f > 2b > 2a > 3c > 3e > 2e > 3f > 3a > 2d > 3b > 3d. Compound 2c shows the strongest acidic properties but compound 3d shows the weakest acidic properties in all compounds. 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*-*t*-butyl(benzyl/benzyliden)amino)-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.

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