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Solvent and molecular structure effects on acidity strength in non-aqueous medium

Şule Bahçeci[1], Zafer Ocak[2*], Nuri Yıldırım[3], Haydar Yüksek[4]

[1]Trabzon University, Fatih Education Faculty, Secondary Education Science and Mathematics Education, 61080, Trabzon, Turkey
[2]Kafkas University, Education Faculty, Mathematics and Science Education,36100 Kars, Turkey
[3]Karadeniz Technical University, Faculty of Science, Department of Chemistry, 61080, Trabzon, Turkey
[4]Kafkas University, Faculty of Science & Letters, Department of Chemistry, 36100 Kars, Turkey

Abstract

The acidic properties of ten 3-alkyl(aryl)-4-[3-hydroxy-4-methoxy benzylidenamino]-4,5-dihydro-1H-1,2,4-triazol-5-one derivatives were investigated. Amphiprotic solvents used in this study were isopropyl alcohol and *tert*-butanol. Acetone and N,N- dimethylformamide (DMF) were preferred as a dipolar aprotic solvent. Compounds were titrated with tetrabutylammonium hydroxide (TBAH) in isopropyl alcohol and titrimetric analyses were used potentiometric method determining the end-points, half-neutralization method determining acidity. Typical S-shaped titration graphs excepted were determined. The acidity strengths of 4,5-dihydro-1H-1,2,4-triazol-5-one derivatives in amphiprotic and dipolar aprotic solvents were calculated using tables and graphs. The pK_a values obtained in the solvents were found to be differentiated. The effects of solvent, molecular structure, autoprotolysis constant dielectric constant, and leveling-differentiation effects of the solvents upon acidity strength of the compounds were discussed.

Keywords: Triazole, amphiprotic solvent, pK_a, potentiometry

1. Introduction

Potentiometry, one of the electrochemical methods, is widely used due to its wide advantages. Potentiometric techniques have long been used in landmark determination. It is simple and inexpensive in potentiometric methods [1]. Potentiometric titrations are one of the most widely used methods for determining acidity constants due to their simple and low cost. In the course of time, many different methods such as spectrometry, conductimetry, electrophoresis, NMR, polarimetry, calorimetry, theoretical, etc. were developed [2]. However, the potentiometric method does not include the restrictions specified in the determination of the equivalent point, so it is the most widely used method among these methods due to its simplicity, accuracy, and precision [3].

Thousands of potentiometric sensors have been successfully developed and applied in many fields such as medicine, environmental monitoring, agriculture, industry and pharmaceutical sciences [4,5].

Among the electrochemical methods of the best techniques for antioxidant activity (AOA) assessment, potentiometry is where the potential shift of the platinum electrode, which is readily applicable and the source of information about AOA, is placed in a mediator system. Their advantages such as usability, speed, and easy measurement offer a direct evaluation of the electron-donor-acceptor properties of the system, ie the properties that determine the antioxidant status [6-8].

Using the dissociation constant, some thermodynamic parameters can be measured, such as enthalpy change (H°), Gibb's energy change (ΔG°), and entropy change (ΔS°). Enthalpy change of the decomposition process (ΔH°) Van't Hoff relation ($d\ln K / dT = \Delta H° / RT^2$) Gibb's free energy (ΔG°) is calculated using the equation $\Delta G° = 2.303RTpK$. Using these calculated values of ΔH° and ΔG°, the entropy change (ΔS°) is determined by the equation $\Delta S° = (\Delta H° - \Delta G°) / T$ [9].

In this article, some 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylideneamino)-4,5-dihydro-1H-1,2,4-triazol-5-one derivates known to have biological

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***Author of correspondence:** zafcak@gmail.com
Tel: +90 (474) 225 12 62
Fax +90 (474) 225 12 64

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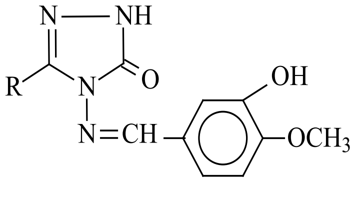
activities and acidic properties were used. The dissociation constants of the compounds were determined by the potentiometric titration method. [10-15]. Acidic properties in solvents were investigated with respect to solvent effect, structure effect, dielectric constant, and autoprotolysis constants. The study will contribute to the literature in the field of acid-bases and buffer solutions.

2. Materials and Methods

2.1. Reagents

Ten 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzyliden-amino)-4,5-dihydro-1H-1,2,4-triazol-5-ones which acidity strengths have been determined are shown in Fig. 1. Compounds 1 has been synthesized according to the literature [16].



1

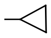
R	1
a	CH_3
b	CH_2CH_3
c	$CH_2CH_2CH_3$
d	$CH_2C_6H_5$
e	$CH_2C_6H_4CH_3(p\text{-})$
f	$CH_2C_6H_4OCH_3$ (p-)
g	$CH_2C_6H_4Cl(p\text{-})$
h	$CH_2C_6H_4Cl(m\text{-})$
i	C_6H_5
j	

Figure 1. 3-Alkyl(Aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one compounds

2.2. Solvents

Isopropyl alcohol as an amphiprotic solvent for the determination of acidity constants of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones, *tert*-butanol, DMF from dipolar aprotic solvents, and acetone were used. The wide potential range of solvents, the solubility of TBAH and 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino) -4,5-dihydro-1H-1,2,4-triazol-5-ones in the solvents, and the working possibility under room conditions were important factors in the selection of solvents. A solution of 0.05 N of TBAH in isopropyl alcohol was preferred as a titrant. Isopropyl alcohol, acetone DMF, and *tert*-butanol were purchased from Merck.

2.3. Titrant

As a titrant, TBAH has been a widely used base against acids. The standard 0.05 N concentration of TBAH in isopropyl alcohol was preferred.

2.4. Apparatus

In the study, measurements were made with a Jenway 3040-model ion analyzer. The sensitivity of the pH meter used in pH readings is ± 0.002, while the sensitivity in mV measurement is ± 0.1, and the precision is ± 0.2. A combined pH electrode was used in the studies. A 50 μL micropipette was used for titrant addition.

2.5. Solutions

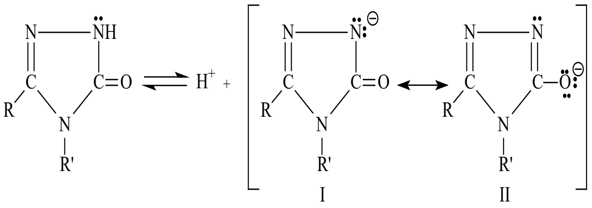
10^{-3} M solutions of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol -5-ones in acetone, *tert*-butanol, isopropyl alcohol, DMF has also been prepared. A 0.05 N solution of TBAH in isopropyl alcohol was prepared as a titrant.

2.6. Methods

Two buffer solutions of pH = 7,0 and pH = 10,0 were used for calibration of the pH meter used. Potentiometric titrations were carried out at 25,0 °C. 3-Alkyl(Aryl)-4-(3-hydroxy-4-methoxy benzyliden amino) -4,5-dihydro-1H-1,2,4-triazol-5-ones in amphiprotic and dipolar aprotic solvents 10^{-3} M 17,0 mL of its solution was taken. The acid solution was made homogeneous by mixing with a magnetic stirrer. With a micropipette, 0.05 mL of titrant each time was added to the stirring acid solution. 10^{-3} M of acid derivatives of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one in amphiprotic and dipolar aprotic solvents. Its solution was titrated with 0.05 N TBAH and the results are expressed as a graph of mV-mL TBAH.

2.7. Determination of acidity constants with Half-neutralization method

Titration graphs of mL TBAH-pH and mL TBAH-mV were drawn with the help of titration data. To determine the equivalent points, the graphs of TBAH - $\Delta E / \Delta V$ (first derivative) and mL TBAH - $\Delta^2E / \Delta V^2$ (second derivative) were used (Fig. 2). From these values, half-neutralization points were calculated [17-21].



(1)

3. Result and Discussion

When the N-H hydrogen in the 4,5-dihydro-1H-1,2,4-triazol-5-one ring is protonated, the equilibrium shifts to the right because the remaining electron pair is delocalized to include oxygen and is easy to accommodate.; hence the acidity increases (Equation 1). This is evidence that the N-H proton in the 4,5-dihydro-1H-1,2,4-triazol-5-one ring system shows acidic properties.

10^{-3} M of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones amphiprotic (isopropyl alcohol, *tert*-butyl alcohol) and dipolar aprotic, (DMF, acetone) as a titrant in solvent mediums, plotted from the data obtained by titration of 0.05 N TBAH solution in isopropyl alcohol, graphs as mV -mL (TBAH) are given in Fig. 3.

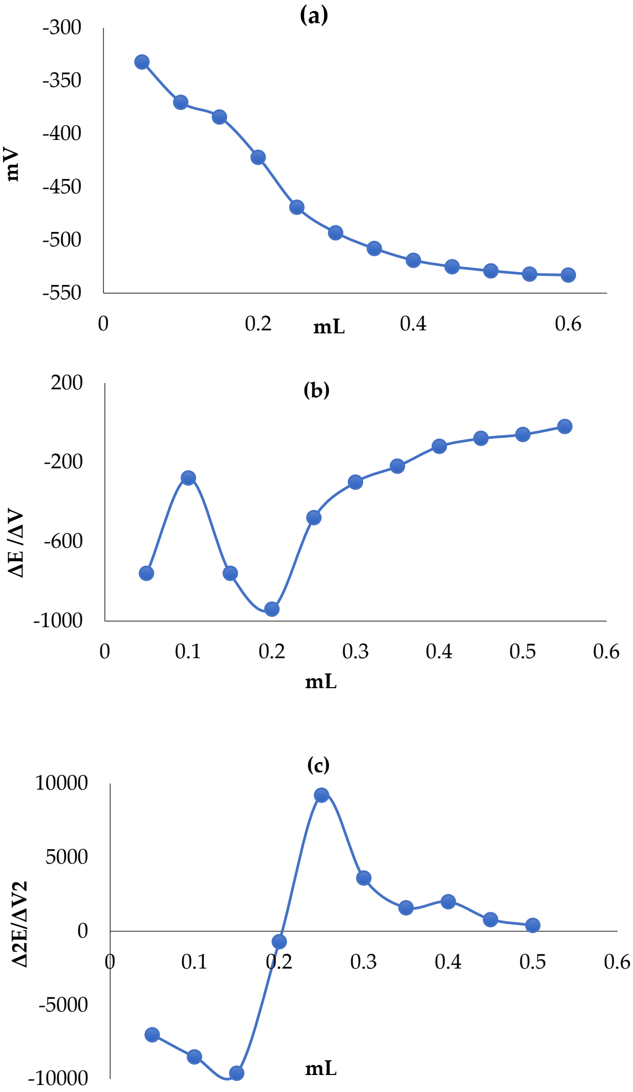


Figure 2. Compound **1b**: **a.** mL-mV curve **b.** ΔE/ΔV curve **c.** $\Delta^2E/\Delta V^2$ curve

Table 1. Acidity strengths of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones in amphiprotic and dipolar aprotic solvents

Compound	Isopropyl alcohol		*tert*-butyl alcohol		Acetone		DMF	
	pK_a	Hnp	pK_a	Hnp	pK_a	Hnp	pK_a	Hnp
1a	15,09	-388	-	-	12,72	-274	15,20	-337
1b	10,23	-168	-	-568	12,72	-248	15,60	-370
1c	14,73	-346	12,77	-290	-	-	15,24	-341
1d	14,43	-317	-	-	16,49	-381	14,47	-307
1e	14,55	-391	-	-	15,38	-361	17,20	-415
1f	15,58	-351	14,20	-290	12,49	-225	14,12	-297
1g	16,02	-370	13,05	-295	15,40	-364	14,56	-313
1h	11,56	-226	-	-	15,85	-372	15,51	-355
1i	13,63	-271	-	-	16,75	-363	18,24	-460
1j	14,98	-331	14,23	-357	12,90	-249	16,50	-390

Half-neutralization potentials were calculated from the graphs obtained and plotted in the excel program. Calculated Hnp and pK_a values are given in Table 1.

3-Alkyl(Aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones determined by potentiometric titration in amphiprotic and dipolar aprotic solvents. Acidity strength (Fig. 4), functional groups, autoprotolysis constant, dielectric constant, and the leveling-differentiation effect was investigated.

Classification of acidity strength in different solvents can be made by the dielectric constant. It was stated that the theoretical increase in pK_a values in four solvents should be *tert*-butyl alcohol < isopropyl alcohol < acetone < DMF. Experimental results suitable for the theoretical sequence were obtained for compounds **1a**, **1b**, **1d**, **1e**, **1h**, and **1i** in amphiprotic solvents. Since typical S-shaped curves for other compounds could not be obtained, acidity constants could not be determined in the *tert*-butanol solvent.

Theoretically, it has been stated that the pK_a values of the compounds in the DMF medium from dipolar aprotic solvents are higher than that of acetone. The experimental results showed a result contrary to the theoretical order of compounds **1d**, **1g**, and **1h**. Typical S-shaped curves could not be obtained for compound **1** in acetone medium, so they could not be compared. For other compounds, theoretical order and experimental results were in agreement. This situation, which is similar to other studies, can be explained as follows.

Solvents such as acetone and N, N-dimethylformamide form lyonium ions but not lyate ions. HX is acid (molecular), S is a solvent and DMF (protophilic solvent) formed the following equilibrium.

$$HX + S \underset{1}{\leftrightarrow} S \cdots\cdots HX \underset{2}{\leftrightarrow} SH^{+}X^{-} \underset{3}{\leftrightarrow} SH^{+} + X^{-} \qquad (2)$$

When protophilic solvents are used for the equilibrium given in Equation 1, the equilibrium number (1) and (2) mostly shifts to the direction in which it is written, while the equilibrium number (3) shifts slightly to the right. In equilibrium number (3), the strongest acid in the free environment is SH^+. This strain reacts directly with the titrant. However, in the case of protophobic solvent such as acetone, the equilibrium shifts slightly to the right in Equation 2. Equilibrium (3) shifts slightly to the right. In this case, SH^+ in protophobic solvent is a much stronger acid.

Considering the autoprotolysis constant, it was seen that the Hnp values of the compounds and the potential ranges of the solvents in *tert*-butyl alcohol, isopropyl alcohol, DMF, and acetone medium are weakly acidic when compared with the data in Table 2.

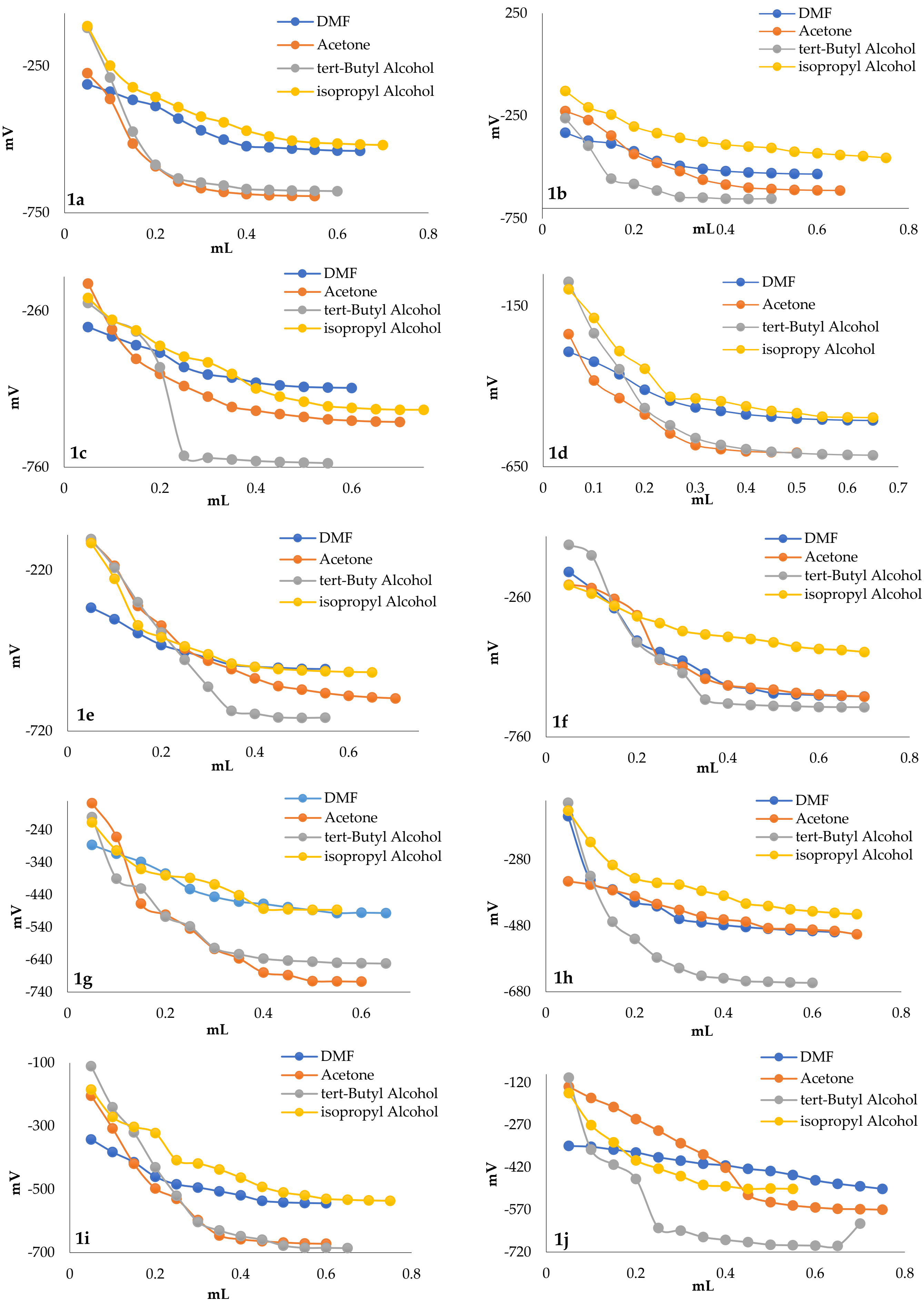


Figure 3. Potentiometric titration graphs of compounds **1a-j** with TBAH in isopropyl alcohol

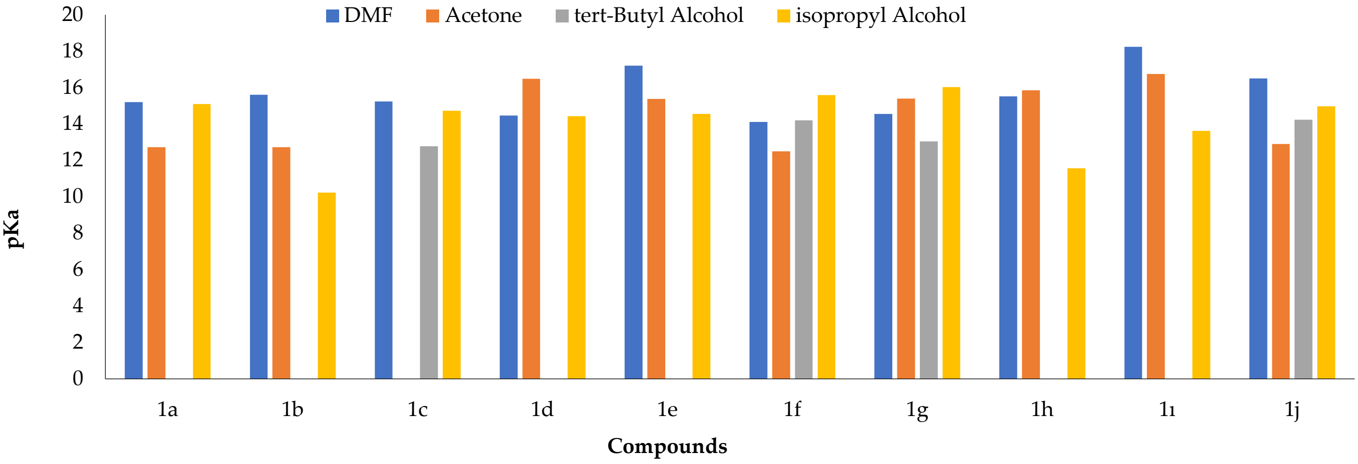


Figure 4. pK_a-compounds plot for compound **1**

Table 2. Potential ranges of solvents and measured Hnp values of 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones

Solvents	**Potential Range (mV)**^{a}		**Potential Range (mV)**^{a}		**Potential Range (mV)**^{b}	**Measured Compounds of the Type 1 Hnp Range**	
***tert*-butyl alcohol**	-	-	-	-	1200	-290	-568
Isopropyl alcohol	-750	+400	-720	+407	1000	-168	-391
Acetone	-970	+660	-965	+598	1550	-225	-381
DMF	-1000	+270	-900	+237	1300	-297	-460

4. Conclusion

Research results; 3-alkyl(aryl)-4-(3-hydroxy-4-methoxybenzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones have proven to be weakly acidic in anhydrous media solvents. When the acidity strength is listed according to the dielectric constant and acidity constant, it has been determined that 1d, 1g, and 1h in DMF and acetone environments are not suitable for the theoretical order [24,25], but suitable for other environments. Compounds **1a** and **1b** were leveled in acetone medium. It has been differentiated in other solvents. However, the molecular effect was examined and it was concluded that there was no significant difference due to the distance of the functional groups to the acidic proton and the solvent effect.

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References

[1] D.A. Skoog, D.M. West, F.J. Holler, S.R. Crouch, Analitik Kimya Temel İlkeler, Translators: E. Kılıç, H. Yılmaz, 2007, Turkey, Bilim Yayıncılık.

[2] J. Reijenga, A. Hoof, A. Loon, B. Teunissen, Development of methods for the determination of pK_a values, Anal Chem Insights, 8, 2013, 53-71.

[3] S. Zafar, S. Akhtar, T. Tariq, N. Mushtag, A. Akram, A. Ahmed, M. Arif, S. Naeem, S. Anwar, Determination of pK_a values of new phenacyl-piperidine derivatives by potentiometric titration method in aqueous medium at room temperature (25 ± 0.5 °C), Pak J Pharm Sci, 27(4), 2014, 925-929.

[4] S. Sharif Manesh, M. Masrournia, Carbon nitride nanoparticles modifed carbon paste electrodes as potentiometric sensors for determination of nickel(II) and chromium(III) ions in tap water samples, J Iran Chem Soc, 18, 2021,1219-1229.

[5] Ö. Işıldak, O. Özbek, Application of potentiometric sensors in real samples, Crit Rev Anal Chem, 2020, doi:10.1080/10408347.2019.1711013.

[6] K. Braininaa, N. Stozhko, M. Bukharinova, E, Khamzina, M. Vidrevich, Potentiometric method of plant microsuspensions antioxidant activity determination, Food Chem, 278, 2019, 653-658.

[7] Kh.Z. Brainina, E.L. Gerasimova, D.P. Varzakova, S.L. Balezin, I.G. Portnov, V.A. Makutina, E.V. Tyrchaninov, Potentiometric method for evaluating the oxidant/ antioxidant activity of seminal and follicular fluids and clinical significance of this parameter for human reproductive function, Open Chem Biomed Methods J, 5, 2012, 1-7.

[8] Kh.Z. Brainina, A.V. Ivanova, E.N. Sharafutdinova, E.L. Lozovskaya, E.I. Shkarina, Potentiometry as a method of antioxidant activity investigation, Talanta, 71, 2007, 13-18.

[9] K.D. Bhesaniya, S. Baluja, Potentiometric determination of dissociation constant and thermodynamic parameters of dissociation process of some newly synthesized pyrimidine derivatives in MeOH/DMF-water medium at different temperatures, J Mol Liq, 190, 2014, 190-195.

[10] Z. Farkas, M. Posa, V. Tepavcevic, Determination of pK_a values of oxocholanoic acids by potentiometric titration, J Surfactants Deterg, 17, 2014, 609-614.

[11] V.R. Almeida, B. Szpoganicza, S. Bonnevilleb, Potentiometric titration and out-of-equilibrium pH response of the biotite-water system, J Brazil Chem Soc, 26(9), 2015, 1848-1860.

[12] A.S. Katea, K.C. Basavaraju, A simple potentiometric titration method for estimation of maleic anhydride in high molecular weight styrene-maleic anhydride copolymer, Polym Test, 65, 2018, 369-373.

[13] M. Lakubowska, B. Bas, E. Niewiara, W. Reczynski, W.W. Kubiak, Potentiometric titration of industrial samples-end-point detection by means of wavelets, AIP Conference Proceedings, 1148, 2009, 613-616.

[14] T. Lisa, D. Chansyanah, S. Marina, K. Nina, S. Andrian, Using potentiometric acid-base titration to determine pK_a from

Mangosteen Pericarps Extract, Perіód Tchê Quím, 16, 2019, 768-773.

[15] N. Demirbaş, R. Uğurluoğlu, A. Demirbaş, Synthesis of 3-Alkyl(Aryl)-4-Alkylidenamino-4,5-dihydro-1H-1,2,4-Triazol-5-Ones as Antitumor Agents, Bioorgan Med Chem, 10, 2002, 3717-3723.

[16] Ş. Bahçeci, N. Yıldırım, Ö. Gürsoy-Kol, S. Manap, M. Beytur, H. Yuksek, Synthesis, characterization and antioxidant properties of new 3-alkyl(aryl)-4-(3-hydroxy-4-methoxy-benzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones, Rasayan J Chem, 9, 2016, 494-501.

[17] E. Kılıc¸ O. Atakol, E. Canel, Z. Alibeşeoğlu, T. Gunduz, F. Köseoğlu, Potentiometric investigation of the effects of several substituents on the basicity of benzilidene-o-hydroxyaniline, Turk J Chem, 22, 1998, 387-391.

[18] H. Yüksek, E. Koca, Ö. Gürsoy-Kol, O, Akyıldırım, M. Çelebier, Synthesis, in vitro antioxidant activity, and physicochemical properties of novel 4,5-dihydro-1H-1,2,4-triazol-5-one derivatives, J Mol Liq, 206, 2015, 359-366.

[19] M. Kurtoğlu, N. Birbiçer, Ü. Kimyonsen, S. Serin, Determination of pK_a values of some azo dyes in acetonitrile with perchloric acid, Dyes Pigments, 41, 1999, 143-147.

[20] N. Gündüz, T. Gündüz, M. Havyalı, Titrations in non-aqueous media: Potentiometric investigation of symmetrical and unsymetrical tetra-aryl porphyrins with 4- nitrophenyl and 4-aminophenyl substituents in nitrobenzene solvent, Talanta, 48, 1999, 71-79.

[21] Z. Ocak, Amfiprotik ve dipolar aprotik çözücülerde 3-(4-Aril) propiyonik asit türevlerinin asitlik kuvvetleri, Iğdır Üniversitesi Fen Bilimleri Enstitüsü Dergisi, 10(3), 2020, 1876-1885.

[22] O. Hakli, K. Ertekin, M.S. Ozer, S. Aycan, Determination of pK_a values of clinically important perfluorochemicals in nonaqueous media, J Anal Chem, 63(11), 2008, 1051-1056.

[23] R.H. Loeppert, L.W. Zelazny, B.G. Volk, Titration of pH-dependent sites of kaolinite in water and selected nonaqueous solvents, Clay Clay Miner, 27 (1), 1979, 57-62.

[24] H. Yüksek, M. Küçük, M. Alkan, Ş. Bahçeci, S. Kolaylı, Z. Ocak, U. Ocak, E. Şahinbaş, M. Ocak, Synthesis and antioxidant activities of some new 4-(4-hydroxy-benzylidenamino)-4,5-dihydro-1H-1,2,4-triazol-5-one derivatives with their acidic properties, Asian J Chem, 18(1), 2006, 539-550.

[25] A. Arslantaş, H. Yüksek, Ö. Gürsoy Kol, Z. Ocak, Z. Tomruk, M. Calapoğlu, Study of antioxidant properties and DNA interaction of some novel 4,5-dihydro-1*H*-1,2,4-triazol-5-one derivates, Asian J Chem, 24(8), 2012, 3327-3334.