Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2009, 1(2): 153-161
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Determination of the protonation constants of some chalcones [(2*E*)-1-(substituted-methylthiophene-2-yl)-3-(substituted-pyridinyl)prop-2-en-1-ones] by the potentiometric method in nonaqueous solvents

Fatih İslamoğlu[1]*, Asu Usta[1], İsmail Aksu[1] and Nurettin Yaylı[2]

*[1]*Department of Chemistry, Rize University, Rize 53100, Turkey.*
[2]Department of Chemistry, Karadeniz Technical University, 61080 Trabzon, Turkey

Abstract

Some Chalcones [(2*E*)-1-(Substituted-Methylthiophene-2-yl)-3-(pyridin-substituted-yl)prop-2-en-1-ones] derivatives were titrated with tetrabutylammonium hydroxide (TBAH) in four non-aqueous solvents (isopropyl alcohol, *tert*-butyl alcohol, *N,N* - dimethylformamide and acetonitrile), using potentiometric method. The half neutralization potential values and the corresponding pKa values were determined for all cases.

Keywords: Tetrabutylammonium hydroxide, potentiometric method, half-neutralization potential.

Introduction

Chalcone is an aromatic ketone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones. They show antibacterial, antifungal, antitumor and anti-inflammatory properties. Some chalcones demonstrated the ability to block voltage-dependent potassium channels [1]. They are also intermediates in the biosynthesis of flavonoids, which are substances widespread in plants and with an array of biological activities. Chalcones are also intermediates in the Auwers synthesis of flavones. Methyl hydroxychalcone (MCHP), found in cinnamon, was thought to be an insulin mimetic, improving insulin response of diabetics [2]. It has since been determined that a flavonoid is responsible for the insulin-like biological activity [3].

Chalcones derivatives of 1,3-diphenylprop-2-enone, are natural products known to act as precursors of flavonoids [4] and cyclobutane-containing dimeric products [5-6]. Azachalcones contain an annular Natom in the phenyl ring, giving rise to a pyridyl moiety. In the past years, the syntheses of azachalcones [7-13] and their N-alkyl-substituted derivatives [7-11] have been studied, as well as their photochemistry [9-10, 14]. Further, the preparation of furan and thiophene analogues of azachalcones have been described [15-21], and some of them have been found to possess a wide variety of biological activities, including antituberculosis, antimicrobial, antioxidant, anti-inflammatory, and antibacterial properties [7-12]. There have been a number of systematic studies of the basicity and acididity in different media using different techniques [22-34], but unfortunately very few have dealt with chalcones derivatives. It is well known that two major factors influence the acidity of a molecule [35-38], namely, structural and solvent effects. In most molecules there are two or more structural effects and it is usually very difficult to assess how much each effect contributes to the acidity of a molecule. Moreover, it is sometimes extremely difficult to differentiate between structural and solvent effects.

In this paper, we tried to investigate structural and solvent effects of several substituents on the basicity or acidity. The chalcones derivatives was titrated potentiometrically as acids with tetrabutyl ammonium hydroxide (TBAH) in four non-aqueous solvents (isopropyl alcohol, *tert*-butyl alcohol, *N*,*N*-dimethylformamide and acetonitrile).

Results and Discussion

There have been studies about the potentiometric titrations of different 6 chalcones derivatives with tetrabutyl ammonium hydroxide in the non-aqueous solvents such as isopropyl alcohol, methyl alcohol, *t*-butyl alcohol and acetone and the pKa values were found between 13.76 – 16.21. In this study, six chalcones derivatives were titrated potentiometrically with tetrabutylammonium hydroxide in non-aqueous solvents such as isopropyl alcohol (ε = 19.4), *t*-butyl alcohol (ε = 12), N,N-dimethylformamide (ε = 36.7) and acetonitrile (ε = 36).

The half-neutralization potential (HNP) values and the corresponding pK_a values of all compounds, obtained from the potentiometric titrations with 0.05 M TBAH in isopropyl alcohol, *tert*-butyl alcohol, acetonitrile and *N*,*N*-dimethylformamide, are presented in Table 1. When the dielectric permittivity of solvents is taken into consideration, the acidic arrangement can be expected as follows: *N*,*N*-dimethylformamide (ε=36.7) > acetonitrile (ε=36) > isopropyl alcohol (ε=19.4) > *tert*-butyl alcohol (ε=12). As seen in Table 1, the acidic arrangement for compounds 1 and 6 is: isopropyl alcohol > *tert*-butyl alcohol > *N*,*N*-dimethyl formamide > acetonitrile, for compounds 2, 3, 4 and 5 is : isopropyl alcohol > *N*,*N*-dimethyl formamide > *tert*-butyl alcohol > acetonitrile. isopropyl alcohol, 1, 2, 3, 4, 5 and 6 compounds show the strongest acidic properties, in acetonitrile 1, 2, 3, 4, 5 and 6 compounds show the weakest acidic properties.

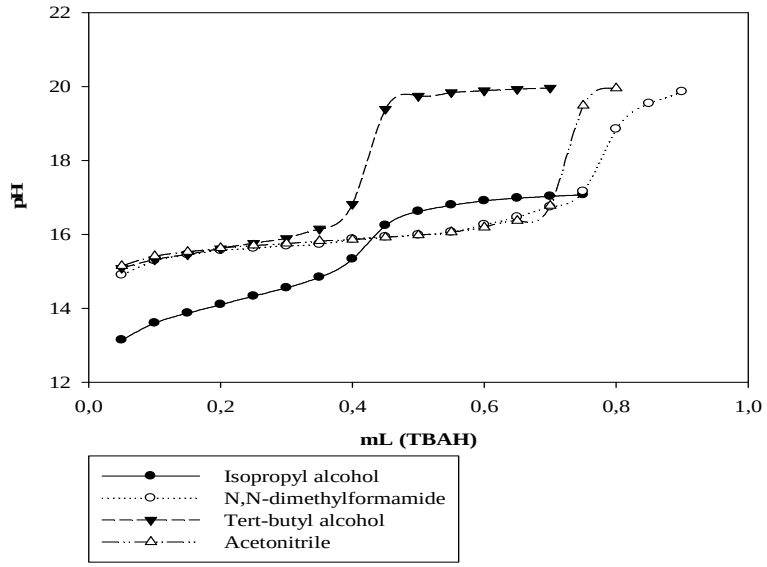


Fig. 2. pH - mL (TBAH) Potentiometric titration curves of 0.001 M solutions of compound 6 (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one) titrated with 0.05 M TBAH in isopropyl alcohol, *t*-butyl alcohol, acetonitrile and N,N-dimethylformamide at 25°C.

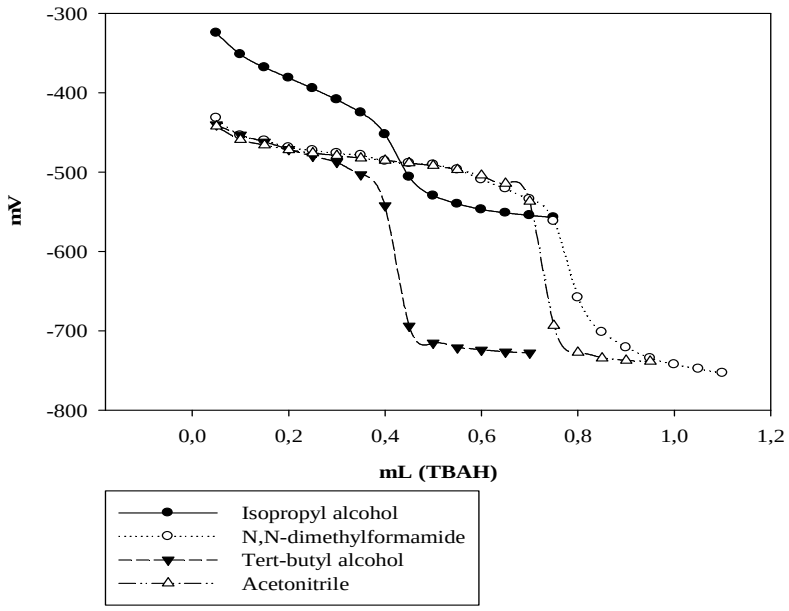


Fig. 3. mV - mL (TBAH) Potentiometric titration curves of 0.001 M solutions of compound 6 (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one) titrated with 0.05 M TBAH in isopropyl alcohol, *t*-butyl alcohol, acetonitrile and N,N-dimethylformamide at 25°C.

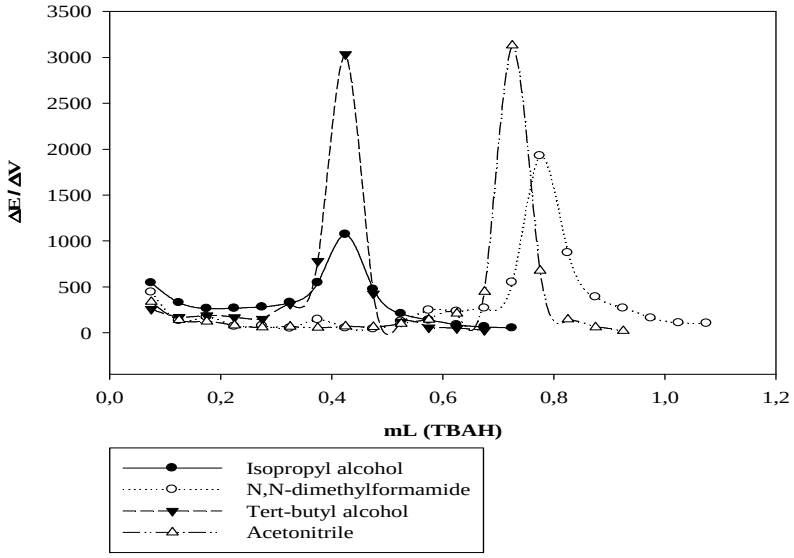


Fig. 4. ΔE/ΔV - mL (TBAH) Potentiometric titration curves of 0.001 M solutions of compound 6 (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one) titrated with 0.05 M TBAH in isopropyl alcohol, *t*-butyl alcohol, acetonitrile and N,N-dimethylformamide at 25°C.

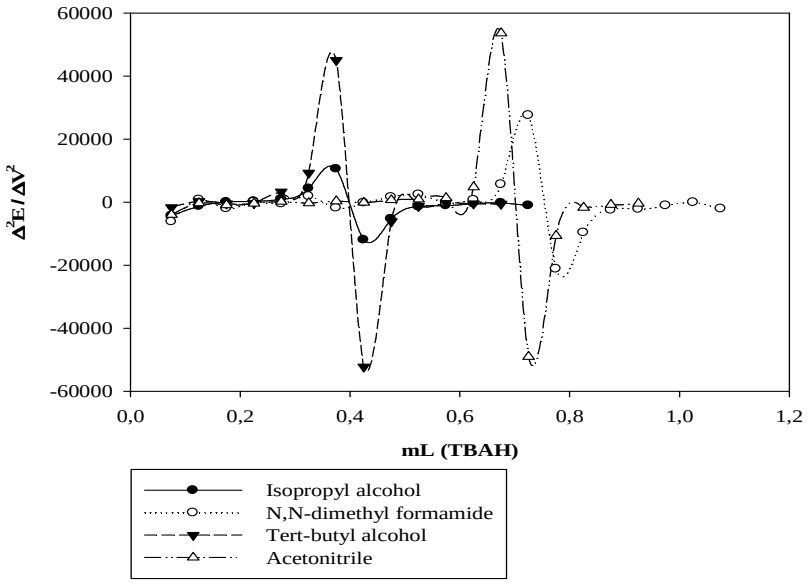


Fig. 5. $\Delta^2E/\Delta V^2$ - mL (TBAH) Potentiometric titration curves of 0.001 M solutions of compound 6 (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one) titrated with 0.05 M TBAH in isopropyl alcohol, *t*-butyl alcohol, acetonitrile and N,N-dimethylformamide at 25°C.

Table 1. The half-neutralization potentials (HNP) and the corresponding pKa values of all compounds in in isopropyl alcohol, *tert*-butyl alcohol, *N,N*-dimethylformamide and acetonitrile.

Compound	Non-aqueous solvents							
	Isopropyl alcohol		*Tert*-butyl alcohol		*N,N*-Dimethyl formamide		Acetonitrile	
	HNP (mV)	pKa	HNP (mV)	pKa	HNP (mV)	pKa	HNP (mV)	pKa
1	-375.8 ± 2.3	14.00 ± 0.04	-458.5 ± 3.1	15.40 ± 0.07	-458.9 ± 2.5	15.42 ± 0.04	-486.5 ± 3.3	15.88 ± 0.09
2	-367.2 ± 1.8	13.86 ± 0.05	-473.3 ± 2.2	15.66 ± 0.03	-465.2 ± 3.1	15.53 ± 0.06	-501.7 ± 2.3	16.13 ± 0.05
3	-375.8 ± 2.7	14.01 ± 0.08	-480.4 ± 2.9	15.77 ± 0.06	-475.7 ± 3.2	15.70 ± 0.09	-505.1 ± 2.8	16.19 ± 0.04
4	-361.4 ± 3.4	13.76 ± 0.07	-450.5 ± 3.7	15.27 ± 0.08	-447.1 ± 3.6	15.25 ± 0.08	-481.1 ± 2.4	15.80 ± 0.06
5	-383.3 ± 2.4	14.12 ± 0.06	-480.2 ± 3.2	15.77 ± 0.06	-447.4 ± 2.8	15.24 ± 0.09	-506.1 ± 2.5	16.21 ± 0.05
6	-385.6 ± 3.3	14.18 ± 0.08	-474.2 ± 2.7	15.67 ± 0.07	-483.7 ± 3.3	15.83 ± 0.05	-483.4 ± 2.1	15.84 ± 0.07

This situation may be attributed to the hydrogen bonding between the negative ions formed and the solvent molecules in the amphiprotic neutral solvents. 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. Table 1 and Figure 1 shows that the HNP values and corresponding pK_a values obtained from the potentiometric titrations rely on the non-aqueous solvents used**.**

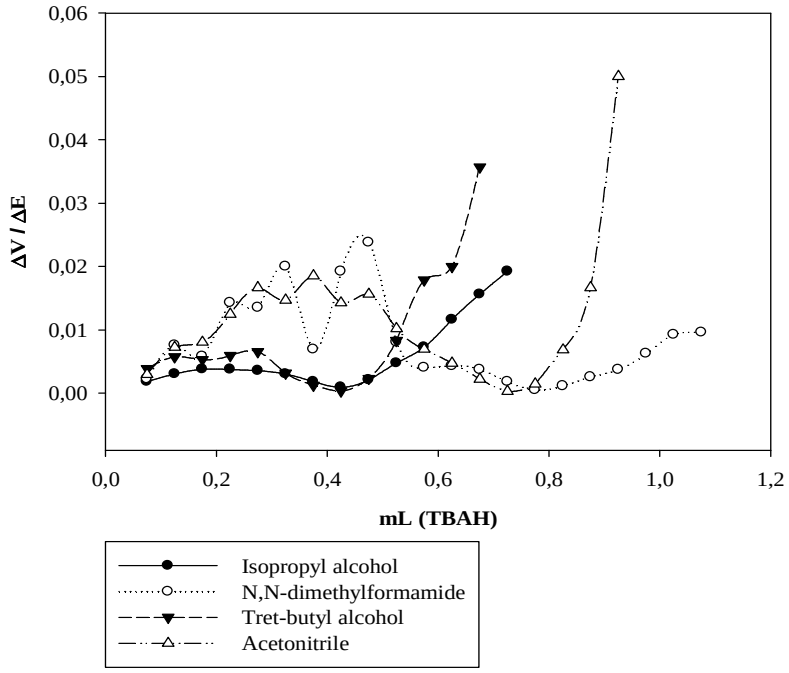


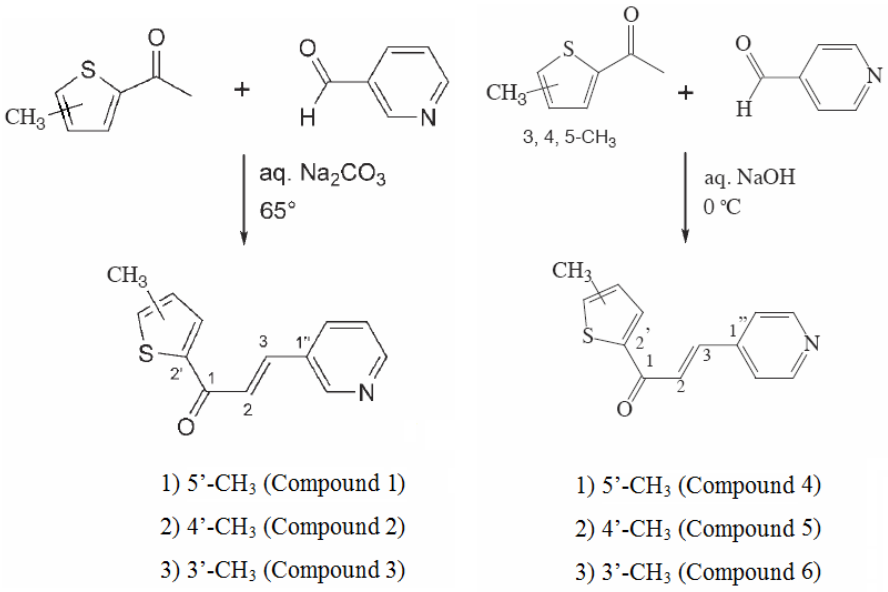
Fig. 6. ΔV/ΔE - mL (TBAH) Potentiometric titration curves of 0.001 M solutions of compound 6 (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one) titrated with 0.05 M TBAH in isopropyl alcohol, *t*-butyl alcohol, acetonitrile and N,N-dimethylformamide at 25°C.

Material and Methods

Experimental

In this study, 6 different chalcones derivatives [(**1**) (2*E*)-1-(5-methylthiophene-2-yl)-3-(pyridin-3-yl)prop-2-en-1-one, (**2**) (2*E*)-1-(4-methylthiophene-2-yl)-3-(pyridin-3-yl)prop-2-en-1-one, (**3**) (2*E*)-1-(3-methylthiophene-2-yl)-3-(pyridin-3-yl)prop-2-en-1-one, (**4**) (2*E*)-1-(5-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one, (**5**) (2*E*)-1-(4-methylthiophene-2-yl)-3-(pyridin-4-yl)prop-2-en-1-one, (**6**) (2E)-1-(3-methylthiophene-2-yl)-3-(pyridin-4-yl) prop-2-en-1-one] were synthesized. All product were synthesized according to the reported procedures [39,40] (**Scheme-I**).

Potentiometric titrations, a HANNA 4521 model Ph-meter equipped with a combined pH electrode (Ingold) and indicator elektrode were used. A magnetic stirrer, a semi micro burette and a 25 mL beaker were also used in titrations. Before potentiometric titrations, the pH meter was calibrated according to the instructions supplied by the manufactures of the pH meter. During the titrations, the titrant was added in increments of 0.05 mL after each stable reading and mV values were recorded.



Scheme-I

The necessary chemicals were supplied from Fluka and Merck. After purifications, isopropyl alcohol was used to prepare 0.05 N tetrabutylammonium hydroxide. For all potentiometric titrations, 0.05 N tetrabutylammonium hydroxide in isopropyl alcohol, which was prepared from 0.1 N tetrabutylammonium hydroxide by dilution, was used.

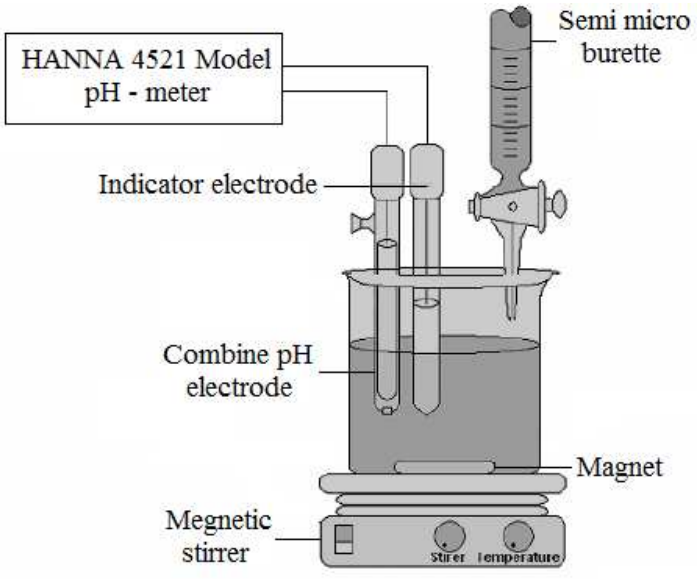


Fig. 1. Potentiometric titration cell

References

[1] O. V. Yarishkin, H. W. Ryu, J. Y. Park, M. S. Yang, S. G. Hong, K. H. Park, *Bioorganic & Medicinal Chemistry Letters*, **2008**, 18(1), 137-140.

[2] K. J. Jarvill-Taylor, R. A. Anderson, D. J. Graves, *Journal of the American College of Nutrition*, **2001**, 20(4), 327-336.

[3] R. A. Anderson, C. L. Broadhurst, M. M. Polansky, W. F. Schmidt, A. Khan, V. P. Flanagan, N. W. Schoene, D. J. Graves, *Journal of Agricultural and Food Chemistry***, 2004,** 52(1), 65–70.

[4] J. B. Harborne; The Flavonoids: Advances in Research, Chapman & Hall, London, **1988**.

[5] V. Seidel, F. Bailleul, P. G. Waterman, *Phytochemistry*, **2000**, 55(5), 439-446.

[6] D. R. Katerere, A. I. Gray, A. R. Kennedy, R. J. Nash, R. D. Waigh, *Phytochemistry*, **2004**, 65(4), 433-438.

[7] Z. Nowakowska, E. Wyrzykiewicz, B. Kedzia, *II Farmaco*, **2002**, 57(8), 657-661.

[8] Z. Nowakowska, E. Wyrzykiewicz, B. Kedzia, *II Farmaco*, **2001**, 56(4), 325-329.

[9] N. Yaylı, O. Uçüncü, A. Yaşar, M. Küçük, N. Yaylı, E. Akyüz, Ş. A. Karaoğlu, *Turkish Journal of Chemistry*, **2006**, 30(4), 505-514.

[10] N. Yaylı, M. Küçük, O. Üçüncü, A. Yaşar, N. Yaylı, Ş. A. Karaoğlu, *Journal of Photochemistry and Photobiology A*, **2007**, 188(2-3), 161-168.

[11] Z. Nowakowska, Magnetic Resonance in Chemistry, **2000**, 38(5), 382-383.

[12] B. Z. Jovanovic´, M. M. Vukovic´, A. D. Marinkovic´, J. Csana´ di, *Journal of Molecular Structure*, **1999**, 482-483, 371-374.

[13] T. Liptaj, V. Mlynarik, M. Remko, J. Durinda, *Collection of Czechoslovak Chemical Communications*, **1981**, 46, 1486-1491.

[14] N. Yaylı, O. Uçüncü, A. Yaşar, Y. Gök, M. Küçük, S. Kolaylı, *Turkish Journal of Chemistry*, **2004**, 28(4), 515-521.

[15] N. Yaylı, Y. Gök, O. Uçüncü, A. Yaşar, Ç. Atasoy, E. Şahinbaş, M. Küçük, *Journal of Chemical Research*, **2005**, 3, 155-159.

[16] M. G. Mamolo, V. Falagiani, L. Vio, E. Banfi, *II Farmaco*, **1999**, 54(11-12), 761-767.

[17] M. D'Auria, L. Emanuele, G. Mauriello, R. Racioppi, *Journal of Photochemistry and Photobiology A*, **2000**, 134(3) ,147-154.

[18] M. D'Auria, L. Emanuele, V. Esposito, R. Racioppi, *Arkivoc*, **2002**, xi, 65-78.

[19] M. D'Auria, R. Racioppi, *Journal of Photochemistry and Photobiology A*, **1998**, 112(2-3), 145-148.

[20] M. D'Auria, R. Racioppi, *Tetrahedron*, **1997**, 53(51), 17307-17316.

[21] M. D'Auria, *Heterocycles*, **2000**, *54*, 475-496.

[22] T. Gündüz, N. Gündüz, E. Kılıç, A. Kenar, *Analyst*, **1986**, 111(9), 1103-1105.

[23] T. Gündüz, N. Gündüz, E. Kılıç, A. Kenar, *Analyst*, **1986**, 111(11), 1345-1347.

[24] M.S.B. Munson, *Journal of the American Chemical Society*, **1965**, 87, 2332-2336.

[25] J.S. Fritz, *Analytical Chemical Society*, **1953**, 25, 407-411.

[26] J.S. Fritz, C.A. Burgett, *Analytical Chemical Society*, **1972**, 44, 1673-1674.

[27] N.V. Meurs, E.A.M.F. Dahmen, *Analytical Chimica Acta*, **1959**, 21, 193-202.

[28] A. Mucci, R. Domain, R. L. Benoit, *Canadian Journal of Chemistry*, **1980**, 58, 953-958.

[29] R.L. Benoit, M.J. Mackinon, L. Bergeron, *Canadian Journal of Chemistry*, **1981**, 59, 1501-1504.
[30] T. Gündüz, N. Gündüz, E. Kılıç, P. Gürkan, *Analyst*, **1987**, 112(7), 1057-1061.
[31] T. Gündüz, N. Gündüz, E. Kılıç, A. Kenar, G. Çetinel, *Analyst*, **1986**, 111(9), 1099-1101.
[32] C.W. Pifer, E.G. Wollish, M. Schmall, *Analytical Chemistry*, **1953**, 25, 310-314.
[33] S. Serin, Y. Gök, S. Karaböcek, N. Gültekin, *Analyst*, **1994**, 119(7), 1629-1631.
[34] A. Kenar, T. Gündüz, E. Kılıç, *Analytical Chimica Acta*, **1996**, 324(1), 57-60.
[35] J.S. Fritz; Acid-Base Titrations in Non-aqueous Solvents, Allynn Bacon, Boston, **1973**.
[36] R.W. Taft, *Prog. Phys. Org. Chem.*, **1983**, 14, 247-350.
[37] J. Hine; Structural Effects on Equilibria in Organic Chemistry, Wiley, New York, **1975**.
[38] J. W. Bayles, A. F. Taylor, *J. Chem. Soc.*, **1961**, 417-425.
[39] A. Usta, A. Yaşar, N. Yılmaz, C. Güleç, N. Yaylı, Ş. A. Karaoğlu, N. Yaylı, *Helvetica Chimica Acta*, **2007**, 90(8), 1482-1490.
[40] A. Usta, A. Yaşar, N. Yaylı, Ş. A. Karaoğlu, N. Yaylı, *Turkish Journal of Chemistry*, **2009**, 33(5), 621-632.