SYNTHESIS AND NON-AQUEUS MEDIUM TITRATIONS OF SOME NEW 3-ALKYL(ARYL)-4-[2-(4-METHOXYBENZOXY)- 3-METHOXY]-BENZYLİDENAMINO-4,5-DIHYDRO-1*H*-1,2,4-TRIAZOL-5-ONES

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Abstract

In this study, seven new 3-alkyl(aryl)-4-[2-(4-methoxybenzoxy)-3-methoxy]-benzylidenamino-4,5-dihydro-1H-1,2,4-triazol-5-ones were synthesized from the reactions of 3-alkyl(aryl)-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-ones with 3-methoxy-2-(4-methoxybenzoxy)-benzaldehyde, which was obtained from the reaction of 2-hydroxy-3-methoxybenzaldehyde with p-methoxybenzoyl chloride by using triethylamine. The new compounds synthesized were characterized by using ^{1}H-NMR, ^{13}CNMR and UV spectral data. In addition, to investigate the effects of solvents and molecular structure upon acidity, the prepared 3-alkyl(aryl)-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-ones were titrated potentiometrically with tetrabutylammonium hydroxide in four non-aqueous solvents, including acetone, isopropyl alcohol, *DMSO* and *N,N*-dimethylformamide. The half-neutralization potential values and the corresponding pK_a values were determined for all cases.

Keywords: 3-alkyl(aryl)-4-[2-(4-methoxybenzoxy)-3-methoxy]-benzylidenamino-4,5-dihydro-1H-1,2,4-triazol-5-ones, potentiometric titration

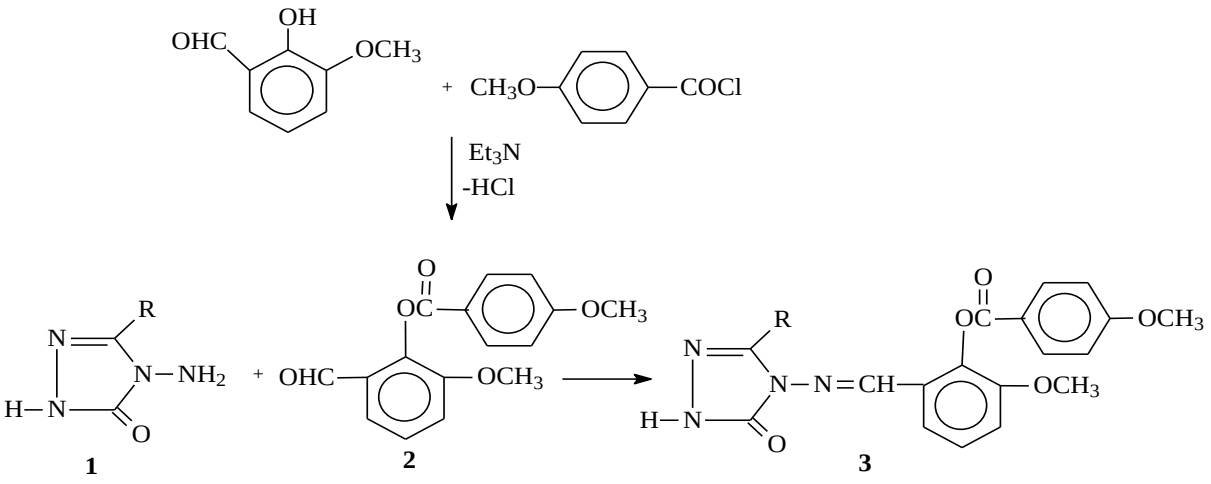
Introduction

Recently, several articles reporting the synthesis of some N-arylidenamino-4,5-dihydro-1H-1,2,4-triazol-5-one derivatives have been published [1-12]. On the other hand, it is known that 1,2,4-triazole and 4,5-dihydro-1H-1,2,4-triazol-5-one rings have weak acidic properties, so some 1,2,4-triazole and 4,5-dihydro-1H-1,2,4-triazol-5-one derivatives were titrated potentiometrically with tetrabutylammonium hydroxide (TBAH) in non-aqueous solvents, and the pK_a values of the compounds were determined [1,2,4-9, 13-15].

Synthesis

In presence of triethylamine, 2-hydroxy-3-meyhoxybenzaldehyde was reacted with p-methoxybenzoylchloride and 3-methoxy-2-(4-methoxybenzoxy)-benzaldehyde compound (2) was obtained. Then, this compound was reacted with 7 new 3-alkyl(aryl)-4-amino-4,5-dihydro-1H-1,2,4-triazol-5-one (1) compounds. As a result, 7 new Schiff Bases (3) were

obtained according to following reaction. Physical data of the new compounds synthesized are compiled in Table **1**. IR, UV and NMR spectral data are presented in Tables **2-4**.



1,3	R
a	CH_3
b	CH_2CH_3
c	$CH_2CH_2CH_3$
d	$CH_2C_6H_5$
e	$CH_2C_6H_4.CH_3$ (*p*-)
g	$CH_2C_6H_4.Cl$ (*p*-)
i	C_6H_5

Table **1**. Physical Data of the Compounds **3a-g**

Compd.	Yield (%)	m.p. (°C)	Crystallized from	Formula	m.w.
3a	98.9	231	Ethanol	$C_{19}H_{18}O_5N_4$	382,38
3b	98.5	213	Ethanol	$C_{20}H_{20}O_5N_4$	396,40
3c	97.6	180	Ethanol	$C_{21}H_{22}O_5N_4$	410,43
3d	96.1	173	Ethanol	$C_{25}H_{22}O_5N_4$	458,47
3e	85.6	193	Ethanol	$C_{26}H_{24}O_5N_4$	472,50
3f	86.4	185	Ethanol	$C_{25}H_{21}O_5N_4Cl$	492,92
3g	87.8	232	Ethanol	$C_{24}H_{20}O_5N_4$	444,45

Table **2**. IR Data (cm^{-1}) and UV Data of the Compounds **3a-g**

Compd.	$\nu_{(NH)}$	$\nu_{(C=O)}$	$\nu_{(C=N)}$	$\nu_{(COO)}$	$\nu_{substituted\ benzenoid\ ring}$	λ_{max}, nm ($\varepsilon \times 10^{-3}$)
3a	3165	1716, 1695	1600	1256	835	304 (11.07), 260 (25.36), 216 (19.56)
3b	3166	1720, 1695	1602	1259	836	303 (16.80), 258 (28.66), 226 (21.27), 214 (19.76)
3c	3198	1735, 1708	1603	1253	812	304 (18.86), 254 (28.82), 232 (23.03), 214 (19.70)
3d	3161	1745, 1705	1605, 1586	1250	821; 756 and 698	304 (9.87), 260 (23.83), 216 (19.73)
3e	3163	1738, 1700	1606, 1578	1254	844	296 (28.25), 256 (29.00), 214 (19.65)
3f	3165	1743, 1705	1605, 1575	1254	844, 820	304 (18.87), 256 (28.79), 232 (23.52), 214 (19.68)
3g	3155	1739, 1704	1604, 1576	1257	801; 763 and 688	304 (11.86), 258 (31.55), 280 (28.39), 216 (23.73)

Table 3. ^{1}H NMR Data of the Compounds **3a-g** (DMSO-d_6, δ/ppm)

Compd.	CH_3	CH_2	OCH_3	OCH_3 (*p*-)	CH_2	Aromatic H	N=CH	NH
3a	2.14 (s)	-	3.80 (s)	3.89 (s)	-	7.14 (d, 2H; *J*=8.85 Hz), 7.33 (d, 1H; *J*=8.24 Hz), 7.40 (t, 1H; *J*=7.97 Hz), 7.58 (d, 1H; *J*=7.83 Hz), 8.11 (d, 2H; *J*=8.85 Hz)	9.89 (s)	11.76 (s)
3b	1.11 (t; *J*=7.47 Hz)	2.51 (q; *J*=7.38 Hz)	3.80 (s)	3.89 (s)	-	7.15 (d, 2H; *J*=8.81 Hz), 7.34 (d, 1H; *J*=8.13 Hz), 7.41 (t, 1H; *J*=7.97 Hz), 7.56 (d, 1H; *J*=7.80 Hz), 8.10 (d, 2H; *J*=8.81 Hz	9.87 (s)	11.78 (s)
3c	0.88 (t; *J*=7.44 Hz)	1.60 (sext; *J*=7.40 Hz)	3.80 (s)	3.88 (s)	2.48 (sext; *J*=7.34 Hz)	7.13 (d, 2H; *J*=8.93 Hz), 7.31 (d, 1H; *J*=8.33 Hz), 7.39 (t, 1H; *J*=7.98 Hz), 7.55 (d, 1H; *J*=7.91 Hz), 8.12 (d, 2H; *J*=8.88 Hz	9.90 (s)	11.80 (s)
3d	-	-	3.79 (s)	3.87 (s)	3.95 (s)	7.12 (d, 2H; *J*=8.93 Hz), 7.23-7.33 (m, 6H), 7.40 (t, 1H; *J*=7.97 Hz), 7.53 (d, 1H; *J*=7.88 Hz), 8.10 (d, 2H; *J*=8.90 Hz	9.87 (s)	11.90 (s)
3e	2.25 (s)	-	3.79 (s)	3.87 (s)	3.89 (s)	7.09-7.16 (d, 6H), 7.32 (d, 1H; *J*=8.29 Hz), 7.40 (t, 1H; *J*=7.99 Hz), 7.54 (d, 1H; *J*=7.90 Hz), 8.09 (d, 2H; *J*=8.88 Hz	9.85 (s)	11.72 (s)
3f	-	-	3.80 (s)	3.87 (s)	3.95 (s)	7.12 (d, 2H; *J*=8.90 Hz), 7.28-7.41 (m, 6H), 7.52 (d, 1H; *J*=7.88 Hz), 8.10 (d, 2H; *J*=8.87 Hz	9.88 (s)	11.73 (s)
3g	-	-	3.80 (s)	3.89 (s)	-	7.12 (d, 2H; *J*=8.81 Hz), 7.34 (d, 1H; *J*=7.59 Hz), 7.40 (t, 1H; *J*=7.90 Hz), 7.51-7.53 (m, 4H), 7.86-7.88 (m, 2H), 8.08 (d, 2H; *J*=8.78 Hz	9.89 (s)	12.20 (s)

Investigation of ^{1}H NMR values of 3 type compounds, while data of aliphatic protons are between δ 0.80-2.10, protons of OCH_3 groups are approximately δ 3,80. Spectrum data of N=CH groups are near δ 9,80. On the other hand, Signals of NH protons are between δ 11,90-12,30. Chemical shift values of all synthesized Schiff Bases are between 7,00-8,90 Hz.

Table 4. ^{13}C NMR Data of the Compounds **3a-g** (DMSO-d_6, δ/ppm)

Compd.	COO	Triazole-C_5	N=CH	Triazole-C_5	Aromatic C	Aliphatic C
3a	164.42	152.11	148.64	144.66	163.42, 151.62, 139.72, 132.68 (2C), 127.78, 127.43, 120.69, 118.42, 115.69, 114.85 (2C)	56.62 (OCH_3), 56.13 (OCH_3-*p*), 11.36 (CH_3)
3b	164.41	152.14	148.86	148.40	163.93, 151.77, 139.69, 132.66 (2C), 127.79, 127.43, 120.75, 118.63, 115.72, 114.83 (2C)	56.65 (OCH_3), 56.13 (OCH_3-*p*), 18.80 (CH_2), 10.36 (CH_3)
3c	164.42	152.15	148.89	147.28	163.93, 151.74, 139.71, 132.67 (2C), 127.82, 127.42, 120.70, 118.58, 115.65, 114.82 (2C)	56.60 (OCH_3), 56.10 (OCH_3-*p*), 26.97 ($CH_3CH_2\underline{CH_2}$), 19.17 ($CH_3\underline{CH_2}CH_2$), 13.80 (CH_3)
3d	164.46	152.11	148.44	146.62	163.93, 151.63, 139.90, 132.67 (2C), 127.76, 127.48, 120.63, 118.13, 115.80, 114.88 (2C); C-3 linked arom. C: [136.11, 129.24 (2C), 128.87 (2C), 127.17]	56.66 (OCH_3), 56.13 (OCH_3-*p*), 31.35 (CH_2)
3e	164.44	152.09	148.33	146.77	163.93, 151.62, 139.87, 132.67 (2C), 127.76, 127.49, 120.59, 118.08, 115.76, 114.88 (2C); C-3 linked arom. C: [136.23, 132.99, 129.44 (2C), 129.11 (2C)]	56.65 (OCH_3), 56.13 (OCH_3-*p*), 30.95 (CH_2), 21.07 (CH_3)
3f	164.45	152.13	148.63	146.27	163.93, 151.62, 139.14, 132.66 (2C), 127.74, 127.45, 120.66, 118.23, 115.82, 114.86 (2C); C-3 linked arom. C: [135.05, 131,93, 131.15 (2C), 128.79 (2C)]	56.66 (OCH_3), 56.11 (OCH_3-*p*), 30.62 (CH_2)
3g	164.41	152.17	150.99	140.07	163.91, 151.76, 140.17, 132.66 (2C), 127.71, 127.57, 120.67, 117.98, 116.01, 114.84 (2C); C-3 linked arom. C: [130.55, 128.92 (2C), 128.47 (2C), 127.01]	56.71 (OCH_3), 56.15 (OCH_3-*p*)

^{13}C NMR data of 3a-i compounds are coherent with ^{1}H NMR values. Signals belonging to OCH_3 carbons are contain standart value which is δ 56,00. Aliphatic CH_3 and CH_2 groups are also contain coherence values. Signals of aromatic carbons are between δ 113,00-151,00. Triazoles C-3 carbon's signal values are between δ 144,00-147,00. C-5 carbons of triazol rings gives signal at δ 153,00. N=CH signals of all of the compounds are δ 148,00. These data are similar to literature values.

Experimental

Apparatus

A Jenway 3040-model ion analyzer was used for potentiometric titrations. An Ingold pH electrode was preferred becauseof the advantage.

Reagents

All chemicals used were of analytical reagent grade or similar. Tetra-n-butylammonium hydroxide (TBAH), isopropyl alcohol, tert-butyl alcohol, acetone, N,N-dimethylformamide and dimethyl sulfoxide (DMSO) (Merck Darmstadt, Germany)) were used throughout the work without further purification.

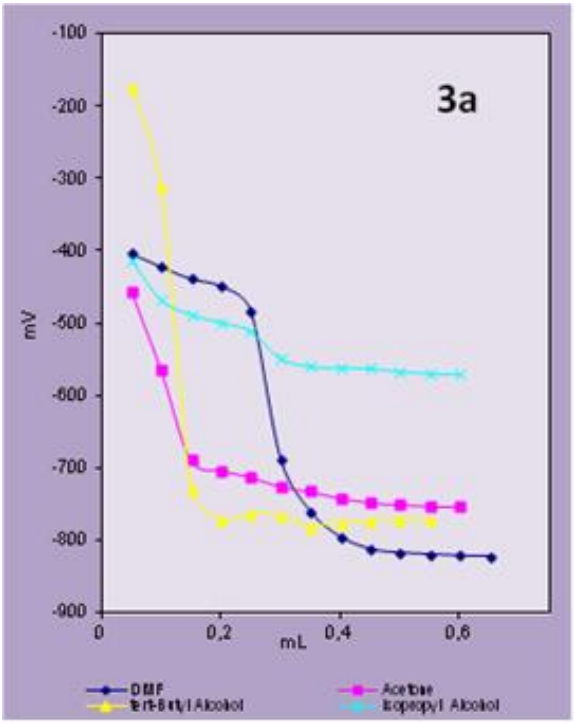
Procedure

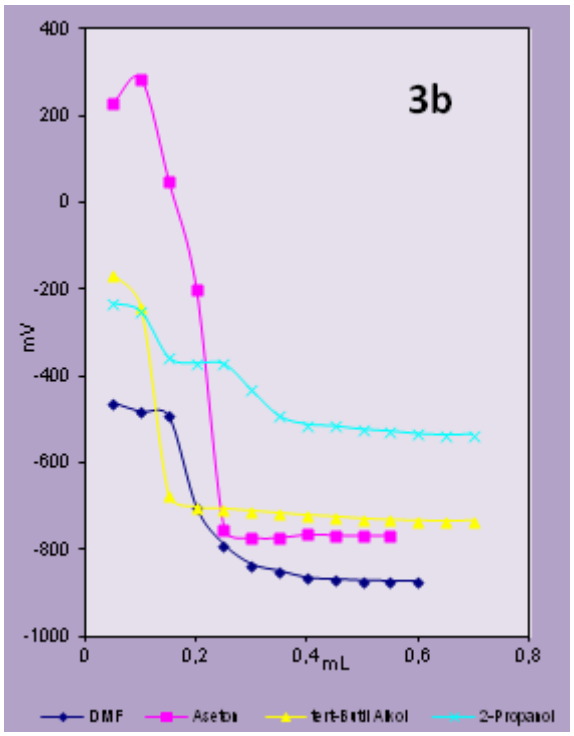
For each compound that would be titrated, the 0.001 M solution was separately prepared in each non-aqueous solvent. The 0.05 M solution of TBAH in isopropyl alcohol, which is widely used in the titration of acids, was used as titrant. The mV values, that were obtained in pH-meter, were recorded. Finally, the half-neutralization potential values and the corresponding pKa values were determined by drawing the mL (TBAH)-mV graphic.

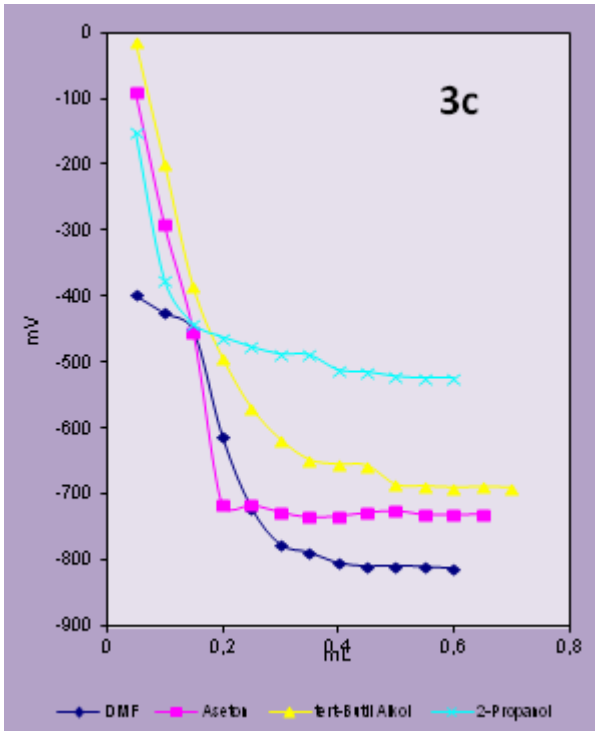
Results and Discussion

There have been several studies about the potentiometric titrations of some new 3-alkyl(aryl)-4-[2-(3-methoxy-4-methoxybenzoxy)-benzylidenamino-4,5-dihydro-lH-l,2,4-triazol-5-ones with tetrabutylammonium hydroxide (TBAH) in the non-aqueous solvents such as isopropyl alcohol, methyl alcohol, tert-butyl alcohol and acetone, and the pKa values were found between 2.71-18.99.

As an example, the potentiometric titration values of 0.001 M some 3-alkyl(aryl)-4-[2-(3- methoxy-4-methoxybenzoxy)-benzylidenamino-4,5-dihydro-lH-l,2,4-triazol-5-ones solutions titrated with 0.05 N TBAH in isopropyl alcohol, tert-butyl alcohol, N,N-dimethylformamide and acetone are presented in Table I; and the graphics formed (3a, 3e) from the potentiometric titrations are given in Figure 2.


3a
mV
mL
DMF
Acetone
tert-Butyl Alcohol
Isopropyl Alcohol


3b
mV
mL
DMF
Aseton
tert-Butil Alkol
2-Propanol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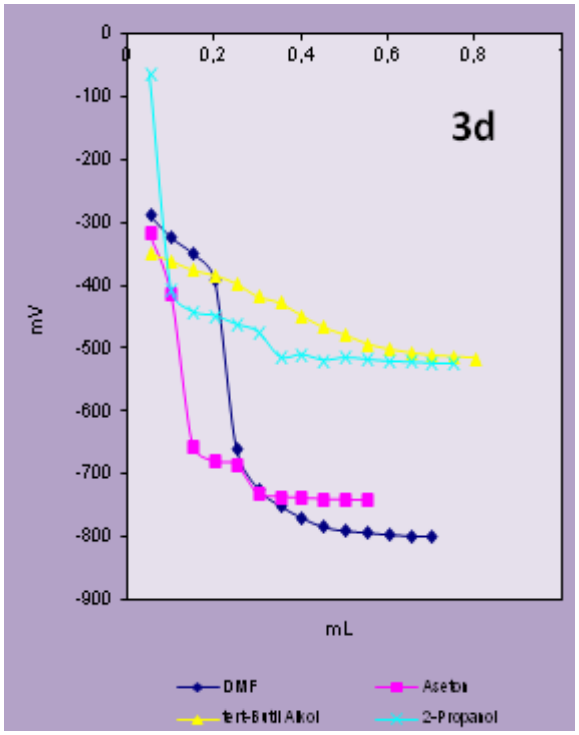
mV
mL
DMF
Aseton
tert-Butil Alkol
2-Propanol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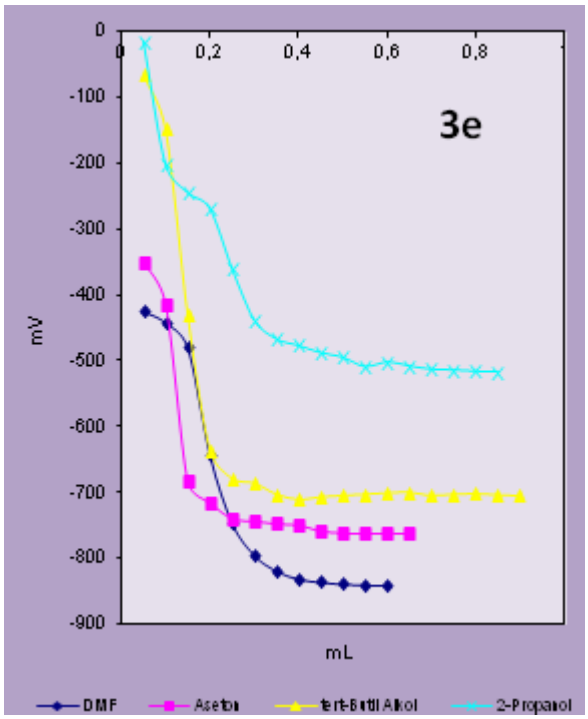

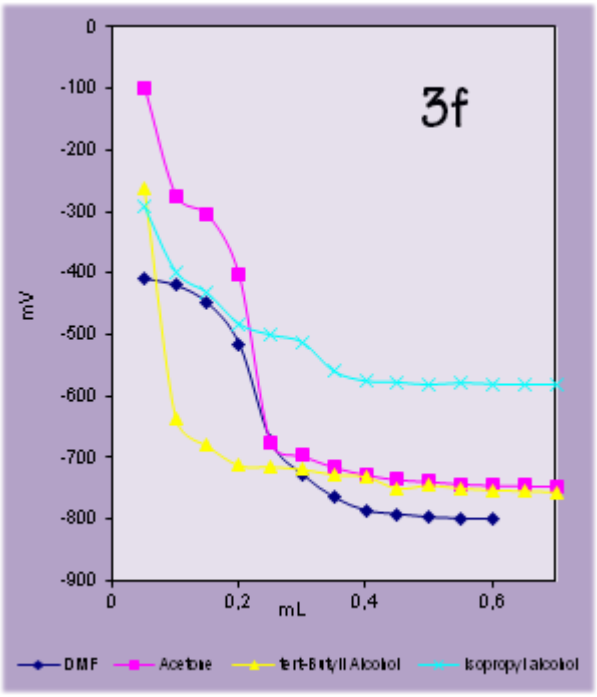

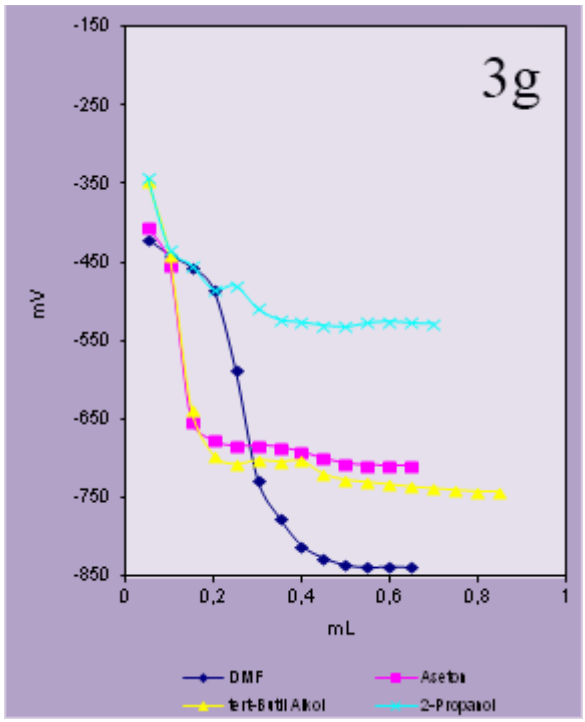

Figure **1 .** Potentiometric Titration Graps of 3a-g Compounds

When the dielectric permittivity of solvents is taken into consideration, the acidic arrangement may be expected as follows: N,N-dimethylformamide (s=37) > acetone (s=20.7) > isopropyl alcohol (s=19.4) > tert-butyl alcohol (s=12). The experimental and theoretical acidic arrangement, along with the error for each compound, these compounds (except for compound 3a in acetone) show the weakest acidic properties in foursolvents.

Table **4.** The half neutralization potentials (HNP) and the corresponding pK_a values of compounds **3a-g** in solvents at 25°C

COMPOUND		DMF		acetone		tert-butyl alcohol		isopropyl alcohol	
		pK_a	HNP	pK_a	HNP	pK_a	HNP	pK_a	HNP
CH_3	3a	17.94	-429	-	-	12.16	-242	18.99	-478
CH_2CH_3	3b	15,24	-324	13,67	-318	16,36	-368	18,37	-442
$CH_2CH_2CH_3$	3c	18.04	-433	14,40	-351	8,68	-67	11,5	-203
$CH_2C_6H_5$	3d	17,33	-411	11,98	-189		-531	18.41	-452
$CH_2C_6H_4CH_3$(p-)	3e	17,41	-419	13,39	-274	-	-712	16,96	-432
$CH_2C_6H_4Cl$ (p-)	3g	18.35	-448	16,82	-405	-	-695	18,26	-442,5
C_6H_5	3i	18.89	-472	2,71	283	11,41	-168	12,95	-231

Typical S-shaped curves were not obtained from the compounds (for compound 3a in acetone) in solvents. Therefore, the HNP values and the pK_a, values were not determined clearly.

As known, the acidity of a compound changes in relation to some factors. The most important two factors of them are the solvent effects and molecular structure [16-20]. It is seen from the Table 4 that the molecular structure of titrated compounds affect the HNP values and the corresponding pK_a values: that is, the HNP values and corresponding pK_a values are connected to the substituents linked to C-3 into some new 3-alkyl(aryl)-4-[2-(3-methoxy-4-methoxybenzoxy)-benzylidenamino-4,5-dihydro-lH-l,2,4-triazol-5-ones ring for the same solvent.

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