

Study of the Electrochemical Redox Characteristics of Some Triazolopyrimidines

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Abstract : An electrochemical study related to the redox characteristics of Ethyl-3-acetyl-6-methyl-1, 4-diphenyl-4, 3a-dihydro-1, 3, 4-triazolino[3, 4-a] pyrimidine-5-carboxylate ester and its derivatives (1a-f) and (2a-e) in nonaqueous solvents such as 1, 2-dichloroethane (DCE), dichloromethane (DCM), acetonitrile (AN), dimethylsulphoxide (DMSO) and tetrahydrofuran (THF) using 0.1 mol dm^{-3} tetrabutylammonium perchlorate (TBAP) as a supporting electrolyte at platinum, glassy carbon and gold electrodes, has been performed using cyclic voltammetry (CV). Controlled potential electrolysis (CPE) is also carried out to elucidate the course of different electrochemical reactions through the separation and identification of the intermediates and final electrolysis products. The redox mechanism is suggested and proved. It was found that all the investigated compounds in all solvents are oxidized in a single irreversible one electron donating process following the well known pattern of the EC-mechanism to give a dimer. On the other hand, these compounds are reduced in a single irreversible one electron step to form the anion radical, which is basic enough to abstract proton from the media forming the radical which undergoes tautomerization and then dimerization processes to give also another bis-compound through N-N linkage formation.

Keywords : Cyclic voltammetry, Oxidation, Reduction, Triazolopyrimidine, Non-aqueous media, Platinum electrode, Glassy carbon electrode, Gold electrode.

1. Introduction

Triazolopyrimidines and its derivatives are known to have many biological, pharmaceutical and analytical applications. Several triazolopyrimidine compounds have potential uses as a potent antibacterial drugs due to their higher antibacterial activity than some commercial antibiotics against bacillus subtilis, staphylococcus aureus and salmonella typhi at MIC (minimum inhibitory concentration) i.e. 10 mg/ml .^{1,2)} Triazolopyrimidine compounds have an important potential role in cardiovascular therapeutics specially in platelet aggregation as an antiplatelet agent or anticoagulant (in the Japanese antiplatelet myocardial infarction study trapidil (triazolopyrimidine) 300 mg/day administered to more than 700 post-MI patients for about 1.5 years resulted in a significant reduction in CV (CV refers to cardiovascular). Events including CV death, reinfarction, and non fatal ischaemic stroke achieving successful advancement more than aspirin. And in other cardiac diseases like angina, peripheral cardiac diseases and stroke.³⁻⁸⁾ Because of this it was found worthwhile to investigate the redox characteristics of substituted triazolopyrimidines (1a-f) and (2a-e). These compounds were extensively studied using cyclic voltammetry in nonaqueous solvents. The number of electrons participating in each electrode reaction was determined using the coulometric technique. Separation and identification of the intermediates and the final products were made through the controlled potential electrolysis (CPE).

2. Experimental

The organic compounds are synthesized according to the procedures outline in literature.⁹⁾ All the synthesized compounds were purified by repeated crystallization, dried under reduced pressure and the purity was checked by thin layer chromatography.

The measurements were carried out using the following apparatus; The EG & G Princeton applied research model 283 Potentiostat/Galvanostat controlled from a PS-486-DX microcomputer via a National Instrument IEEE-488 through GPIB board by means of M270/250 program was used for the electrochemical control.

All measurements were carried out with $2.5 \times 10^{-5} \text{ mol}$ of the reactant in 15 ml dry oxygen free solvent with 0.1 mol dm^{-3} tetra-n-butylammonium perchlorate as supporting electrolyte. 1, 2-Dichloroethane (DCE), dichloromethane (DCM), acetonitrile (AN), tetrahydrofuran (THF) and dimethylsulfoxide (DMSO) were used as solvents.

During the solvent purification, all the processes were performed under a dry oxygen-free argon atmosphere. Fractionation was carried out using a 120 cm column filled with glass spirals.

At a recoil ratio of 50 : 1. All purified solvents were stored under argon in the dark. Purification of the different solvents was carried out as follows; EtCl_2 (Merck, P. a.) was boiled for 24h with PCl_5 and then distilled. The main fraction was stirred with KMnO_4 for 24h and distilled. Finally, the solvent was fractionated.

AN was purified according to the modified methods of

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Walter and Rumaloy.^{10,11)}

THF (Uvasol Merck) was boiled successively for 12h with calcium hydride (Merck), 12h with basic aluminium oxide (Woelm, Act. I), 6h with sodium metal and 6h with potassium metal and distilled after each process. In the last two steps the solvent was fractionated.

DMSO (Merck) was boiled four times with calcium hydride (Merck) for 14h (5 g/L) and subsequently fractionated at 14 Torr. Finally, the main fraction was carefully fractionated.

The working electrode was a Pt electrode 1.3 mm in diameter, the auxiliary electrode was a Pt wire immersed in the corresponding electrolyte. The reference electrode was Ag/AgCl/Cl⁻ (sat. AN) and the redox potential (E_p) values are referred to the potential of cobaltocinium/cobaltocene system.¹²⁾

2.1. Controlled Potential Electrolysis (CPE)

CPE experiments were carried out in dry acetonitrile containing 0.1 mol. dm⁻³ tetra-n-butylammonium perchlorate (TBAP) as supporting electrolyte, compound 1a and 2d are reported here as examples. The potential was controlled at the current plateau of the oxidation or reduction peaks (300 mV more

positive or more negative than the E_p in oxidation and reduction processes, respectively). As a working electrode, a platinum gauze electrode (ca. 80 cm²) was used. The progress of the electrolysis was followed by recording periodically the decrease in current with time. From time to time the working electrode was removed from the cell, sprayed with pure acetone and burned in a direct flame, cooled and replaced in the cell. After the electrolysis was completed, the cell was disconnected from the circuit and the solvent was evaporated in vacuum. The residue was shaken with dry ether and the supporting electrolyte was filtered off. The ethereal layer was evaporated in turn. The obtained residue was chromatographed on thin layer silica gel plates using chloroform as an eluent. The main electrolysis product obtained was scraped off the plate and extracted with acetonitrile, filtered and evaporated in vacuum. The resulting solid compound was identified.

2.1.1 The Oxidation product of 1a

The ¹H NMR of the obtained oxidative product of 1a reveals that, the absence of the band corresponding to the C-

Table 1. Cyclic voltammetric data of compounds (1a-f) at pt, Glassy C and Au electrodes in different solvents (scan rate = 100 mv/s).

Compounds	Sol.	D.N.	Temp.	Electrode	Reduction	Oxidation	$\Delta E = E_p^{Ox} - E_p^{Red}$	Log K	
					E_p (V)	E_p (V)			
1a	DCM	1.000	0°C	Pt	-1.493	1.529	3.022	51.219	
				C	-1.482	1.528	3.010	51.016	
				Au	-1.477	1.512	2.989	50.66	
	DCE	0.100	25°C	Pt	-1.491	1.520	3.011	51.033	
				C	-1.453	1.544	2.997	50.796	
				Au	-1.462	1.520	2.982	50.54	
	AN	14.100	25°C	Pt	-1.394	1.396	2.790	47.321	
				C	-1.395	1.384	2.779	47.118	
				Au	-1.385	1.378	2.763	46.897	
	THF	20.000	0°C	Pt	-1.790	1.960	3.750	63.558	
				C	-1.760	1.610	3.370	57.118	
				Au	-1.750	1.770	3.520	59.660	
	DMSO	29.800	25°C	Pt	-1.449	1.280	2.729	46.253	
				C	-1.490	1.263	2.753	46.66	
				Au	-1.435	1.440	2.875	48.728	
	Compounds	Sol.	D.N.	Temp.	Electrode	Reduction	Oxidation	$\Delta E = E_p^{Ox} - E_p^{Red}$	Log K
						E_p (V)	E_p (V)		
	1d	DCM	1.000	0°C	Pt	-1.800	1.454	3.254	55.152
C					-1.774	1.442	3.216	54.508	
Au					-1.740	1.454	3.194	54.135	
DCE		0.100	25°C	Pt	-1.592	1.427	3.019	51.169	
				C	-1.718	1.416	3.134	53.118	
				Au	-1.710	1.429	3.139	53.203	
AN		14.100	25°C	Pt	-1.623	1.308	2.931	49.677	
				C	-1.740	1.333	3.073	52.084	
				Au	-1.653	1.305	2.958	50.135	
THF		20.000	0°C	Pt	-1.680	1.960	3.64	61.694	
				C	-1.620	1.600	3.22	54.575	
				Au	-1.420	1.740	3.16	53.219	
DMSO		29.800	25°C	Pt	-1.700	1.265	2.965	50.253	
				C	-1.736	1.255	2.991	50.694	
				Au	-1.733	1.429	3.162	53.592	

H at carbon number four in pyrimidine ring at $\delta = 5.98$ compared with starting material 1a which gives a sharp band at $\delta = 5.91$ (S, 1H, CH). Also the mass spectral data gives $m^+/z = (738)$.

2.1.2 The Reduction product of 1a

The ^1H NMR of the obtained reductive product of 1a reveals that, the presence of the band corresponding to C-H at carbon number four in pyrimidine ring at $\delta = 5.98$ (S, 2H, 2CH) compared with starting material 1a which gives sharp band at $\delta = 5.9$ (S, 1H, CH). Also C-H of triazole ring appear at $\delta = 5.2$ (S, 2H, 2CH aliphatic). Also the mass spectra data gives m^+/z (742).

2.1.3 The oxidation product of 2d

The ^1H NMR of the obtained oxidative product of 2d reveals that, the absence of the band corresponding to the C-H at carbon number four in pyrimidine ring at $\delta = 5.82$ ppm compared with starting material 2d which gives a sharp band at $\delta = 5.62$ ppm (S, 1H, CH). Also the mass spectra data gives m^+/z (780).

2.1.4 The Reduction product of 2d

The ^1H NMR of the obtained reductive product of 2d reveals that, the presence of the band corresponding to the C-H at carbon number four in pyrimidine ring at $\delta = 5.83$ ppm (S, 2H, 2CH) compared with starting material 1a which gives a sharp band at $\delta = 5.82$ ppm (S, 1H, CH). Also the C-H of triazole ring appear at $\delta = 5.5$ ppm (S, 2H, 2CH aliphatic). Also the mass spectra data gives m^+/z (784).

3. Results and Discussion

Cyclic voltammetric data are listed in Tables 1 and 2. Fig. 1 and 2 show as an example the cyclic voltammograms of some investigated compounds. Compounds (1a-f) and (2a-e) in all solvents are oxidized in a single irreversible one-electron donating process following the well known pattern of EC-mechanism; forming cation radical followed by a proton removal from the 4-position in the pyrimidyl ring forming the unstable intermediate (radical) which tautomerize and then dimerize to give the corresponding bis-compound (dimer) as in (scheme 1). On the other hand the reduction center in

Table 2. Cyclic voltammetric data of compounds (2b-2e) at Pt, Glassy C and Au electrodes in different solvents (scan rate = 100 mv/s).

Compounds	Sol.	D.N.	Temp.	Electrode	Reduction	Oxidation	$\Delta E = E_p^{Ox} - E_p^{Red}$	Log K	
					E_p (V)	E_p (V)			
2b	DCM	1.000	0°C	Pt	-1.648	1.446	3.094	51.219	
				C	-1.568	1.417	2.985	51.016	
				Au	-1.620	1.389	3.009	50.660	
	DCE	0.100	25°C	Pt	-1.590	1.435	3.025	51.034	
				C	-1.545	1.420	2.965	50.796	
				Au	-1.585	1.429	3.014	50.542	
	AN	14.100	25°C	Pt	-1.508	1.327	2.835	47.321	
				C	-1.449	1.325	2.774	47.118	
				Au	-1.472	1.309	2.781	46.898	
	THF	20.000	0°C	Pt	-1.120	1.600	2.720	63.559	
				C	-1.110	1.580	2.690	57.118	
				Au	-1.102	1.590	2.692	59.660	
	DMSO	29.800	25°C	Pt	-1.554	1.217	2.771	46.254	
				C	-1.550	1.203	2.753	46.660	
				Au	-1.536	1.330	2.866	48.728	
	2d	DCM	1.000	0°C	Pt	-1.559	1.45	3.009	50.999
					C	-1.504	1.457	2.961	50.186
					Au	-1.518	1.458	2.976	50.406
DCE		0.100	25°C	Pt	-1.508	1.455	2.963	50.219	
				C	-1.454	1.444	2.898	49.118	
				Au	-v1.518	1.458	2.976	49.898	
AN		14.100	25°C	Pt	-1.412	1.341	2.753	46.660	
				C	-1.381	1.304	2.685	45.508	
				Au	-1.395	1.345	2.740	46.44	
THF		20.000	0°C	Pt	-1.490	1.685	3.175	53.898	
				C	-1.500	1.690	3.190	53.898	
				Au	-1.300	1.680	2.980	50.508	
DMSO		29.800	25°C	Pt	-1.454	1.286	2.740	46.440	
				C	-1.458	1.277	2.735	46.356	
				Au	-1.450	1.370	2.820	47.796	

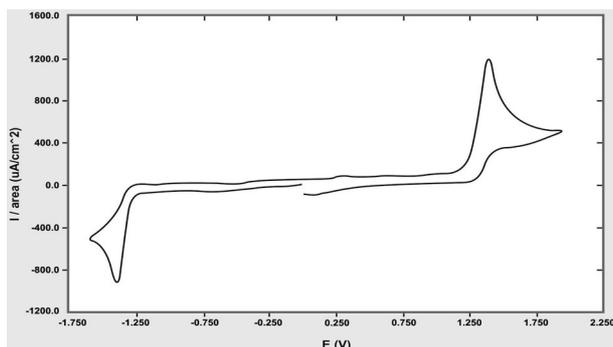


Fig. 1. CV-voltammogram of compound 1a in (AN) at Pt-electrode (scan rate = 100 mV/s; T = 25 °C)

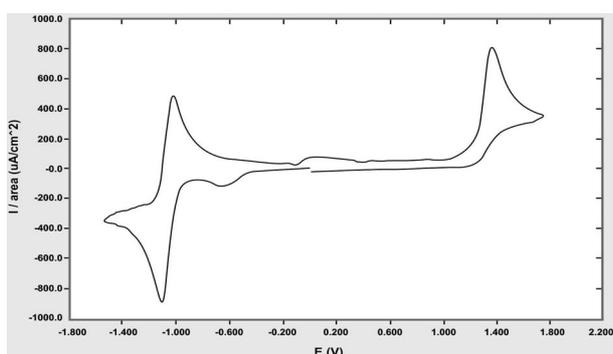
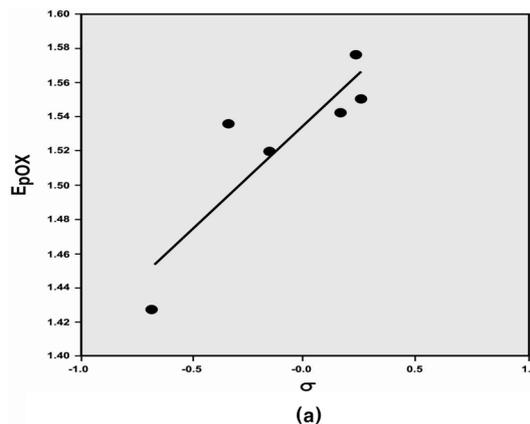
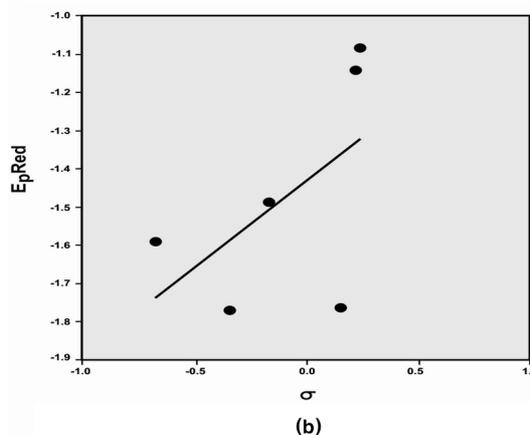


Fig. 2. CV-voltammogram of compound 1c in (AN) at glassy C-electrode (scan rate = 100 mV/s; T = 25 °C).

the investigated compounds seems to be the (C = N) in the triazole ring.^{13,14} Although the reported studies¹⁵⁻¹⁸ gave the chance for dimerization through N-N coupling in the pyridine rings but in our case the presence of the more active center in the triazene ring favours the coupling through the atoms of this ring which have been proved in this work. Compounds (1a-f) and (2a-e) are reduced in an irreversible one electron gain to form the anion-radical, which is basic enough to abstract proton from the media¹⁹⁻²² forming the radical which undergoes tautomerization and then dimerization process to give also another bis-compound through N-N linkage formation (Scheme 1). The stability of this anion-radical can be seen from the shape of the reduction peak and also from the values of ΔE_p and I_p^c/I_p^a .



(a)



(b)

Fig. 3. Dependence of ΔE_p (ox) of compound (1a-f) in (DCE) on Hammett substitution constant (σ), (b): Dependence of ΔE_p (red) of compound (1a-f) in (DCE) on Hammett substitution constant (σ).

3.1. Substituent Effect

The effect of substituents on the redox mode of an electro-active site can be illustrated by applying the well-known modified Hammett equation of the form.²³

$$E_p^* = \rho_x \sigma_x + E_p^H \quad (1)$$

Where σ_x is the Hammett constant, ρ_x is the polarographic reduction or oxidation constant and E_p^* , E_p^H are the peak potentials of the substituted and unsubstituted compounds respectively. Fig. 3(a), (b) illustrate the Hammett equation correlations of the peak potentials of compounds (1a-f) for both oxidation and reduction processes. The equations of the regression lines obtained for the series (1a-f) are listed in

Table 3. The Linear relation parameter between Hammett constant and potential for compounds (1a-f).

Solvent	Pt	C	Au
AN	$(E_p^{ox})_1 = 0.130 \sigma_x + 1.392$	$(E_p^{ox})_1 = 0.062 \sigma_x + 1.374$	$(E_p^{ox})_1 = 0.081 \sigma_x + 1.374$
	$(E_p^{red})_1 = 0.394 \sigma_x - 1.414$	$(E_p^{red})_1 = 0.597 \sigma_x - 1.356$	$(E_p^{red})_1 = 0.515 \sigma_x - 1.352$
DCE	$(E_p^{ox})_1 = 0.123 \sigma_x + 1.538$	$(E_p^{ox})_1 = 0.104 \sigma_x + 1.530$	$(E_p^{ox})_1 = 0.097 \sigma_x + 1.525$
	$(E_p^{red})_1 = 0.448 \sigma_x - 1.432$	$(E_p^{red})_1 = 0.544 \sigma_x - 1.415$	$(E_p^{red})_1 = 0.537 \sigma_x - 1.435$
DCM	$(E_p^{ox})_1 = 0.077 \sigma_x + 1.529$	$(E_p^{ox})_1 = 0.079 \sigma_x + 1.517$	$(E_p^{ox})_1 = 0.067 \sigma_x + 1.513$
	$(E_p^{red})_1 = 0.576 \sigma_x - 1.477$	$(E_p^{red})_1 = 0.541 \sigma_x - 1.447$	$(E_p^{red})_1 = 0.514 \sigma_x - 1.442$
THF	$(E_p^{ox})_1 = 0.021 \sigma_x + 1.800$	$(E_p^{ox})_1 = 0.101 \sigma_x + 1.659$	$(E_p^{ox})_1 = 0.015 \sigma_x + 1.767$
	$(E_p^{red})_1 = 0.160 \sigma_x - 1.614$	$(E_p^{red})_1 = 0.165 \sigma_x - 1.560$	$(E_p^{red})_1 = 0.070 \sigma_x - 1.455$
DMSO	$(E_p^{ox})_1 = 0.054 \sigma_x + 1.307$	$(E_p^{ox})_1 = 0.0280 \sigma_x + 1.275$	$(E_p^{ox})_1 = -0.021 \sigma_x + 1.369$
	$(E_p^{red})_1 = 0.550 \sigma_x - 1.370$	$(E_p^{red})_1 = 0.581 \sigma_x - 1.388$	$(E_p^{red})_1 = 0.609 \sigma_x - 1.363$

Table 3.

It is obvious from equations in Table 3 that the magnitude of the oxidation constant ρ_x^{ox} is smaller than that of the corresponding reduction constant ρ_x^{red} . This indicates that the electroreduction is much more susceptible to substituent effect than electrooxidation. This fact implies that, there is more significant resonance interaction between the substituent and the reduction center (C = N group) in the triazole ring which is in good agreement with the proposed reduction of adjacent (C = N group).

To show the effect of solvent on the redox mode of the investigated compounds, the electrochemical characteristics of these compounds are extensively studied in 1, 2-dichloroethane (DCE), dichloromethane (DCM), acetonitrile (AN), tetrahydrofuran (THF) and dimethylsulfoxide (DMSO) with 0.1 mol dm⁻³ tetra-n-butylammonium perchlorate as supporting electrolyte. The effect of scan rate (V) on ΔE_p and I_p^c/I_p^a of the reversible reduction process is presented in Table 4, and Fig. 2 represents as example the cyclic voltammogram of both oxidation and reduction of these compounds. The voltammetric data are listed in Tables 1 and 2. As shown from the data and voltammograms (Fig. 1 and 2) compounds (1a-f) show that in the other used non-aqueous solvents; (DCE, DCM, THF and DMSO) the redox mechanism of all the investigated compounds seems to be like that in AN in which the oxidation occurs in a single irreversible one electron donating processes; forming cation radical followed by a proton removal from the 4-position in the pyrimidyl ring forming the unstable intermediate (radical) which tautomerize

and then dimerize to give the corresponding bis-compound (dimer) as in (Scheme 1).

On the other hand the reduction center in the investigated compounds seems to be the (C = N) in the triazole ring.^{13,14} These compounds are reduced in an irreversible one electron gain to form the anion-radical, which is basic enough to abstract a proton from the media^{17,19,20} forming the radical which undergoes tautomerization and then dimerization process to give also another bis-compound through N-N linkage formation (Scheme 1). The reversibility and irreversibility of reduction can be obtained from the presence of the reverse peaks in the cyclic voltammograms of compound 1c and 1 Fig. 2 and from the variation of the values of ΔE_p and I_p^c/I_p^a with scan rate (Table 4). The results show that the reduction process of both 1c and 1e satisfy the requirements of quasi-reversible mechanism in the three solvents at least at low scan rates. The substituents in these compounds will stabilize "to some extent" the intermediate. The formation of the radical-anion during the reduction has been proved by others.²⁴⁻²⁶ The verification and adjustment of the redox scheme will be established through controlled potential electrolysis which give us the possibility to separate and identify the final oxidation and reduction products. The analysis and the spectral data of the separated products are coincide with the structure of the products. No difference appears in the redox mode of these compounds (Series 1 and 2) by using either Pt, glassy C or Au electrodes. Generally it appears that, the peak current in the oxidation process is more or less higher at the Au-electrode than at the Pt-electrode which may be attributed to

Table 4. CV-voltammetric data for the compounds (1_c) and (1_e) in different solvents at Pt, glassy C and Au electrodes (at different scan rates).

Scan rate (mV/sec)	1 _c on Pt electrode								1 _e on glassy C electrode							
	AN		DCE		DCM		DMSO		AN		DCE		DCM		DMSO	
	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a	ΔE_p (mV)	I_p^c/I_p^a
30	117	1	138	1.135	152	1.013	126	1.2	112	1.1	128	0.83	126	1.034	155	1.24
50	112	0.95	168	1.28	155	1.03	134	0.9	97	1.17	143	0.946	143	1.143	259	1.08
70	112	0.98	173	1.236	172	0.984	90	1.07	97	0.97	153	0.88	149	1.27	174	0.93
90	121	0.976	189	1.243	193	0.986	154	1.16	97	1.09	143	0.865	166	1.29	135	1.13
100	97	1	178	1.013	188	0.84	110	0.82	92	1.02	163	1.095	187	0.866	98	1.2
200	121	1	229	1.19	234	0.94	130	1.02	107	1	204	0.893	206	1.28	106	1
300	91	1	275	1.15	265	0.91	126	0.98	97	0.987	219	1.178	211	1.14	118	1.012
400	132	1.03	280	1.142	290	1.047	138	0.97	102	1	244	0.973	252	1.03	106	1.077
500	131	1.02	320	1.087	316	0.905	138	0.9	102	1	249	0.964	263	1.04	118	0.94

Table 5. Difference in solvation energies of compounds (1a-f) in different solvents.

Solvent transition	Electrode	F(DE _p) _A - F(DE _p) _A in two different solvents					
		1a	1b	1c	1d	1e	1f
DCM‡DCE	Pt	F(11)	F(13)	F(31)	F(235)	F(46)	F(15)
	C	F(13)	F(30)	F(36)	F(82)	F(35)	F(32)
	Au	F(7)	F(86)	F(55)	F(55)	F(31)	F(87)
DCE‡AN	Pt	F(221)	F(242)	F(74)	F(88)	F(187)	F(331)
	C	F(218)	F(240)	F(224)	F(61)	F(211)	F(304)
	Au	F(219)	F(337)	F(191)	F(181)	F(162)	F(328)
DCM‡AN	Pt	F(232)	F(229)	F(43)	F(323)	F(233)	F(346)
	C	F(231)	F(210)	F(260)	F(143)	F(246)	F(272)
	Au	F(226)	F(251)	F(246)	F(236)	F(193)	F(241)

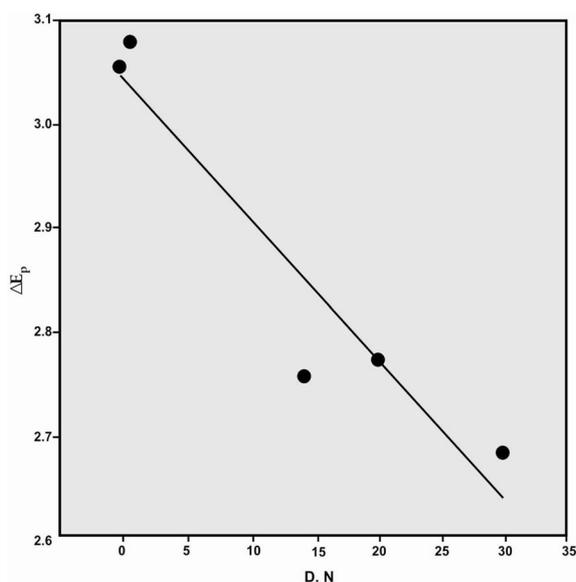


Fig. 4. Dependence of ΔE_p of compound 2d on the donor number of the solvents.

the complexing ability of the Au-electrode with the oxidation product of these compounds.²⁷⁻²⁹⁾

Increasing the donor number (DN)³⁰⁾ of the solvent makes both the oxidation and reduction of the triazolopyrimidines easier (Tables 1 and 2). This behavior can be attributed to the solvation effect, as already reported by many workers.^{31,32)}

According to the Born-Haber cycle,³³⁾ the E_p values for one triazolopyrimidine in two different solvents A and B and the solvation energies of the corresponding ions can be derived as follows:

$$\begin{aligned} F(\Delta E_p^{\text{ox}} - \Delta E_p^{\text{red}}) &= F\{[E_p^{\text{ox}}(\text{A}) - E_p^{\text{ox}}(\text{B})] - [E_p^{\text{red}}(\text{A}) - E_p^{\text{red}}(\text{B})]\} \\ &= F\{[E_p^{\text{ox}}(\text{A}) - E_p^{\text{red}}(\text{A})] - [E_p^{\text{ox}}(\text{B}) - E_p^{\text{red}}(\text{B})]\} \\ &= -\delta\Delta G_{\text{solv}}(\text{TD}^+, \text{A}) + \delta\Delta G_{\text{solv}}(\text{TD}^+, \text{B}) \\ &\quad -\delta\Delta G_{\text{solv}}(\text{TD}^-, \text{A}) + \delta\Delta G_{\text{solv}}(\text{TD}^-, \text{B}) \\ &= [\delta\Delta G_{\text{solv}}(\text{TD}^+, \text{B}) + \delta\Delta G_{\text{solv}}(\text{TD}^-, \text{B})] \\ &\quad -[\delta\Delta G_{\text{solv}}(\text{TD}^+, \text{A}) + \delta\Delta G_{\text{solv}}(\text{TD}^-, \text{A})] \end{aligned}$$

where TD represents the triazolopyrimidine derivative, $\delta\Delta G_{\text{solv}}$ is the differential Gibbs solvation energy, F is the faraday constant and $E_p^{\text{ox}} - E_p^{\text{red}} = \Delta E_p$ is the difference

between the oxidation and reduction peaks potential in the same solvent. According to the equation, when the solvent is changed the sum of the solvation energies is greater if the difference ΔE_p is smaller. As can be seen in Tables 1 and 2, ΔE_p for all the investigated triazolopyrimidines (1a-f and 2a-e) decreased when the solvent changed from 1, 2-dichloroethane to acetonitrile; i.e. the sum of the solvation energies increased which is in full agreement with the results obtained for hydrazyl.^{30,34)} This is in accordance with Gutmann's donor model.³⁰⁾ In all cases there is a linear relationship between the electrochemical parameters (E_p , ΔE_p and $\log k$) and the donor number (Fig. 4).

Accordingly, the sum of the solvation energies of a particular triazolopyrimidine in a given solvent depends on the donor number of the solvent. This suggests that solvation process is mainly attributable to electrostatic interaction. It is possible that the unusual results for the oxidation and reduction of all the investigated triazolopyrimidines in THF and DMSO is due to perturbation of the solvent by, for example, formation of an ion pair.³⁴⁻³⁶⁾ Also, the solvation of the formed ion radical of two different substituted triazolopyrimidines in the same solvent can be expressed as follows according to the principle of the cyclic process.³²⁾

$$F[E_p^{\text{ox}} - E_p^{\text{red}}]_{1b} - [E_p^{\text{ox}} - E_p^{\text{red}}]_{1c} = [\delta\Delta G_{\text{solv}}(\text{1b})^{\bullet} + \delta\Delta G_{\text{solv}}(\text{1b})^{\bullet-}] - [\delta\Delta G_{\text{solv}}(\text{1c})^{\bullet} + \delta\Delta G_{\text{solv}}(\text{1c})^{\bullet-}]$$

This can only be applied if $I(\text{R}) - E_A(\text{R})$ is a constant, where I is the ionization potential and E_A is the electron affinity.

Tables 1 and 2 show a regular increase in ΔE_p for the compounds using different solvents. Taking in consideration the allowed experimental error, the increase follows the order:

$$\begin{aligned} (\Delta E_p)_{1e} < (\Delta E_p)_{1c} < (\Delta E_p)_{1a} < (\Delta E_p)_{1d} < (\Delta E_p)_{1b} < (\Delta E_p)_{1f} \\ (\Delta E_p)_{2d} < (\Delta E_p)_{2a} < (\Delta E_p)_{2e} < (\Delta E_p)_{2c} < (\Delta E_p)_{2b} \end{aligned}$$

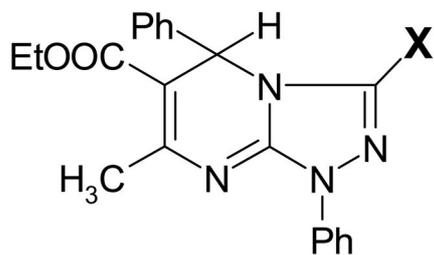
i.e. the sum of the solvation energies for compounds in the two series (1a-f) and (2a-e) increase in the order: (Tables 5 and 6)

$$1f > 1b > 1d > 1a > 1c > 1e ; 2b > 2c > 2e > 2a > 2d$$

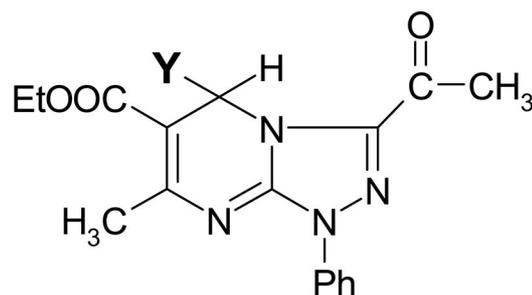
This can be explained from the fact that the substituents are far away from the oxidation center of the molecules due to tautomerization process see (Scheme 1), and they only affect the reduction process, which is in full agreements with the proposed mechanism. Accordingly, if it is assumed that

Table 6. Difference in solvation energies of compounds (2a-e) in different solvents.

Solvent transition	Electrode	$F(\Delta E_p)_A - F(\Delta E_p)_B$ in two different solvents				
		2a	2b	2c	2d	2e
DCM → DCE	Pt	F(11)	F(69)	F(23)	F(46)	F(52)
	C	F(13)	F(20)	F(48)	F(63)	F(22)
	Au	F(7)	F(5)	F(32)	F(32)	F(24)
DCE → AN	Pt	F(221)	F(190)	F(298)	F(210)	F(195)
	C	F(218)	F(191)	F(214)	F(213)	F(267)
	Au	F(219)	F(233)	F(221)	F(204)	F(215)
DCM → AN	Pt	F(232)	F(259)	F(321)	F(256)	F(247)
	C	F(231)	F(211)	F(262)	F(276)	F(245)
	Au	F(226)	F(233)	F(253)	F(236)	F(239)



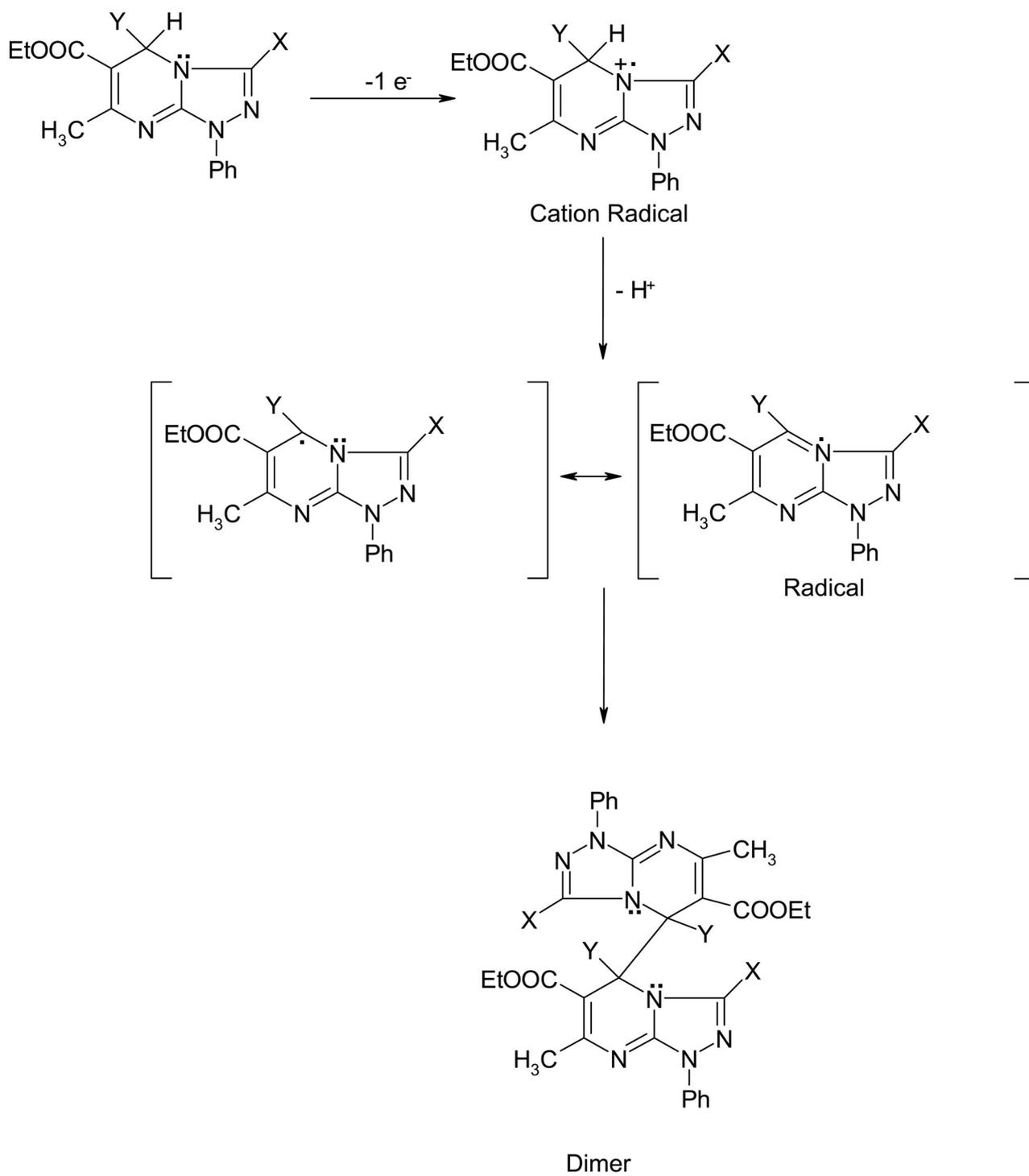
series 1



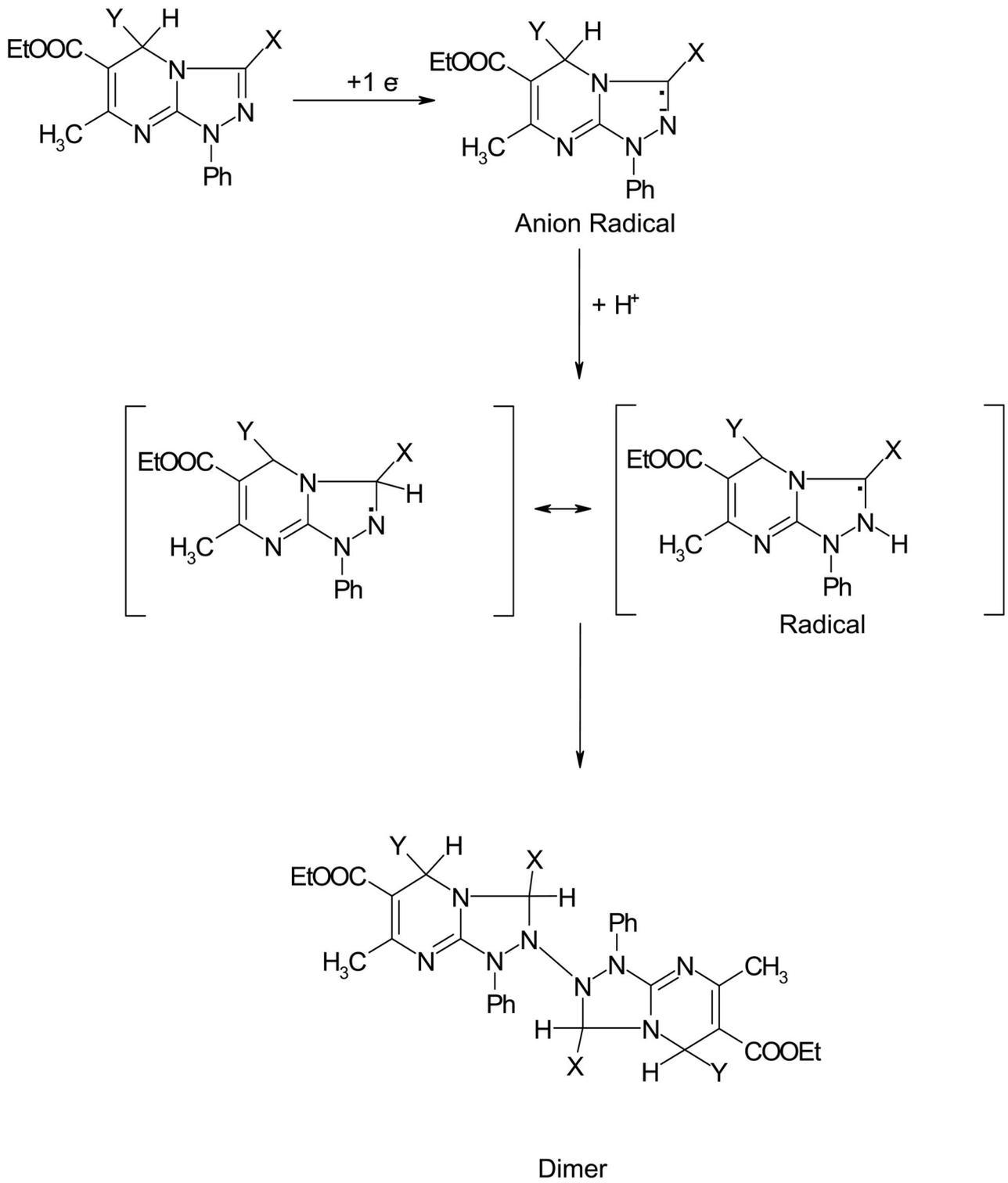
series 2

Compounds	Series 1	Compounds	Series 2
	X		Y
1a	COCH ₃	2a	Ph
1b	COOC ₂ H ₅	2b	
1c		2c	
1d		2d	
1e		2e	
1f	COOCH ₃		

● 1a and 2a is the same compound.



(Scheme 1 oxidation)



(Scheme 1 reduction)

the difference in the ionization potentials is small, the change of the solvation energies of the different investigated compounds in different solvents which obtained are listed in Tables 5 and 6. On the basis of substituent dependence it is expected that the oxidation potential will decrease, while the reduction potential will increase, when the substituent is less electronegative.

4. Conclusions

The electrochemical redox characteristics of some triazolopyrimidines of 1a-f and 2a-e are studied and the redox mechanism is suggested and proved.

All compounds are oxidized in a single irreversible one electron donating process following EC-mechanism to give a dimer. They are reduced in a single irreversible one electron step gives anion radical which abstract a proton from the media forming the radical which tautomertize and dimerizes through N-N linkage formation.

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References

1. F. A. Eid, A.H. Abd El-Wahab, *Acta pharm*, **54**, 13-26 (2004).
2. A. M. El-Agrody, M. H. El-Hakim, M. S. Abd El-Latif and K. A. El-Ghareeb, *Acta pharm*, **50**, 111-120 (2000).
3. Yasue H, Ogawa H, Tanaka H, et al. *Am J Cardiol*, **83**, 1308-1313 (1999).
4. Alfredo R. Galassi, C. Tamburino, A. Nicosia, G. Russo, R.Grassi, A. Monaco and G. Giuffrida, *Journal of Catheterization and Cardiovascular Interventions*, **46**, 162-168 (1999).
5. ASPECT Research Group. Effect of long-term oral anticoagulant treatment on mortality and cardiovascular morbidity after myocardial infarction. *Lancet*, **343**, 499-503 (1994).
6. M W H Behan and R F Storey, *Postgrad Med J*, **80**, 155-164 (2004).
7. A. Hirayama, K. Kodama, Y. Yui, H. Nonogi, T. Sumiyoshi, H. Origasa, S. Hosoda, C. Kawai and JMIC-M Investigators, *The American Journal of Cardiology*, **92**, 789-793 (2003).
8. Mest HJ. Trapidil : a potent inhibitor of platelet aggregation. *J Drug Dev*, **3**, 143-149 (1990).
9. A. O. Abdelhamide unpublished work, chem. Dep. Fac. of science, Cairo uni (2005).
10. M.Walter and L. Rumolay, *Anal.Chem.*, **45**, 165 (1973).
11. Privat Communication, J. Heinze, Chr. Heyne, H. Magg, F. Strohbuch Suttinger, Freiburg (1976).
12. G. M. Abou-Elenien, *J. Electroanal. Chem.*, **345**, 303 (1993).
13. G. M. Abou-Elenien, A. A. El-Maghraby and H. R. Abdel-Tawab, *Electroanalysis*, **13**(7), 587 (2001).
14. G. M. Abou-Elenien, N. A. Ismail, A. A. El-Maghraby and G. M. Al-Abdallah, *Electroanalysis*, **13**(12), 1022 (2001).
15. J. E. O'Reilly and P. J. Elving, *J. Electroanal. Chem.*, **75**, 507-532 (1977).
16. R. Battistuzzi, M. Borsari, D. Dallari, G. Gavioli, C. Tavagnacco and G. Costa, *J. Electroanal. Chem.*, **368**, 227-234 (1994).
17. I. Navarro, M. Rueda, G. Ramirez and F. Prieto, *J. Electroanal. Chem.*, **384**, 123 (1995).
18. G. M. Abou-Elenien; A. O. Abdelhamide; N. A. Ismail; A. A. EL-Maghraby and M. A. I. EL-Hamadi, (The Electrochemical Society of Japan) **69**(9), 652-658 (2001).
19. G. M. Abou-elenien, *J. Electroanal. Chem.*, **375**, 301 (1994).
20. G. M. Abou-Elenien, N. A. Ismail and A. A. El-Maghraby, *Electrochimica Acta*, **36**, 927 (1991).
21. V. Gutmann and R. Schmid, *Monatsh. Chem.*, **100**, 2113 (1969).
22. J. E. O'Reilly and P. J. Elving, *J. Electroanal. Chem.*, **75**, 507-532 (1977).
23. H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).
24. P. E. Iversen, *synthesis*, **484** (1972).
25. Y. Zhang, D. K. Gosser, Jr., P. H. Rieger, D. A. Swiegart *J. Am. Chem. Soc.* **113**, 4062 (1991).
26. A. J., Bard, L. R. Faulkner, *Electrochemical. Methods*, 1st ed. John. Wiley and sons: New York (1980).
27. Th. Wandlowski, P. chaiyasith and H. Baumgartel, *J. Electroanal. Chem.*, **346**, 271 (1993).
28. R. Gabert, H. Baumgartel, *J. Electroanal. Chem.*, **183**, 315 (1985).
29. R. Gabert, H. Baumgartel, *J. Electroanal. Chem.*, **185**, 147 (1985).
30. V. Gutmann, *Monatsh. Chem.*, **104**, 990 (1973).
31. I. V. Nelson and R. T. Iwamoto, *Anal. Chem.*, **33**, 1795 (1961).
32. V. Gutmann and R. Schmid, *Monatsh. Chem.*, **100**, 2113 (1969).
33. B. Case, N. S. Hush and R. Parsons, *J. Electroanal. Chem.*, **10**, 360 (1965).
34. G. M. Abou-Elenien, *J. Electroanal. Chem.*, **345**, 303-321 (1993).
35. S. Patai (ed.), "The Chemistry of Ether Linkage", Interscience, London, Ch. 6. (1967).
36. S. Searles Jr. and M. Tamres, "Basicity and Complexing Ability of Ethers" Interscience London, pp. **295** (1967).