

Polarographic Behaviour of α - and γ -Substituted Acetoacetanilide Derivatives in Alcoholic Aqueous Media

M. A. Aboutabl, M. F. Abo El-Ghar, and H. M. Fahmy*

Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt

Abstract. A polarographic study on a series of newly synthesized compounds, namely N-(3'-pyridyl)-2,3-dioxobutanamide-2-arylhydrazones (**1 a–f**) in a wide range of *pH* is reported and discussed. CPE indicated that these compounds are reduced in the hydrazono form. A scheme is proposed and confirmed through isolation and identification of 2,5-dimethyl-3,6-di[N-(3'-pyridyl)amide]-1,4-dihydro-pyrazine as an electrolysis product.

Keywords. Polarography; Acetoacetanilides, polarography of.

Das polarographische Verhalten von α - und γ -substituierten Acetoacetanilid-Derivaten in alkoholisch-wässrigem Medium

Zusammenfassung. Es wird über eine polarographische Untersuchung einer Reihe von neu synthetisierten Verbindungen, die N-(3'-pyridyl)-acetoacetamid- α -arylhydrazone **1 a–f**, in einem weiten *pH*-Bereich berichtet. Kontrollierte Potential-Elektrolyse (CPE) zeigte, daß diese Verbindungen in ihrer Hydrazonoform reduziert werden. Es wird ein Reaktionsschema vorgeschlagen und auch mit der Isolierung und Identifizierung von 2,5-Dimethyl-3,6-di[N-(3'-pyridyl)amid]-1,4-dihydropyrazin als Elektrolyseprodukt belegt.

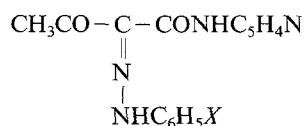
Introduction

Our group has been involved for some time in investigations dealing with the electroactivity of the hydrazone linkage at the DME [1–4]. Recently the azo-hydrazone tautomerisation attracted our attention [5, 6]. In the course of our work the actual location of the hydrazono linkage in a molecule of specific configuration seemed of great value in the estimation of its electrochemical behaviour. In continuation we report the polarographic behaviour of N-(3'-pyridyl)-2,3-dioxobutanamide-2-arylhydrazones (**1 a–f**), in which the hydrazono moiety is linked between a carbonyl (CO) and an amide(CONH) group in a parent basic molecule (pyridine ring).

Experimental

N-(3'-pyridyl)-2,3-dioxobutanamide-2-arylhydrazones (**1 a–f**)

1 g N-(3'-pyridyl)-3-oxobutanamide and 1.5 g sodium acetate were dissolved in 30 ml ethanol and cooled in an ice-bath. The cold solution was stirred and treated gradually with an equimolecular



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- 1 a, X = H 1 d, X = 4 - OCH₃
 1 b, X = 3 - CH₃ 1 e, X = 4 - Cl
 1 c, X = 4 - CH₃ 1 f, X = 3 - NO₂

amount of appropriate diazotized aromatic amine. The mixture was left for 1 h, then the precipitate was collected, washed and crystallized from the proper solvent; pertinent data are given in Table 1.

i-E Curves

All DC current-voltage curves were recorded on a Sefram X-Y recorder in conjunction with a Wenking POS 73 potentiostat.

Potentiostat and Its Auxiliaries

(a) For controlled potential electrolysis, a tutorial T6 transistorized potentiostat (Birmingham, England) was used.

(b) A laboratory valve voltmeter (type U 720 Elpo, Poland) was used to check the value at which the potential was controlled (accuracy of $\pm 2\%$).

(c) A universal avometer (model 6X mark III-Motwane Manufacturing, India) was used for recording the current of the current-time coulometric curves.

Table 1. Characteristic data of N-(3'-pyridyl)-2,3-dioxobutanamide-2-arylhydrazones (1 a-f)

Compound no.	-x	Formula (M)	M.p./°C Solvent	Yield %	Analysis (calcd./found)		
					C	H	N
1 a	H	C ₁₅ H ₁₄ N ₄ O ₂ (282.29)	124 dil. EtOH	82	63.82	5.00	19.85
					63.5	5.1	20.1
1 b	3-CH ₃	C ₁₆ H ₁₆ N ₄ O ₂ (296.32)	130 EtOH	85	64.85	5.44	18.91
					65.1	5.5	19.2
1 c	4-CH ₃	C ₁₆ H ₁₆ N ₄ O ₂ (296.32)	130 EtOH	85	64.85	5.44	18.91
					64.5	5.6	19.2
1 d	4-OCH ₃	C ₁₆ H ₁₆ N ₄ O ₃ (312.32)	165 EtOH	78	61.53	5.16	17.94
					61.8	5.4	18.3
1 e	4-Cl	C ₁₅ H ₁₃ N ₄ O ₂ Cl ^a (316.74)	176 EtOH	74	56.88	4.14	17.69
					57.1	5.4	18.0
1 f	3-NO ₂	C ₁₅ H ₁₃ N ₅ O ₄ (327.29)	212 AcOH	75	55.04	4.00	21.4
					54.7	4.3	21.7

^a Analysis of Cl calcd./found 11.20/11.4

pH-Meter

A pH-meter type Titrimeter T54N Prolabo (France) was used for measuring the *pH*-values.

Controlled Potential Electrolysis of N-(3'-pyridyl)-2,3-dioxobutanamide-2-phenylhydrazone (1a)

50 mg of **1a** was dissolved in 50 ml absolute ethanol and 30 ml of 0.1 N HCl. The potential was controlled at -0.74 V vs. SCE, the solution was deaerated with a stream of pure hydrogen gas which was present throughout the period of electrolysis. After approximately 3 h the colour changed from yellow to colourless and a polarogram was taken which showed the absence of any wave indicating that the starting compound was completely reduced. The electrolysis was then stopped and the solution was separated from the mercury and evaporated to $1/4$ of its original volume. The remaining solution was neutralized with a concentrated NaOH solution to $\sim pH$ 8 and evaporated till dryness on a waterbath. The obtained residue was washed carefully with petroleum ether ($60-80^{\circ}C$) to remove aniline, then the mixture was decanted and the remaining ether was evaporated. Finally, the residue was treated with distilled water to dissolve the sodium chloride present. The brown precipitate was collected through filtration and washed several times with distilled water. The obtained product (56% yield) was collected and identified as 2,5-dimethyl-3,6-di[N-(3'-pyridyl)amide]-1,4-dihydro-pyrazine; m.p. $300^{\circ}C$. Elem. anal.: found % (calcd.) for $C_9H_9N_3O$: C 61.2 (61.7), H 5.1 (5.1) (5.1), N 26.1 (24). IR in KBr ν/cm^{-1} : 3 550–3 000 broad band (NH), 1 660 (CONH), 1 600 (C=C). 1H NMR δ/ppm : NH (anilide) singlet at 12.9, aromatic and NH multiplet at 7.3–8.9, CH_3 singlet at 2.1. The disappearance of the CH resonance indicates the dimerization of the amino compound. On the other hand, an aniline standard spot test [7] gave positive results.

Results and Discussion*Nature of the Polarographic Waves A and B*

Routine analyses such as the effect of variation of Hg-height and concentration on the limiting current i_{1a} and i_{1b} indicated that waves A and B are controlled by diffusion. Also, logarithmic analyses (Tables 2 and 3) showed that these electrode processes are irreversible in nature as revealed from the values of αn and α .

Table 2. Half-wave potentials expressed in function of pH^a for compounds **1a-f** in 50% ethanolic Britton-Robinson buffers

Compound no.	Wave A	Wave B
1a	$E_{1/2}^b = -0.40 - 0.080 pH$	$E^{1/2} = -0.86 - 0.073 pH$
1b	$E_{1/2} = -0.41 - 0.081 pH$	$E_{1/2} = -0.85 - 0.073 pH$
1c	$E_{1/2} = -0.43 - 0.079 pH$	$E_{1/2} = -0.90 - 0.069 pH$
1d	$E_{1/2} = -0.42 - 0.078 pH$	$E_{1/2} = -0.86 - 0.072 pH$
1e	$E_{1/2} = -0.39 - 0.076 pH$	$E_{1/2} = -0.90 - 0.065 pH$
1f	$E_{1/2} = -0.42 - 0.080 pH$	distorted ^c

^a Equations valid in the pH range 2–12

^b $E_{1/2}$ are expressed vs. SCE

^c Due to the interference of the wave with the wall of the supporting electrolyte

Table 3. Logarithmic analysis data of *N*-(3'-pyridyl)-2,3-dioxobutanamide-2-arylhydrazones **1 a-f** on wave A in ethanolic Britton-Robinson buffers

Compound no.	<i>pH</i> ^a	<i>R T</i> / <i>α nF</i> ^b	<i>α n</i>	<i>α</i> ^c (<i>n</i> = 4)
1 a	3.55	0.053	1.12	0.28
	7.81	0.069	0.86	0.22
	11.30	0.036	1.64	0.41
1 b	3.48	0.044	1.34	0.34
	6.87	0.055	1.07	0.27
	11.48	0.047	1.26	0.32
1 c	3.60	0.048	1.23	0.38
	6.76	0.047	1.26	0.32
	11.16	0.040	1.48	0.37
1 d	3.20	0.054	1.09	0.27
	7.20	0.049	1.21	0.33
	11.60	0.031	1.91	0.48
1 e	2.93	0.061	0.97	0.27
	7.19	0.059	1.00	0.25
	11.47	0.037	1.60	0.40
1 f	3.60	0.027	2.19	0.55
	7.01	0.067	0.88	0.22
	11.56	0.046	1.28	0.32

^a Individual *pH* values at which logarithmic analysis was carried out

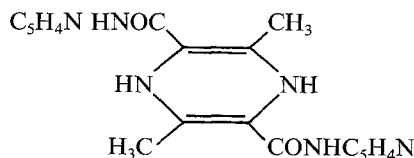
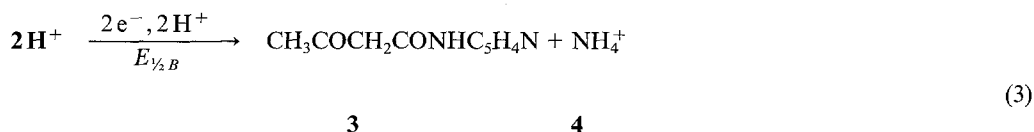
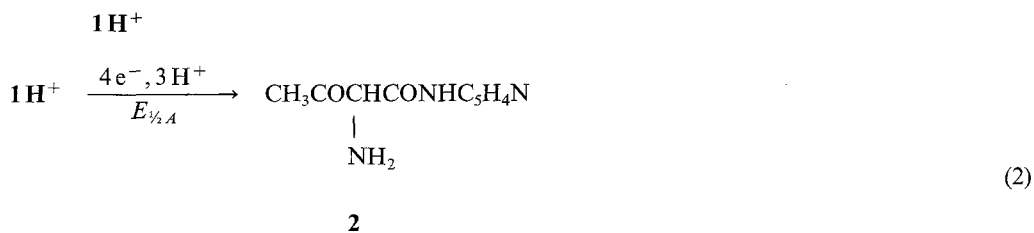
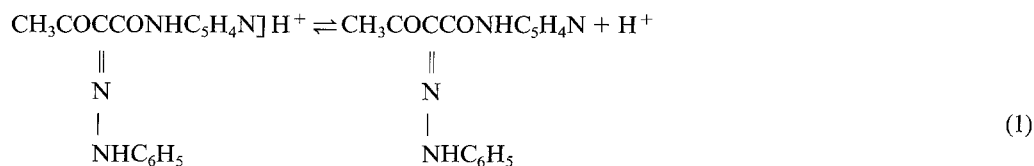
^b Slope of logarithmic analysis

^c Transfer coefficient

Assignment of Waves A and B of Compounds 1 a-f

The behaviour of wave A is in good agreement with the reported behaviour of compounds containing the hydrazone linkage [8–11] and different from those containing the azo-N=N-moiety [12–14]. Thus the magnitude of their $E_{1/2}$ values are within the limits of those of aromatic acyclic hydrazones, but more negative than those of azo compounds. This interpretation is confirmed by the fact that the wave corresponding to the reduction of the nitro moiety in **1 f** appeared prior to wave A; if an azo function was the reducible species the nitro wave should appear at more negative potential [8]. On the other hand, the two electron irreversible diffusion controlled wave B which appeared in **1 a-f** could only be assigned for either (i) the cleavage of the C–NH₂ bond in the product of the first process wave A or (ii) the electroreduction of the acetyl carbonyl in N-(3'-pyridyl)-2-amino-3-oxobutanamide. Assignment (ii) was rejected since N-(3'-pyridyl)-acetoacetamide was found to be inactive under the same experimental conditions. Furthermore, the resulting electrolysis of a sample solution of $2 \cdot 10^{-4}$ M **1 a** in acid medium at *pH* ~ 2 gave a positive ammonium ion spot test [15] indicating that in wave B the cleavage of the C–NH₂ bond occurs [16]. These results are in accordance with those previously reported by Shawali et al. for 3-phenyl-3-oxopropanilide-2-arylhydrazone [17], whereas Malik et al. reported that 2,3,4-pentanetrione-3-arylhydrazone gave only one 4 electron wave [18].

Based on the foregoing results, and isolation and identification of 2,5-dimethyl-3,6-di-N-(3'-pyridyl)-amide-1,4-dihydro-pyrazine as main product of electrolysis, Scheme 1 is suggested for the electro reduction of **1 a-f** in acid media.



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Scheme 1

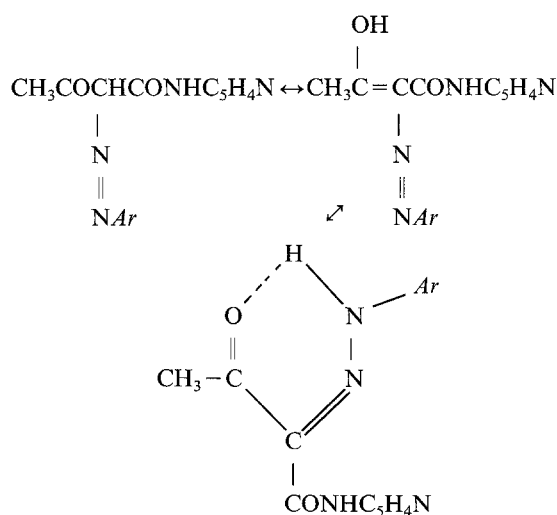
The protonation/deprotonation step in Eq. (1) is confirmed from the $dE_{1/2}/dpH$ dependency of **1 a-f** which assumes the preprotonation of the molecule prior to its reduction according to [19]

$$dE_{1/2}/dpH = (RT/\alpha nF)p,$$

where p is the number of protons. Using the proper values of αn as obtained from the slopes of logarithmic analysis will give a value of ~ 1 which is usually the number of protons in preprotonation of the molecule in the bulk of solution.

The inactivity of **3** has been confirmed by running an authentic sample of N-(3'-pyridyl)-acetoacetamide under the same experimental conditions which showed that **3** is polarographically inactive at the DME. This is in accordance with acetoacetanilide **6** which is also inactive. It is important to mention that while **3** and **6** are inactive, benzoyl- (**7**) and naphthoyl- (**8**) acetanilides [20, 21] are electrochemically active. This can be rationalized for by the fact that the conjugation of

the carbonyl (CO) with the aromatic ring facilitates its reduction. That 2-amino-N-(3'-pyridyl)-3-oxobutanamide was not obtained as product of electrolysis at $pH \sim 2$ and only the cyclized product **5** was the main product can be explained by the fact that on evaporation of the solvent reaction (4) occurred [22]. Finally, the detection of ammonia using Nessler's reagent (spot test) [15] confirms step (3), a similar reductive splitting for the protonated amino group has been reported in literature [16]. It remains that usually hydrazones are reduced in acid medium or in both media when the hydrazono NH is ionizable. It was thus found mandatory at this stage to see whether these hydrazones are ionizable or not, and therefore we tried to calculate their pK_a values through UV scanning and potentiometric titrations. The results indicated that these molecules are stable and unionizable in the studied pH limits (~ 2 – 12). This can only be explained by the fact that the NH of the hydrazono linkage is stabilized by tautomerization (Scheme 2).



Scheme 2

Table 4. Diffusion coefficients of compounds **1 a–f** in ethanolic Britton-Robinson buffers ($c=0.1 \text{ mM}$, $m=1.3 \text{ mg s}^{-1}$, $t=2.75 \text{ s drop}^{-1}$, $n=4 e^-$ for $h=50 \text{ cm}$)

Compound no.	Average i_t (μA)	Diffusion coefficient (D) ($\text{cm}^2 \text{ s}^{-1}$)
1 a	0.8072	$4.09 \cdot 10^{-6}$
1 b	0.7333	$3.37 \cdot 10^{-6}$
1 c	0.8266	$4.29 \cdot 10^{-6}$
1 d	0.7981	$4.00 \cdot 10^{-6}$
1 e	0.8318	$4.34 \cdot 10^{-6}$
1 f	0.6225	$2.43 \cdot 10^{-6}$

Therefore, it may be concluded that these molecules are basic in nature due to the presence of the pyridyl ring and therefore are even protonated in alkaline media and thus are reduced within the whole *pH* range with *pH*-independent limiting current.

To terminate this work it was found of value to calculate the diffusion coefficients of all studied compounds to obtain final consistent electrochemical data. Thus, using the Ilkovic equation [23–25], the diffusion coefficients were computed and compiled in Table 4. The obtained values are of the order $10^{-6} \text{ cm}^2 \text{ s}^{-1}$ which are more or less compatible with molecules having related structure and similar molecular weights [12, 18, 26].

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