© *Proc. Indian natn. Sci. Acad.*, 52, A, No. 2, 1986, pp. 521–530.
Printed in India.

POLAROGRAPHIC BEHAVIOUR OF SOME ARYLAZOGUANYLPYRAZOLE NITRATES

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(*Received 17 February 1986*)

Polarographic reduction of arylazoguanylpyrazole nitrates takes place in a 2-electron transfer, giving a diffusion controlled irreversible wave in B. R. buffers of *p*H range 2.0–11.0. For evaluating the mechanistic steps, orientation at d.m.e. and assigning inner or outer sphere path of electrode process, studies have been carried out in the presence and absence of surfactants. Results have been explained on the basis of formation of phenylazo-functionalised surfactant as an intermediate species.

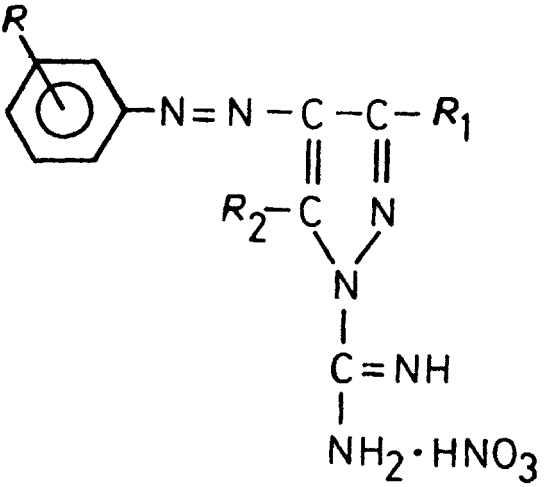
Key Words : Polarography; Potential Antidiabetic; Reduction; Pyrazoles Hammett Equation; Surfactants

INTRODUCTION

DRYHURST in a review of the electrochemistry of some biologically interesting organic molecules provides an excellent illustration of how modern electrochemical techniques can provide biologically significant informations. The ongoing studies of McCreery and coworkers on the electrochemistry of phenothiazine tranquilizer drugs[2–6] represent examples of the biologically relevant information which can be deduced from electrochemical studies. An underlying rationale for my studies on the electrochemical reduction of biologically important N-heterocyclic molecules is that such studies can lead to information bearing on the reaction routes and mechanisms of biological redox reactions. One of the various reasons for investigating the electrochemical behaviour of biologically important compounds is the development of possible correlation based on the mechanistic paths involved and the characteristic potentials associated with them, e.g., half-wave potentials, are a function of electron density and other factors, which are simply related to some biological, clinical, physical, or chemical property and activity.[7,8] The resulting linear relationship between $E_{1/2}$ for a series of closely related compounds allows prediction of the magnitude of the property of a compound from its easily determined $E_{1/2}$. Moreover, correlation of $E_{1/2}$ with structural reactivity, and other characteristics may provide a better understanding of the structure on the redox behaviour of the compounds.*

Keeping this in view it was considered worthwhile to study critically the electrochemical behaviour of some potential antidiabetic[9,10] 4-arylazo-N-guanyl-3 methyl/phenyl-5-methyl/phenylpyrazole nitrates (A) at D.M.E. with special reference to the effect of substituents in the phenyl ring as well as in the pyrazole ring on their redox mechanism involved therein.

*See Ref. 16.



(A)

where R represents various substituents.

$R_1 = CH_3$ or C_6H_5, $R_2 = CH_3$ or C_6H_5

Experimental

4-Arylazo-N-guanyl-3-methyl/phenyl-5-methyl/phenylpyrazole nitrates having substituent in the benzene ring, viz., H, 2-CH_3, 4-CH_3 , 2-Cl, 4-Cl, 2-OCH_3, 3-OCH_3, 4-OCH_3, 2-OC_2H_5 and 4-OC_2H_5 were prepared by the literature method.[10] All the compounds were recrystallised from DMF-water mixture. Their purity was ascertained by TLC.

Reagents and Solutions

The stock solutions (1.0×10^{-3}M) of all the compounds were prepared in DMF. Britton-Robinson buffers in the *p*H range 2.0–11.0 and 1.0M KCl, 0.01M cetyltrimethyl ammonium bromide (CTAB) were prepared in doubly distilled water. All the chemicals and solvents used were of A.R. grade. Solutions for polarographic measurements were prepared by mixing 1.0ml of the compound, 2.0ml of DMF (which was necessary to keep the compound in solution), 1.0ml of 1.0M KCl and 6.01ml. of the appropriate B.R. buffer. Polarograms were than recorded by adding CTAB 0.1ml to 1.0ml to each solution. Dissolved oxygen was removed from the solution by passing purified nitrogen gas for about 10.0 min.

Apparatus

Polarograms were recorded on an ELTICO DC CL-25 recording polarograph. The capillary characterstics were $1.55 mg^{2/3}\ S^{-1/2}$ at $h = 45$cm at a zero applied potential in 1.0M KCl solution. The temperature of the solution was maintained

at 25 + 0.2 °C by keeping the polarographic cell in a thermostatic bath. The *p*H metric measurements were made on the Expanded Scale LI 10 *p*H meter with glass electrodes. The electronic spectra of the solution during electrolysis were recorded at different time intervals on a UV-VIS Carl Zeiss Spectrophotometer. Saturated Calomel Electrode was used as the reference electrode. Temperature coefficient was calculated by the Nejedly's method.[11] The number of electrons, *n*, involved in the reduction was determined by the method of Devries and Kroon[12] using a mercury pool cathode. Azobenzene was used as the reference depolarizer for the evaluation of the values of '*n*' of arylazoguanylpyrazole nitrate. The formula used was :

$$n_2 = n_1 \left(\frac{i_d \text{ (azobenzene)}}{i_d \text{ (azobenzene)}} \right) \left(\frac{i_d \text{ (sub.)}}{i_d \text{ (sub.)}} \right) \frac{V_1 C_1}{V_2 C_2},$$

where i_d (azobenzene) is the original diffusion current for azobenzene V_1, C_1 and Δi_d (azobenzene) are its volume, concentration and change in the diffusion current after electrolysis. i_d (sub.), V_2, C_2 and Δi_d (sub.) are corresponding quantities for the substance. The controlled potential electrolysis was carried out in a potential corresponding to the plateau of the wave. After complete electrolysis (12hr) the catholyte was subjected to product analysis.

Results and Discussion

All the compounds (I–XXX) gave a single 2*e* reduction wave in B.R. buffers of *p*H range 2.0–11.0. The nature of the wave was diffusion-controlled as shown by the linear dependence of limiting current on $1/h$ and the concentration of depolarizer. The constancy of wave height in the *p*H range studied, together with the fact that temperature coefficient[13] had low values (1.3–1.52 per cent deg.) further confirmed that the reduction waves were fully diffusion controlled. The wave characteristics are compiled in Table I. The half-wave potentials of these compounds were found to be dependent on *p*H and shifted towards more negative potential with increase in *p*H. The plots of $E_{1/2}$ *vs* *p*H were linear with slopes in the range 0.052 to 0.060 V/*p*H upto *p*H 9.0, thereafter, there was a small change in $E_{1/2}$ and the values of the slope was significantly small. The irreversible nature of the waves was confirmed by log plots.[13] The fact that $E_{1/2}$ shifted towards more negative potential with increasing concentration of depolarizer further points towards the irreversible nature of the waves.

The possible reduction sites in these compounds are —N = N— and —C = N—. Out of these, the former is more susceptible[14] to reduction than the latter as it will require a much higher negative potential for reduction. The value of *n* and *p* were determined as usual[13] and on the basis of number of electrons and protons involved in the rate determining step and overall electrode process a mechanism for the reduction of above azo compounds may be proposed as reported elsewhere[15,25] :

Effect of Substituents

For evaluating the effect of substituents, the compounds under investigation were classified in the following manner: 4-arylazo-N-guanyl-3,5-dimethylpyrazole

TABLE I

Polarographic characteristics of some arylazoguanylpyrazole nitrates at pH 8.2
Compounds I—X, $R_1 = R_2 = CH_3$; XI—XX, $R_1 = CH_3$, $R_2 = C_6H_5$; XXI–XXX, $R_1 = R_2 = C_6H_5$ (Concn. 1.0×10^{-4}m.)

No.	R	$-E_{1/2}$, V	$\Delta E_{1/2}$, V	$i_d/\mu A$	$\frac{dE_{1/2}, V}{dpH\,pH}$	αn
I	H	0.67	0.00	0.80	0.055	0.65
II	2-CH_3	0.66	0.01	0.85	0.052	0.63
III	4-CH_3	0.69	0.02	0.85	0.052	0.63
IV	2-Cl	0.63	0.04	0.85	0.055	0.65
V	4-Cl	0.66	0.01	0.80	0.055	0.61
VI	2-OCH_3	0.69	0.02	0.84	0.054	0.62
VII	3-OCH_3	0.69	0.02	0.84	0.055	0.65
VIII	4-OCH_3	0.70	0.03	0.80	0.052	0.65
IX	2-OC_2H_5	0.68	0.01	0.85	0.052	0.63
X	4-OC_2H_5	0.71	0.04	0.85	0.052	0.65
XI	H	0.71	0.00	0.88	0.057	0.69
XII	2-CH_3	0.71	0.00	0.91	0.055	0.69
XIII	4-CH_3	0.73	0.02	0.90	0.055	0.68
XIV	2-Cl	0.66	0.05	0.90	0.052	0.69
XV	4-Cl	0.69	0.02	0.92	0.055	0.71
XVI	2-OCH_3	0.71	0.00	0.90	0.054	0.69
XVII	3-OCH_3	0.72	0.01	0.90	0.055	0.71
XVIII	4-OCH_3	0.75	0.04	0.92	0.055	0.71
XIX	2-OC_2H_5	0.70	0.01	0.92	0.057	0.69
XX	4-OC_2H_5	0.73	0.02	0.90	0.055	0.69
XXI	4	0.77	0.00	1.00	0.054	0.72
XXII	2-CH_3	0.75	0.02	1.00	0.057	0.75
XXIII	4-CH_3	0.79	0.02	0.95	0.058	0.75
XXIV	2-Cl	0.73	0.04	0.95	0.058	0.70
XXV	4-Cl	0.76	0.01	1.00	0.054	0.70
XXVI	2-OCH_3	0.78	0.01	1.05	0.060	0.75
XXVII	3-OCH_3	0.78	0.01	1.07	0.058	0.77
XXVIII	4-OCH_3	0.81	0.04	1.00	0.054	0.70
XXIX	2-OC_2H_5	0.76	0.01	0.95	0.058	0.70
XXX	4-OC_2H_5	0.80	0.03	1.05	0.054	0.72

nitrate was chosen as the parent substance of compounds I–X, further 4-arylazo-N-guanyl-3-methyl-5-phenylpyrazole nitrate and 4-arylazo-N-guanyl-3,5-diphenylpyrazole nitrate were selected of compounds XI–XX and XXI–XXX respectively. Since the values of αn, $dE_{1/2}/dpH$ are practically constant for all compounds of the series, indicating that their reduction is taking place by the same mechanism and therefore, the conditions for the application of Hammett equation are fulfilled[16]. The $E_{1/2}$ of substances I–X, XI–XX and XXI–XXX were plotted against the values of Hammet substituent constant (σ). The values of σ_{o-} were taken from the literature[17] The linear plots of $E_{1/2}$ *vs* σ in B.R. buffer of *p*H 8.2, for the three series are depicted in Fig.1. In these plots and para derivatives fit in the straight line in all cases, whereas *ortho* derivatives deviate from the straight line. The values of the specific reaction constant (ρ) obtained from these plots are 0.11V,

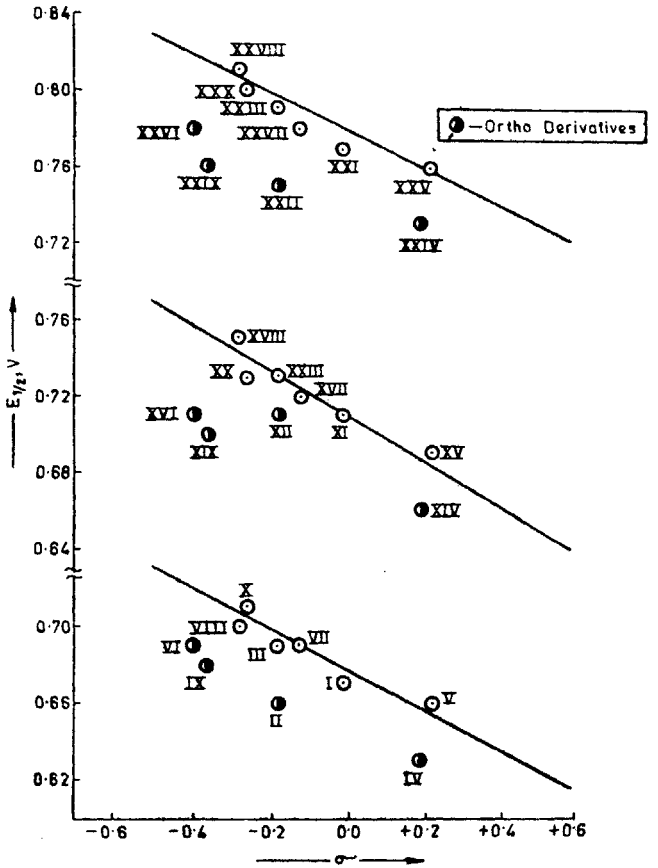


FIG 1 Plot of $-E_{1/2}$ *vs.* σ for arylazoguanylpyrazole nitrates at *p*H 8.2.

0.12V and 0.10V for compounds I–X, XI–XX and XXI–XXX respectively. For the ortho derivatives the corrected values of $E_{1/2}$ were obtained from the relationship[16]

$$(E_{1/2})\ \text{corr.} = E_{1/2} - [\delta\pi,\ R(Es)_{o-x}],$$

where steric reaction constant ($\delta\pi$, R) is

$$\delta\pi,\ R = (\Delta E_{1/2} - \rho\pi,\ R\sigma_{o-x})/(Es)_{o-x}.$$

The plot of corrected $E_{1/2}$ *vs* o gave a straight line in which ortho derivatives also fall on the regression lines. The practically identical values of the specific reaction constant for all the three series indicate that observed values of ρ are similar to those found for other azobenzenes and fit the $\rho - E_H^0$ plot. Furthermore, the positive values of ρ can be regarded as evidence[18] that the mechanism of the electrode process is nucleophilic.

Comparison of values of $E_{1/2}$ for I, XI and XXI show that the replacement of methyl group by phenyl group in pyrazole ring shifts the $E_{1/2}$ towards more negative potential (Table I). This effect is slightly more marked when the two methyl groups at position 3 and 5 are replaced by phenyl groups. Polarographic ortho shift ($\Delta 0$)[19] was determined at different *p*H values for various groups viz., methyl, methoxy, chloro and ethoxy, and are given in Table II. All compounds show positive polarographic shift indicating that *ortho* substituted compounds undergo reduction more easily than the corresponding para substituted analogues. Polarographic *ortho* shift was found to be independent of *p*H in the entire reaction series.

Effect of supporting electrolyte concentration, cations and anions and solvent was found to be similar as reported earlier for other series of azo compounds.

TABLE II

Values of polarographic ortho shift (ΔO) *for arylazo-guanylpyrazole nitrates at pH* 8.2
(Concn. 1.0×10^{-4}M)

R	R_1	R_2	$\Delta O/V$
Methyl	CH_3	CH_3	0.03
Chloro	CH_3	CH_3	0.03
Methoxy	CH_3	CH_3	0.01
Ethoxy	CH_3	CH_3	0.03
Methyl	CH_3	C_6H_5	0.02
Chloro	CH_3	C_6H_5	0.03
Methoxy	CH_3	C_6H_5	0.04
Ethoxy	CH_3	C_6H_5	0.03
Methyl	C_6H_5	C_6H_5	0.04
Chloro	C_6H_5	C_6H_5	0.03
Methoxy	C_6H_5	C_6H_5	0.03
Ethoxy	C_6H_5	C_6H_5	0.04

Effect of Surfactants

The electrochemical reaction at an electrode may either take place in the close vicinity of the electrode or a little far off from the electrode surface i.e. at 'Inner Helmholtz Plane' (IHP) or 'Outer Helmholtz Plane' (OHP). This distinction can be very well evaluated by carrying out reduction studies in the presence of strongly adsorbable substances.

Literature survey revealed that such studies have not been undertaken with organic compounds. Recently, we have reported[20,21] the polarographic reduction of a number of heterocyclic compounds without evaluating the mechanistic steps and their respective position at the d.m.e. during reduction.

For carrying out these studies polarograms were recorded in presence of differents amounts of CTAB (0.1–1.0ml). In presence of surfactant also, diffusion-controlled but more irreversible waves were obtained. $E_{1/2}$ of these waves were also *p*H dependent and the i_d remained *p*H independent. A perusal of the slope

values of log plots reveals that the irreversible reduction of above pyrazoles becomes more irreversible when the surfactant concentration is gradually increased and $E_{1/2}$ records a negative shift as their concentration is increased. The αn_a shows a decrease with the increase in surfactant concentration indicating that the transfer of electrons is made increasingly difficult. The decrease in the value of $K^0_{f,h}$ with increasing surfactant concentration lends support to this conclusion.

Rate of reduction (K_{app}) for both inner and outer sphere reduction at the mercury electrode surface is given by the equation[22]

$$\log K_{app} = \log \frac{i}{FCb},$$

where i is the current density at the rising part of the waves at a potential $-E$, Cb— the bulk concentration of the deplarizer and K_{app} the rate constant for reduction. In the presence and absence of CTAB, values of K_{app} for all these compounds were calculated and are given in Table II. The above equation can be used successfully to differentiate between the two paths by monitoring the changes in the K_{app} in absence and presence of surfactants. If surfactants cause some change in the values of K_{app} it may be taken as a proof of inner sphere path otherwise it indicates outer sphere path.

It may be further observed that for a particular solution of constant concentration of the depolarizer and the supporting electrolyte, the plot of log K_{app} (determined at various potentials $-E$ on the rising part of the wave) against $-E$ should be linear and is given by the equation[22]

$$\frac{\partial \log K_{app}}{\partial E} = \frac{\alpha}{2.303\,RT}\left(\frac{(\partial \Delta G^0_{AR} + F)}{\partial E}\right) - \frac{1-\alpha_1}{2.303\,RT}\left(\frac{\partial \Delta E^0_{AR}}{\partial E}\right).$$

Since the magnitude and sign of the free energy terms will significantly vary for an inner and outer sphere path, the value of α_{app} will also vary. The α_{app} values thus can be utilised to differentiate between the two paths. The values of α_{app} has been evaluated from the slopes of plots (Tafel plots) of k_{app} against—E, which gives:

$$\alpha_{app} = -\frac{2.303\,RT}{F}\left(\frac{\partial \log K_{app}}{\partial E}\right),$$

when values of α_{app} are above 0.5, the electrode process in assumed to be taking in outer sphere whereas lower values than 0.5 indicates inner sphere path. Hence, it is obvious that values of K_{app} and α_{app} for a particular compound may be utilised to distinguish between the inner and outer sphere path of the electrode reactions. K_{app} and α_{app} values for above compounds are given in Table III. On reviewing the data in Table III it appears that K_{app} as well as α_{app} decrease in the presence of surfactant indicating that reduction is taking place at the inner sphere of the electrode.

The lower rate (K_{app}) of the electrode process in the presence of cationic surfactant (CTAB) may be due to the formation of surfactant-depolarizer complex.

TABLE III

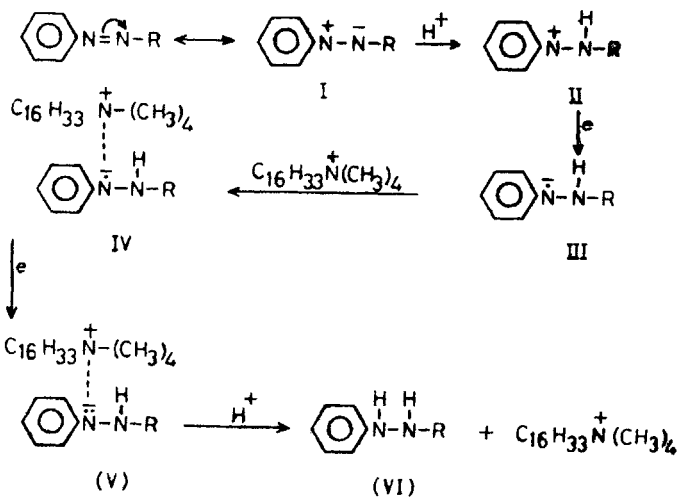
Values of $-\log K_{app}$ and α_{app} for electroreduction of some typical arylazoguanylpyrazole nitrates at pH 8.2 (Concn. 1.0×10^{-4}M)

R	R_1	R_2	$-\log K_{app}$ (cm^{-1})		α_{app}	
			(a)*	(b)**	(a)*	(b)**
H	CH_3	CH_3	0.27	0.31	0.36	0.41
4—CH_3	CH_3	CH_3	0.30	0.32	0.36	0.40
4—Cl	CH_3	CH_3	0 26	0.30	0.38	0.41
H	CH_3	C_6H_5	0.30	0.32	0.37	0.39
4—CH_3	CH_3	C_6H_5	0.32	0.33	0.38	0.41
4—Cl	CH_3	C_6H_5	0.28	0.34	0.37	0.42
H	C_6H_5	C_6H_5	0.31	0.35	0.36	0.40
4—CH_3	C_6H_5	C_6H_5	0.33	0.39	0.38	0.41
4—Cl	C_6H_5	C_6H_5	0.33	0.35	0.35	0.40

*(a) In the absence of surfactant.
**(b) In the presence of surfactant.

The surfactant micelles do not diffuse as such in the outer plane of the Helmholtz double layer but it is the surfactant-depolarizer complex which reaches the inner part of the double layer, orients itself towards electrode surface and subsequently get reduced. The possible mechanism may be as follows (H^+, e, e, H^+).[16]

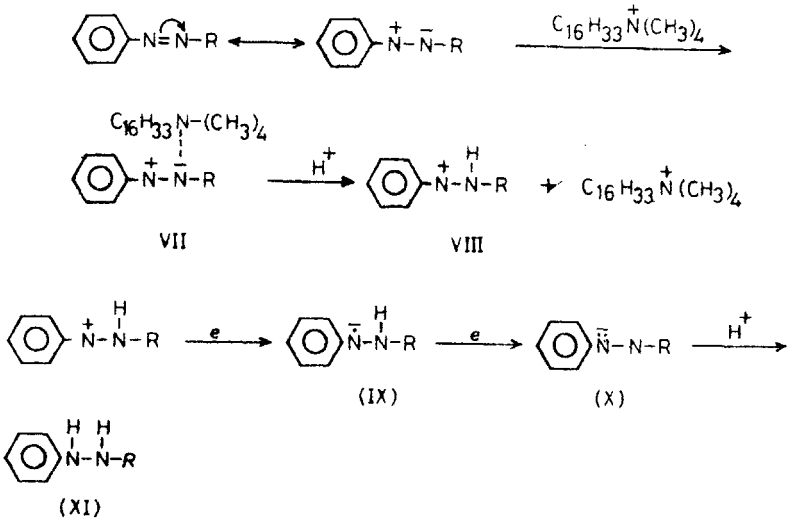
Mechanism I



In this mechanism free radical (III) form surfactant-depolarizer complex with cationic surfactant (CTAB). This surfactant-depolarizer complex may diffuse to the inner part of the double layer and get reduced to (IV) after the uptake of an electron and a proton, and releasing the surfactant as such.

This mechanism appears to be more probable due to the easy availability of species $C_6H_5-\overset{+}{N}-\overset{-}{N}-R$ in the solution. After the formation of phenylazo-functionalised[23,24] surfactant (VII) (formed by the interaction of depolarizer —N—N—group) it gets protonated to give protonated species (VIII). The protonated intermediate then reducts to (XI) similarly as in the case of mechanism 1.

Mechanism II



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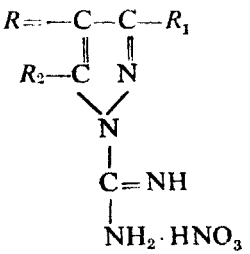

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