Polarographic Reduction and Tautomeric Structure of 2-Amino-5-arylazothiazoles

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The polarographic behaviour of a series of 2-amino-4-phenyl-5-arylazothiazoles has been investigated at a dropping mercury electrode. Each of the compounds studied exhibits one wave which was shown to correspond to the reductive cleavage of the azo linkage by a 4e irreversible step. On the basis of the polarographic data, it was concluded that the compounds exist only in one tautomeric form, namely the aminoazo structure **1**. The results of $E_{1/2} - \sigma_X$ correlations and HMO calculations of bonding energies of the various possible tautomeric forms **1-3** indicate that the aminoazo form **1** is the most stable structure of the compounds examined.

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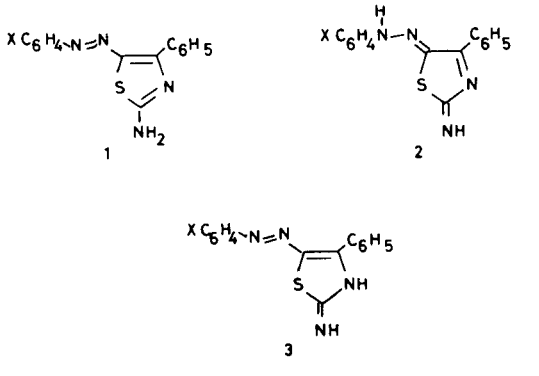
Introduction.

An enormous amount of research into the chemistry and properties of thiazole and benzothiazole has been reported [2-12] as many of their derivatives become important in pharmaceutical, biochemical and technical fields. Among the many products which have emerged are antibiotics [8], diuretics [8], antihistamines [8], anthelmintics [8], mitodepressives [9], mitostatics [9], antiparasitics [12], antiinflammatories [12], and antiviral [9]. Recent industrial uses encompass vulcanization accelerators and antioxidants [9], photochromics [10-12] and dyestuffs [10-12]. In spite of this, a literature survey revealed that the electroreduction of thiazole derivatives has received no attention until recently. To remedy this situation, we have studied the polarographic reduction of a series of 2-amino-4-phenyl-5-arylazothiazoles **1a-e**. Our objective was, on one hand, to elucidate the mechanism of the reduction of **1** at the dropping mercury electrode (dme), and on the other hand, to shed some light on the tautomeric structure of such compounds for which three tautomeric forms **1-3** can be written (Scheme 1). Also, it was desirable to examine the effect of substituents on the polarographic reactivity of such dyes. Such information will help in understanding the relation between the structure of these compounds and their biological and industrial properties.



a, X = p-CH_3O b, X = p-CH_3 c, X = H d, X = p-Cl e, X = m-Cl

Scheme 1

Results and Discussion.

Typical polarograms of **1c**, taken as an example of the series studied, in 50% (v/v) ethanolic buffered solutions of *p*H values ranging from 4.0 to 11.5 are reproduced in Figure 1. The polarograms of other compounds **1b-e** exhibit similar pattern. It is obvious that each compound gives one well defined wave in the *p*H range 4.0-11.5. The polarographic data of **1a-e** are summarized in Table 1. Besides the main reduction wave no other wave was obtained except for the hydrogen reduction wave which appears at -1.6 V *vs.* SCE. Keeping in mind the feasibility of the various reduction sites (namely N=C_2, C_4=C_5, and N=N) it may be inferred that the observed wave corresponds to the reduction of the azo group. The limiting current of the wave of each compound was found to decrease with increasing the *p*H of the solution. The decrease has the form of a dissociation curve (Figure 2). Also, the half-wave potential of the wave observed in each case is *p*H-dependent, it shifts towards more negative values with increasing the *p*H of the solution. The plots of $E_{1/2}$ *vs.* *p*H were linear. The equations of the regression lines obtained are given in Table 1. These results indicate that the group undergoing

Table 1

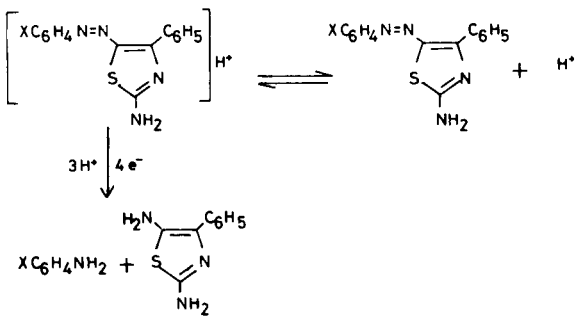
Data of Arylazothiazoles **1a-e**

Compound No.	$-E_{1/2} = a_o + a_1$ *p*H [a]	$-(RT/\alpha nF) \times 10$ [b]	*p*H [c]
1a	$-E_{1/2} = 0.220 + 0.05$ *p*H	0.207	7.62
1b	$-E_{1/2} = 0.159 + 0.0575$ *p*H	0.222	7.79
1c	$-E_{1/2} = 0.154 + 0.0575$ *p*H	0.213	6.44
1d	$-E_{1/2} = 0.075 + 0.062$ *p*H	0.241	7.62
1e	$-E_{1/2} = 0.039 + 0.064$ *p*H	0.231	7.83

[a] Equation valid in the *p*H range studied. [b] Slope of logarithmic analysis plots. [c] Individual *p*H value at which logarithmic analysis was carried out.

reduction in this electrode process is more difficult to be reduced in alkaline medium, and suggest the participation of hydrogen ions in the rate determining step of the electrode reaction.

To shed light on the nature of the cathodic wave of **1** the effects of mercury height and the molar concentration of **1** on the limiting current were also investigated. The results show that the wave observed is controlled by diffusion throughout the whole *p*H range, since the slope of the plot of log i *vs.* log h is about 0.5, and plots of current *vs.* molar concentration were straight lines passing through the origin. Logarithmic analysis of the wave at different *p*H values using the fundamental equation for polarographic waves [13] indicated that the electrode process is an irreversible one. The values of the slopes of such plots are given in Table 1. The present data indicate that the course of the polarographic reduction of **1** is different from that reported for arylhydrazones [15] and is closely related to the behaviour of azo compounds [14]. Thus, it is not unreasonable to exclude the tautomeric hydrazone structure **2** for the compounds studied. This conclusion is further substantiated by the results of the study of substituent effects and controlled potential electrolysis and by comparison of the values of the bonding energies of the possible tautomeric structures calculated by the Hückel molecular method (HMO) as outlined in the following section. As the number of electrons transferred in the electrode reaction was found to be four, the general reaction sequence shown in Scheme 2 can be proposed for the reduction of **1** at the dme. The first step represents protonation of **1** at the expense of the hydrogen ions from the solution and the second step represents the reduction of the protonated species of step 1. This sequence finds support from the results of controlled potential electrolysis. Thus, the electronic absorption spectrum of **1c** in ethanol exhibits two absorption maxima near 265 and 412 nm assignable to the π-π^* transitions of the thiazole and azo chromophores respectively. However, the product obtained from cpe experiment exhibits only one band at 278 nm. Also, the identification of aniline among the products of cpe by spot test and tlc confirms the reductive cleavage of the azo group.



Scheme 2

At a given *p*H value, the influence of substituents is as expected, *m*-chlorophenylazo derivative **1e** exhibits the most positive value of $E_{1/2}$, whereas the *p*-methoxy analog **1a** exhibits the most negative one. For a quantitative study of the substituent effects, the values of the half-wave potentials at any *p*H can be used because it was found that the value of the transition coefficient (αn) remains approximately constant at any given *p*H within the reaction series. This was ascertained by examination of the values of the slopes ($RT/\alpha nF$) of the linear plots obtained from the logarithmic analysis of the waves (Table 1). As for the majority of the polarographic reductions [16], the values of $E_{1/2}$ of the compounds **1a-e** were correlated with the Hammet substituent constants, σ_X, which were taken from the tabulation by Ritchie and Sager [17]. The results of the statistical treatment of the data by the least squares method [18] are summarized in Table 2. The values obtained from the reaction constant, ϱ, at different *p*H's have signs expected for a nucleophilic attack by electrons. The observed linear correlations between $E_{1/2}$ and σ_X, as evidenced by the correlation coefficients (Table 1) substantiate the conclusion that the compounds studied exist in one tautomeric form, namely **1**. The coexistence of other tautomeric forms in equilibrium with **1** would lead to nonlinear relations between $E_{1/2}$ and σ_X [19].

Table 2

Results of Statistical Treatment of $E_{1/2}$ Data with Hammett Equation [a]

*p*H	$E^X_{1/2} = -E^H_{1/2} + \varrho\sigma_X$	r [b]	± s [c]
6.0	$-E_{1/2} = -0.482 + 0.162\ \sigma_X$	0.995	0.005
7.0	$-E_{1/2} = -0.542 + 0.138\ \sigma_X$	0.992	0.005
8.0	$-E_{1/2} = -0.596 + 0.114\ \sigma_X$	0.990	0.005
9.0	$-E_{1/2} = -0.654 + 0.098\ \sigma_X$	0.962	0.008

[a] $E^X_{1/2}$ and $E^H_{1/2}$ are the half-wave potentials of the substituted and unsubstituted phenylazothiazoles respectively. [b] Correlation coefficient. [c] Standard deviation.

Also, the tautomeric hydrazone structure **2** and the iminoazo form **3** can be excluded on the basis of their lower bonding energies. HMO calculations have shown that the bonding energies of structures **1a**, **2a** and **3a** are 30.817 β, 30.614 β and 30.688 β, respectively [20,21]. It has been shown that only one tautomer exists when the value of $|\Delta(BE)_{A-H}/n|$ is greater than 0.002 β, where $\Delta(BE)_{A-H}$ is the difference in bonding energies of the azo (A) and hydrazone (H) forms and n is the number of π electrons in the system [22].

EXPERIMENTAL

5-Arylazo-4-phenyl-2-aminothiazoles **1a-e** were prepared by coupling the appropriate diazotized aniline to 2-amino-4-phenylthiazole as previously described [23]. The crude products were brought to analytical puri-

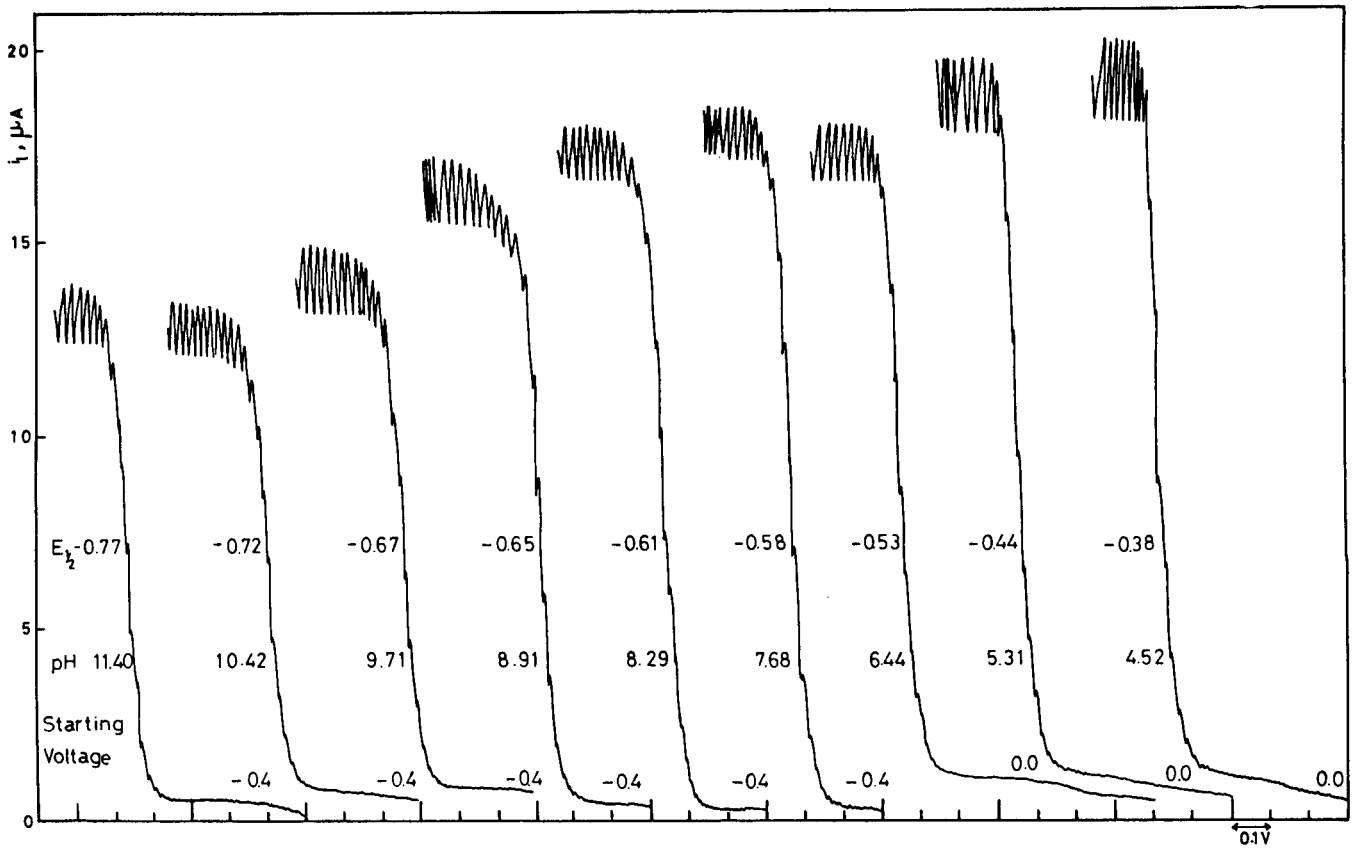


Figure 1. Polarograms of $10^{-4}M$ 2-amino-4-phenyl-5-phenylazothiazole in 50% v/v ethanolic Britton-Robinson buffers.

ty by several (at least three) recrystallizations from ethanol. Stock solutions ($10^{-3}M$) were prepared in ethanol. Britton-Robinson buffers [24] were prepared and used as supporting electrolyte. All chemicals used were of AnalaR grade. The electronic absorption spectra of **1a-e** were recorded on a Unicam SP8000 spectrophotometer.

All polarograms were recorded on a Metrohm E261R polarograph. A digital Radiometer *p*H meter type 63 equipped with a combined glass electrode type GK2311C was used for measuring the *p*H. It was calibrated before and checked after each measurement using standard Radiometer aqueous buffers of *p*H's 4.01 and 7.00 ± 0.01. The *p*H meter readings (B) recorded in ethanol-water solutions were converted to hydrogen ion concentration [H^+] by means of the relation of van Uitert and Hass [25] namely:

$$-\log [H^+] = B + \log U_H$$

where log U_H is the correction factor for the solvent composition and ionic strength for which B is read. The value of log U_H was found to be −0.25 for 50% (v/v) ethanol-water solution at 25° [26].

Polarography.

Polarographic i *vs.* E curves were recorded in solutions placed in a water jacketed thermostated cell (25.0 ± 0.1°) which is fitted with a saturated calomel electrode (SCE) and a dropping mercury electrode. The capillary used possessed the following characteristics in third distilled water open circuit: drop-time t = 3.0 sec/drop; out-flow velocity m = 2.91 mg/sec at mercury height h = 60 cm.

Ethanol (10 ml), the appropriate buffer solution (12 ml) and gelatin solution (0.5%, 0.5 ml) were introduced into the cell and the mixture was deaerated by a stream of purified nitrogen for 5 minutes, then 2.5 ml of the azothiazole stock solution was added. After further deaeration for 5 minutes the polarographic curve was recorded, and then the apparent *p*H of the test solution was measured.

The half-wave potentials were measured graphically and expressed *vs.* SCE with an accuracy of ± 0.001 V. The accuracy of the applied voltage was checked by recording the polarograms of standard thallous solutions of different concentrations ($E_{1/2}$ = 0.45 V *vs.* SCE).

Controlled Potential Electrolysis.

The determination of the number of elecrons transferred in the electrode process was carried out coulometrically following the method of Lingane [27]. In each experiment, 35 ml of $-0^{-3}M$ solution of the appropriate arylazothiazole at *p*H 2.6 were used. The progress of electrolytic reduction was followed by recording the decrease in current with time. The number of electrons (n) involved was calculated using the equation:

$$n = \frac{i_o}{2.3\,CFv(\text{dlog } i/dt)}$$

where i_o is the current at time t = 0, when C = C_o, v is the volume in litres of the solution, and (dlog i/dt) is the slope of the plot of log i **vs.** t.

Identification of Controlled-Potential Electrolysis Products.

The solutions obtained after complete electrolysis of **1c** in four runs were combined and concentrated to one tenth of their original volume.

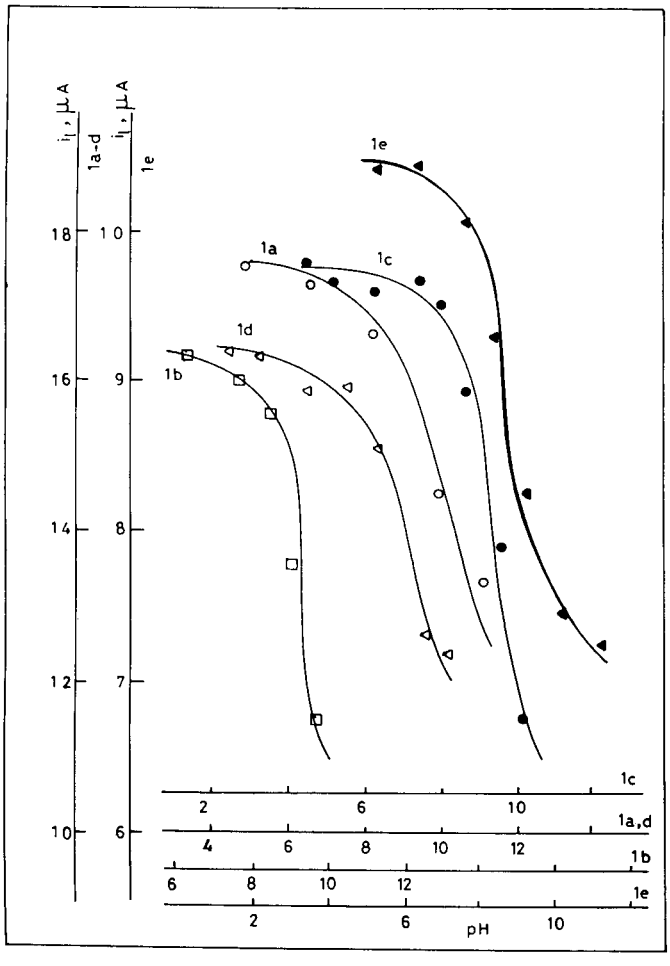


Figure 2. Dependence of the limiting currents of the polarographic waves of arylazothiazoles **1a-e** on *p*H in 50% (v/v) ethanolic Britton-Robinson buffers.

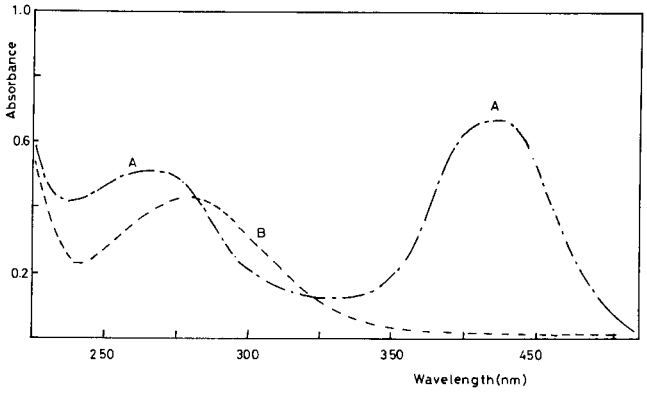


Figure 3. Electronic absorption spectra of 2-amino-4-phenyl-5-phenylazothiazole **1c** in 50% (v/v) ethanolic Britton-Robinson buffer of *p*H 2.6 (Curve A) and of the product of CPE of **1c** (Curve B).

The mixture was extracted twice with ether (50 ml) and the ether extracts were combined, dried over anhydrous sodium sulfate, filtered and the solvent was evaporated. Analysis (tlc) of the remaining residue using silica gel as the adsorbent and benzene as the eluent revealed the presence of two components one of which was identified as aniline. The latter was also identified in the product mixture by standard spot test [28]. The electronic absorption spectrum of the mixture in ethanol is shown in Figure 3.

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[20] Bonding energy, BE, is defined as $BE = E_\pi - \Sigma n_i\alpha_i$, where E_π is the total π-electronic energy of the system, n_i the number of π-electrons contributed by the atom i to the system, and α_i is the Coulomb integral of the atom i. The use of bonding energies for studies of tautomerism in various organic systems is described in one of our previous publications [21].

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