

Polarographic Behaviour of Some 5-Arylmethylene-2-phenylhydrazonothiazolidin-4-ones in Aqueous Medium

Hussein M. Fahmy,* Hamed Abdel-Reheem Ead, and Mohamed Abdul-Wahab
Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt

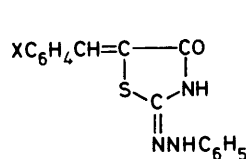
The electrochemical reduction of a series of 5-arylmethylene-2-phenylhydrazonothiazolidin-4-ones has been investigated. The mechanism of the electrode processes over a wide range of pH is proposed, discussed, and clarified.

1,3-Thiazolidin-4-one and its derivatives are known to have many biological, pharmaceutical, and analytical applications.¹⁻⁴ Consequently, hydrazones (1) are anticipated to have similar applications. In the present investigation the electrochemical behaviour of (1a-h) has been studied over a wide range of pH. For the sake of comparison two model compounds namely 2-phenylhydrazonothiazolidin-4-one (2) and 5-diphenylmethyl-2-phenylhydrazonothiazolidin-4-one (3) were also studied under similar conditions.

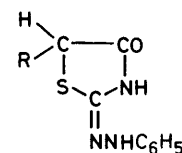
Experimental

Instrumentation.—An LP60 polarograph (Laboratorni Pristrojé, Prague) was used. The capillary possessed the following characteristics: t 3.75, m 2.15 mg s⁻¹ for h 55 cm. A pH-meter type Titrimeter TS4N (Prolabo, France) was used for measuring the pH values. For controlled-potential electrolysis (c.p.e.) a T6 transistorized potentiostat was used. The number of electrons consumed during electrolysis was calculated automatically with a Tacussel electronic integrator type IG3A.

Compounds.—5-Arylmethylene-2-phenylhydrazonothiazolidin-4-ones (1a-h), 2-phenylhydrazonothiazolidin-4-one (2), and 5-diphenylmethyl-2-phenylhydrazonothiazolidin-4-one (3) were synthesized according to previously reported procedures.⁵⁻⁷



(1)



(2) R = H

(3) R = (C₆H₅)₂CH

- | | |
|-----------------------------------|----------------------------------|
| a; X = H | e; X = <i>p</i> -Cl |
| b; X = <i>p</i> -CH ₃ | f; X = <i>p</i> -Br |
| c; X = <i>p</i> -OCH ₃ | g; X = <i>p</i> -NO ₂ |
| d; X = <i>p</i> -OH | h; X = <i>m</i> -NO ₂ |

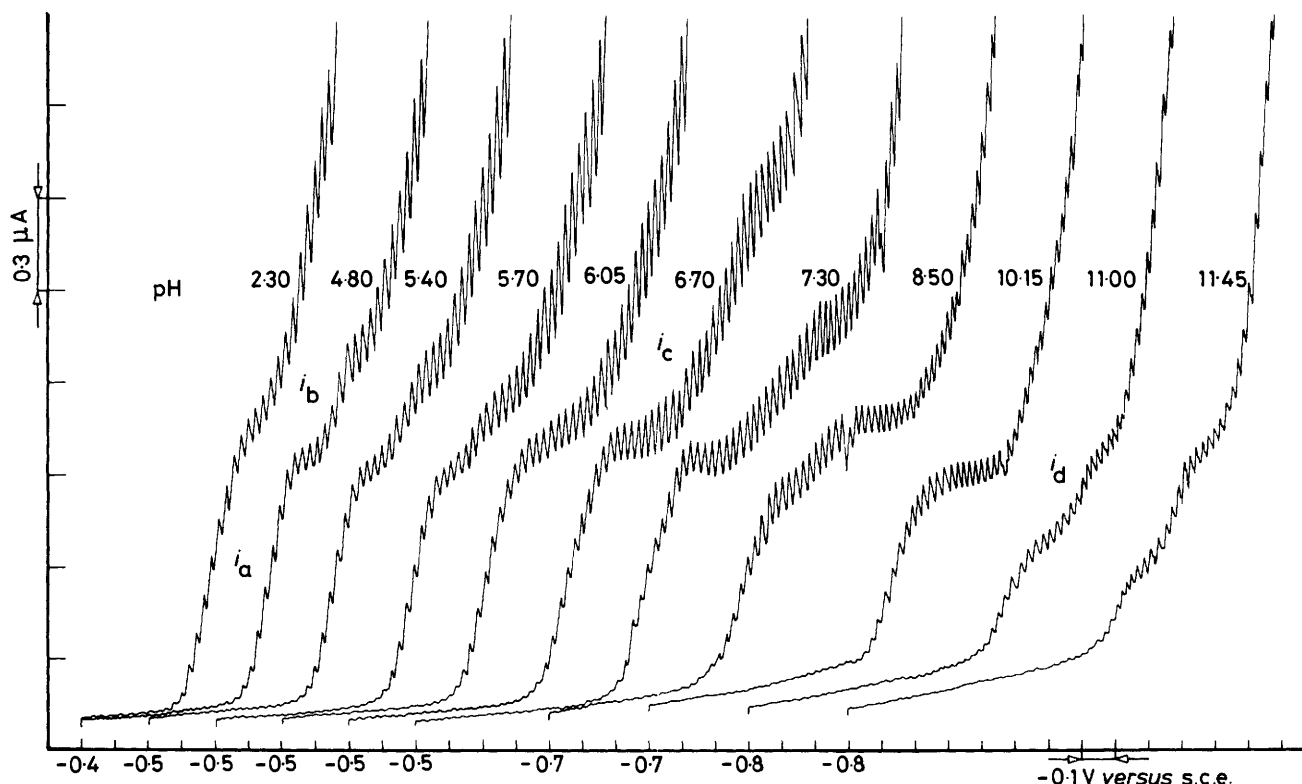


Figure 1. Polarograms of 10⁻⁴M-(1a) in 40% v/v ethanolic aqueous buffers

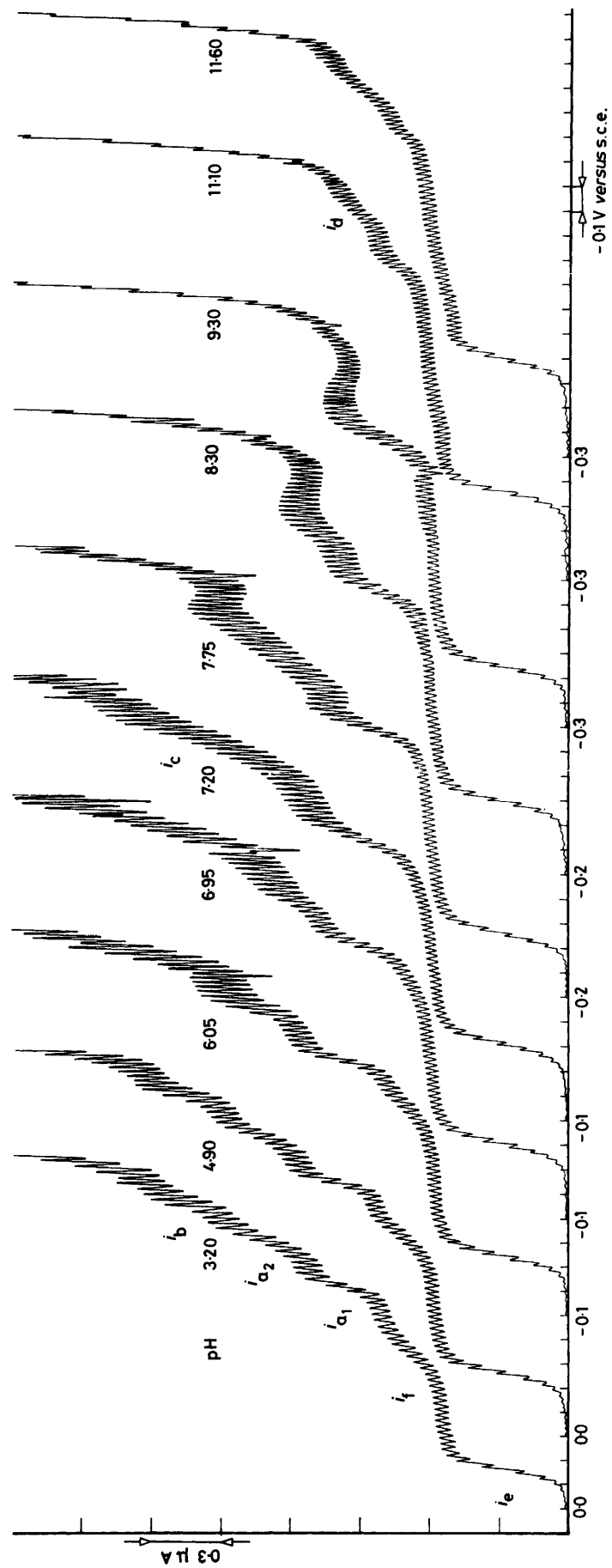


Figure 2. Polarograms of 10^{-4} M-(1h) in 40% v/v ethanolic aqueous buffers

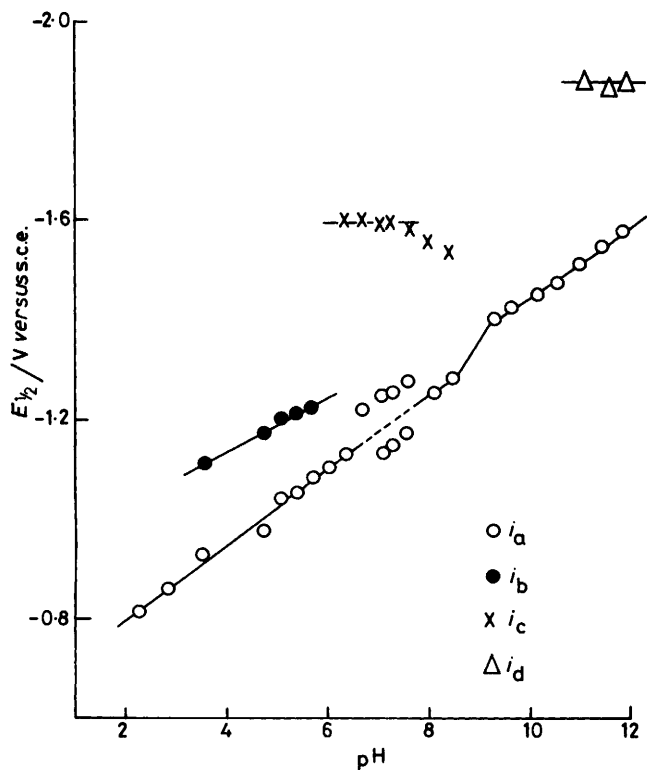


Figure 3. Variation of the half-wave potential $E_{1/2}$ of the various polarographic waves of (1a) with pH of solution

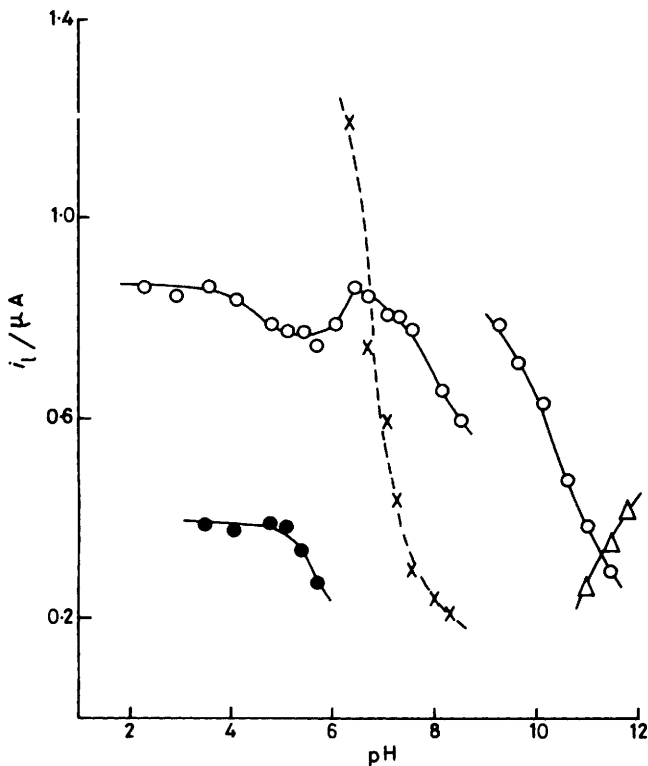


Figure 4. Variation of the limiting current i_l of the various polarographic waves of (1a) with pH of solution

Solutions and Procedures.—Britton–Robinson buffers⁸ were used as supporting electrolytes. Ethanol and the appropriate buffer solution were introduced into the cell. The mixture was

then deaerated for 5 min by bubbling a stream of hydrogen through it. The calculated volume of the stock solution was then introduced into the cell so that the final concentration was 10^{-4} M in 40% ethanolic buffer (10 cm^3). All experiments were carried out at $25 \pm 1^\circ \text{C}$. The half-wave potentials were measured graphically and expressed versus saturated calomel electrode (s.c.e.) with an accuracy of $\pm 0.005 \text{ V}$.

Controlled-potential Electrolysis.—**General procedure.** C.p.e. was carried out using a mercury pool electrode in the appropriate supporting electrolyte (200 cm^3) which contains 40% ethanol and 2×10^{-3} M-hydrazone. The electrolysis cell was a 250 cm^3 conical flask on top of which were fixed the s.c.e. and auxiliary and hydrogen inlets. The mercury pool was stirred with a magnetic stirrer. The progress of the electrolysis was followed by recording the decrease in current with time. After the reduction was terminated, the volume was reduced by evaporation *in vacuo* to a quarter of its original volume and the appropriate separation and identification were carried out.

C.p.e. of hydrazone (1a). (i) In acid medium. HCl (10^{-2} M) was used as supporting electrolyte. The hydrolysis was performed at -1.0 V versus s.c.e. At the end of electrolysis the solution was neutralized with few drops of concentrated NH_4OH and evaporated *in vacuo*. The concentrated solution was then extracted with benzene. The extract was dried (Na_2SO_4) followed by evaporation to dryness. The obtained crude material was crystallized from light petroleum and gave a yellow powder identified as 5-benzyl-2-aminothiazolidin-4-one, m.p. 160°C , ν_{max} (KBr) 3 320 (NH), 2 930 (CH), 1 680 (CO), and 710 cm^{-1} (monosubstituted benzene); m/e 206, 177, 77, 75, 69, and 45 (Found: C, 58.1; H, 5.3; S, 15.0. Calc. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{OS}$: C, 57.7; H, 5.8; S, 15.4%).

Aniline was also detected in the electrolysed solution using the anthranilic acid spot test.⁹

(ii) In neutral medium. Electrolysis was carried at a potential of -1.6 V versus s.c.e. at pH 6.7. The electrolysed solution was reduced and ammonia was detected with Nessler' reagent.¹⁰

C.p.e. of hydrazone (2). Electrolysis was conducted in dilute HCl (10^{-2} M) at a controlled potential of -1.0 V versus s.c.e. After complete electrolysis the solution was neutralized to pH 6 and extracted by ether several times. The extract was then evaporated to dryness and the remaining residue was crystallized from methanol. A yellow crystalline substance was obtained and it is identified as 2-aminothiazolidin-4-one, m.p. 230°C (Found: C, 31.1; H, 4.95; S, 26.8. Calc. for $\text{C}_3\text{H}_6\text{N}_2\text{OS}$: C, 30.5; H, 5.1; S, 27.1%); ν_{max} (KBr) 3 280 (NH), 2 930 (CH), and $1 675 \text{ cm}^{-1}$ and absence of characteristic benzene bands. Using the anthranilic acid spot test,⁹ aniline could also be identified among the electrolysis products.

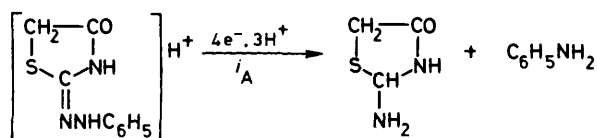
Results and Discussion

Representative polarograms for hydrazones (1a and h) selected as typical examples of the series are illustrated in Figures 1 and 2. The curves display four waves according to the pH of the medium. Thus at $\text{pH} < \text{ca. } 6.5$ reduction takes place in two steps, i_a and i_b . In neutral to faintly alkaline solution (6.5–8.5) a third wave i_c appears. At $\text{pH} > 10$ a more negative wave i_d is formed. In addition to these waves, the nitro-derivatives (1g and h) showed two more positive waves i_e and i_f . It is noteworthy that i_a always splits into two steps (i_{a_1} and i_{a_2}) in hydrazones (1g and h) whereas for hydrazones (1a–d), i_a only divides in the pH range 6.5–8.5.

The shift of $E_{1/2}$ and variation of i_l with pH is illustrated in Figures 3 and 4 for compound (1a) taken as a representative example. The polarographic data for the series (1a–h) are compiled in the Table. The effects of both concentration and

Table. Polarographic data of 5-arylmethylene-2-phenylhydrazonothiazolidin-4-ones (1a-h)

Compound	$dE_{\frac{1}{2}}/mV$		$RT/2nF$			$i_1/\mu A$		
	Wave i_a (pH 2.6-6)	Wave i_b (pH 3-6)	Wave i_a (pH 3-4)	Wave i_b (pH 4-5)	Wave i_c (pH 7-7.5)	Wave i_a (pH 3-4)	Wave i_b (pH 4-5)	Wave i_c pH 7-7.5
(1a)	0.074	0.056	0.073	0.065	0.164	0.870	0.392	0.75
(1b)	0.074	0.054	0.075	0.063	0.133	0.900	0.390	0.81
(1c)	0.076	0.052	0.092	0.052	0.145	0.900	0.450	1.05
(1d)	0.072	0.056	0.073	0.071	0.152	0.795	0.390	0.84
(1e)	0.077	0.054	0.077	0.056	0.162	0.795	0.364	0.81
(1f)	0.074	0.058	0.065	0.056	0.165	0.780	0.390	1.05
(1g)	0.074 (i_a)	0.054	0.055 (i_a)	0.063	0.138	0.530	0.500	1.35
	0.061 (i_a)		0.067 (i_a)			0.530		
(1h)	0.078 (i_a)	0.055	0.063 (i_a)	0.072	0.156	0.530	0.500	1.32
	0.062 (i_a)		0.072 (i_a)			0.500		



Scheme 1.

mercury-height together with logarithmic analysis indicated that all the waves are diffusion controlled with the exception of i_c which showed catalytic behaviour.

The c.p.e. of hydrazone (1a) in acid medium at the potential of the limiting-current plateau of wave i_b gave 5-benzyl-2-aminothiazolidin-4-one together with aniline. These products reveal that the electrode processes in acid medium (waves i_a and i_b) involve the reductive splitting of the N-N bond and the saturation of both the azomethine group C=N and the ethylene bond C=C. However, the resulting electrolysis products do not show the sequence by which the reduction proceeds. For a clear understanding of the course of electroreduction occurring in steps i_a and i_b it was found worthwhile to consider the behaviour of models (2) and (3) under the same experimental conditions.

Hydrazone (2) was found to be reduced in acid medium in a four-electron irreversible wave i_A which decreases in height with increase of pH in the form of a dissociation curve. The shift of the half-wave potential follows a straight line with a slope of 72 mV/pH. These polarographic characteristics are compatible with those previously reported for typical hydrazones and the reduction follows the classical four-electron reduction mechanism proposed by Lund.¹¹

On the other hand, hydrazone (3) displayed two waves i_1 and i_2 in acid medium (Figure 5). These two waves have approximately the same height and both $E_{\frac{1}{2}}$ and i_1 of the two waves are pH dependent (Figures 5 and 6). Comparison of these waves in acid medium with the four-electron wave of hydrazone (2) showed that: (i) each of the waves i_1 and i_2 corresponds to a two-electron uptake, (ii) the half-wave potential of wave i_1 nearly coincides with the one-fourth potential of the wave i_A of hydrazone (2). In addition to these observations hydrazones (2) and (3) are identical in all aspects except that (3) is substituted at C-5 by the electroinactive diphenylmethyl group. Hence, one can conclude that the two waves i_1 and i_2 of hydrazone (3) correspond to the stepwise reduction of the hydrazone moiety, via a c.e.c. (H^+ , $2e^-$, H^+) mechanism, i.e. cleavage followed by saturation.

The fact that the reduction of the hydrazone moiety takes place as one step in (2) and stepwise in (3) is most probably due to the effect of the substituent at position 5. Substitution at

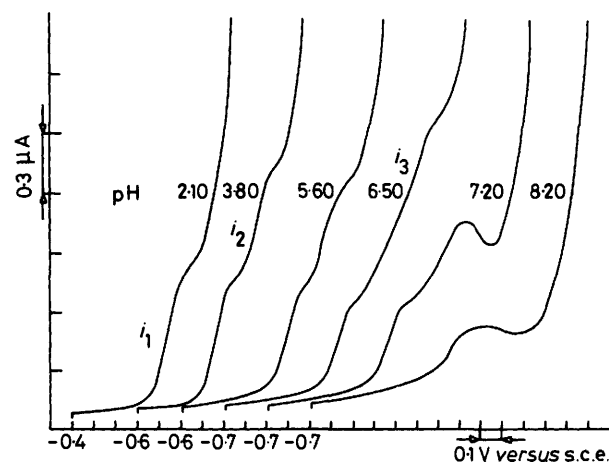
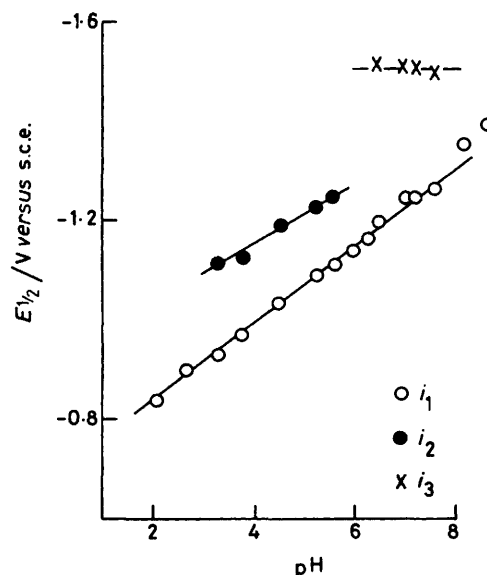
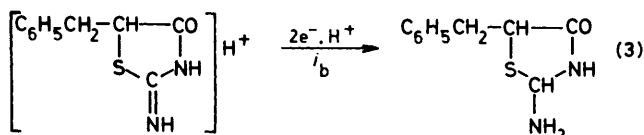
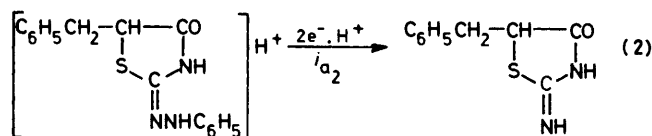
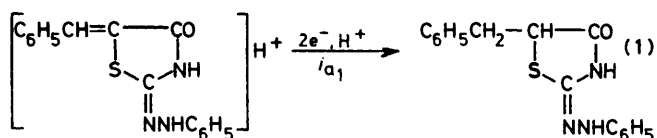


Figure 5. Polarographic behaviour of model (3) in alcoholic aqueous buffered media

Figure 6. Variation of $E_{\frac{1}{2}}$ with pH of the polarographic waves of model hydrazone (3)

C-5 of thiazolidinones is known to influence the half-wave potentials of various processes.¹²

The assignment of the course of reduction of compound (1a)



Scheme 2.

in acid medium can be achieved through comparison of its waves with those of model (3). Thus wave i_b of the parent compound (1a) is similar in all aspects to the wave i_2 . Also, the three-fourth potential of wave i_a is comparable with the $E_{\frac{3}{4}}$ value of wave i_1 . Hence, one may conclude that the reduction of (1a) in acid medium follows the sequence C=C, N-N, C=N according to Scheme 2.

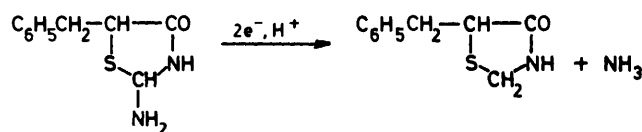
The reduction processes in the first step i_a ($i_{a1} + i_{a2}$) correspond to equations (1) and (2). The half-wave potentials of steps i_{a1} and i_{a2} differ by so little that only one wave, i_a , is observed at most pH values. Equation (3) corresponds to step i_b in which the reduction of the imine formed in step i_{a2} occurs. The dependence of $E_{\frac{3}{4}}$ of the waves of pH (cf. Table) is a direct indication that the protonation precedes the electron uptake. It is of interest to mention that use of equation (4)¹³ shows that the

$$\frac{dE_{\frac{3}{4}}}{dpH} = -\frac{0.0591}{\alpha n} \cdot p \quad (4)$$

number of protons (p) consumed in the rate-determining step is one per molecule for each wave i_a and i_b . Because the shift of $(E_{\frac{3}{4}})_b$ is smaller than that of wave i_a , the two waves merge at pH 6.

All other hydrazones (1b–h) showed similar behaviour in acid medium. The nitro-derivatives exhibited additional waves i_c and i_f at less negative potentials. Wave-height ratios indicate that four and two electrons are consumed in these waves. Thus, they can be ascribed to the reduction of the nitro group according to the previously reported mechanism for *p*-nitrophenol^{14,15} and *p*-nitroaniline.^{16,17}

In almost neutral to just alkaline solution (pH range 6.5–8.5) the acid reduction mechanism (Scheme 3) is considered still to operate. In addition hydrazone (1a) displayed a third more negative wave i_c with an abnormal height. Its half-wave potential is practically pH independent whereas its height decreases sharply with increasing pH. This wave is also exhibited by the other hydrazones (1b–h), (2) (wave i_b), and (3) (wave i_3) but splits into two poorly developed steps i_c and i_e in hydrazones (1d and f). The height of the more negative step i_c is strongly pH dependent while that of step i_e is almost constant within 1 pH unit (and then amalgamates with i_c). The more negative step i_e was found to be catalytic in nature. This has been proved by the increase of the wave with lowering mercury head,



Scheme 3.

by non-linear dependence of the wave height on concentration, and by a steep increase with decreasing pH value.¹⁸

Based on the above observations one may conclude that wave i_c of hydrazone (1a) involves a reduction process (step i_c). It is possible to assign the reduction current i_c either to saturation of the C=O group in position 4 or to the reductive splitting of the C-N bond of the amine formed in step i_b . When hydrazone (1a) is reduced at a large-scale mercury pool electrode at $(E_{\frac{3}{4}})_c$, ammonia could be detected in the electrolysed solution. Thus, the reduction process in step i_c corresponds most probably to the reductive splitting of the C-N bond (Scheme 3). By analogy with other substances bearing a reducible C-N bond,¹⁹ the reductive splitting of ammonia results most probably from the protonated form. The pH independence of $(E_{\frac{3}{4}})_c$ may be attributed to the interference of catalytic hydrogen evolution. The reduction of hydrogen ions may be catalysed by ammonia or the hydrated^{20,21} imine following one of the mechanisms reported by Heyrovsky,²² Frumkin,²³ and Stackelberg.^{24,25}

At higher pH values (pH > ca. 10) a fourth wave i_d appears. This wave increases with increasing pH of the solution and hence can be ascribed to the reduction of the unprotonated C=C bond.^{26,27}

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