Effect Of Substituents On The Polarographic And Spectrophotometric
Behaviour Of 2- [N-(phenyl)- acetimidoyl] -1,3-Indandione

by

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Effect Of Substituents On The Polarographic And Spectrophotometric Behaviour Of 2- [N-(phenyl)- acetomidoyl] -1,3-Indandione

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ABSTRACT:

The effect of a variety of substituents on the polarographic behaviour and acid-base equilibrium (revealed spectrophotometrically) of 2-[N-(phenyl)- acetomidoyl]-1,3-indandione has been studied in wide pH range buffer solutions (pH~3-12). The application of the linear free energy relationships using $E_{1/2}$ values with different $\sigma$ sets showed a weak dependence while $pK_a-\sigma$ sets showed a good correlation.

Introduction

1,3-indandione and some of its substituted derivatives showed wide applications in medicinal chemistry\(^1,2,3\), as antiinflammatory agent\(^4\) and miticides\(^5\). Relevant studies to the electrochemistry of this class of compounds were recently reviewed by Stradins\(^6\). Due to its wide applicability our group was involved with the polarographic and spectrometric studies for different groups of substituted 1,3-indandione\(^7,8\). The polarographic reduction of 2-[N-(phenyl) acetomidoyl] -1,3-indandione ($I_a$) was found to proceed along two-electronic, $E_{1/2}$-pH dependent wave (A), which is assigned to reduction of the $\geq C=\text{N}-$ linkage according to:

\[
\begin{array}{c}
\text{CH}_3
\end{array}
\xrightarrow{2e, 2H^+, H_2O}
\begin{array}{c}
\text{CH}_3
\end{array}
+ \begin{array}{c}
\text{NH}_2
\end{array}
\]

Wave A
At pH > 8 wave (A) started to decrease in height with appearance of one electronic $E_{1/2}^\text{pH}$ independent wave (B) assigned to reduction of the carbonyl group resulting from the alkaline hydrolysis of the azomethine bond:

![Chemical structure](image)

**Wave B**

In continuation to this direction we report here the effect of electron-withdrawing groups (p-Cl, m-NO$_2$, p-NO$_2$) and electron-donating group (p-CH$_3$) on the polarographic reduction waves (A) and (B) and the degree of ionization of H in position 2 of 2-[(N-(phenyl) acetimidoyl]-1,3-indandione:

![Chemical structure](image)

Meanwhile the fidelity of existence of linear free energy relationship (LFER) was tested through correlation of the experimentally determined $E_{1/2}$ and pK$_a$ values with different $\sigma$ sets.

**Experimental**

Organic Syntheses:

Compounds $I_{a-c}$ were prepared following procedures previously reported by Amer et al. A mixture of 2-acetyl-1, 3-indandione (0.01
mole) and aniline, or the respective substituted aniline, in 30 ml acetic acid was heated at 80°C for 30 minutes. The solid that obtained after cooling or dilution with water, was recrystallized from ethanol to give $I_{a-e}$. Credit of purity was checked by m.p. and elemental analysis which agreed well with the theoretical values.

Polarography:

(a) Apparatus. Polarographic curves were recorded with an E 506 pen-type recorder polarograph (Metrohm, Switzerland). The capillary possessed the following characteristics in H$_2$O open circuit: $t = 5.1$ s/drop, $m = 1.49$ mg s$^{-1}$ for $h = 40$ cm.

(b) Solution. $10^{-3}$M-Stock solutions were prepared by dissolving an accurately weighed quantity of material in the appropriate volume of absolute ethanol. Britton-Robinson modified universal buffers$^{10}$ were used as supporting electrolyte.

(c) Measurements. All experiments were carried at 25 ± 2°C. The half-wave potentials were measured graphically and expressed versus the saturated calomel electrode (SCE) with an accuracy ± 0.005 V.

(d) Procedure. Ethanol (7 ml) and the appropriate buffer solution (12 ml) were introduced in the polarographic cell. The mixture was then deaerated by bubbling a stream of hydrogen for 12 min. 1 ml of $10^{-3}$ M depolarizer was then introduced into the cell so that the final concentration was $5 \times 10^{-5}$ M in 20 ml of 40 % (V/V) ethanolic buffer. Controlled Potential Electrolysis:

Mercury pool electrolysis was carried out 40 % V/V ethanol $10^{-2}$M-HCl solution (200 ml) and substance ($I_a$) (200 mg) taken as a typical example. The electrolysis cell was a 250 ml conical flask in which the reference, auxiliary electrodes, and the gas inlet were added by means of a cork. The potential was controlled by a tutorial T$^6$ transistorized potentiostat at -1.0 V vs. SCE (i.e. on the limiting current plateau of wave A). The progress of the electrolysis was followed by recording the decrease in current with time and the number of electrons was computed from i-t curves following the procedure outlined by Lingane$^{11}$ and found to be 2e. After disconnecting the electrolysis cell, 1 ml of the resulting solution was withdrawn and the presence of aniline
in this solution was revealed by a standard spot test\textsuperscript{12}. Trials to separate and crystalize a solid product were unsuccessful where almost resinous material was obtained.

Spectrophotometric Measurements and Determination of the Apparent Dissociation Constant:

These were carried out using PYE Unicam 1800 spectrophotometer supplemented with Unicam SP 1805 programme controller automatic recording unit. The runs in the visible and UV range were carried out for 5 x 10\textsuperscript{-5}M I\textsubscript{aq}, 40 % alcoholic Britton - Robinson buffer solutions at roughly increasing 0.5 pH unit. The pH of the solution was measured and the spectrophotometric run was recorded within few minutes. The pK\textsubscript{a} was then calculated using the equation\textsuperscript{13},

\[
pH = \text{pK}_a + \log \left( \frac{A - A_{\text{min}}}{A_{\text{max}} - A} \right)
\]

where \(A_{\text{max}}\) is the absorbance of the undissociated acid, \(A\) is the absorbance of the organic reagent at a given pH value and \(A_{\text{max}}\) is the absorbance of the completely dissociated acid at high pH medium. The intersection of the straight line of pH vs. log \(\frac{A - A_{\text{min}}}{A_{\text{max}} - A}\) with the pH axis, at log \(\frac{A - A_{\text{min}}}{A_{\text{max}} - A}\) = 0 gave directly the pK\textsubscript{a}.

Results And Discussion

Polarographic Reduction:

The polarographic behaviour of the p-CH\textsubscript{3} and p-Cl substituents (compounds I\textsubscript{b} & I\textsubscript{c}) were found identical with that reported for the parent compound I\textsubscript{a}\textsuperscript{8}. On the other hand the polarograms obtained with the m-NO\textsubscript{2}(I\textsubscript{d}) and p-NO\textsubscript{2} (I\textsubscript{e}) derivatives (schematically given in Figs. 1 and 2 respectively) are somewhat complicated due to the interference of the reduction waves of the nitro group with that of the \(>\text{C} = \text{N}\)-linkage. Thus at pH < 4 the nitro group of the m-NO\textsubscript{2} substituent (Fig. 1) showed 4-electronic and 2-electronic waves successively; these were followed by a two-electronic wave at more negative potentials assigned to reduction of the \(>\text{C} = \text{N}\)-linkage (wave A). At 6.5 < pH > 4 the 2-electronic wave of the nitro group amalgamates with wave (A) and at pH 7.38 the amalgamated wave splits again into two two-electronic waves: the more negative wave (assigned to reduction of \(>\text{C} = \text{N}\)-
Fig 1: Schematic representation of the polarograms of $5 \times 10^{-4}$M 2-N-(m-NO$_2$-phenyl) acetomidoyl -1,3-indandione ($I_g$) in 40% V/V ethanolic Britton-Robinson buffers.
group) decreases in height with pH increase and the more positive wave to reduction of the NO₂ group. At pH > 9 the reduction waves of the nitro decreases in height to a four electronic process and remains constant up to the highest pH. In acidic, neutral and fairly alkaline media (pH < 9) the m-NO₂ group reduces to the respective amine along six electronic process as follows:

\[ \text{m-NO}_2 \rightarrow \text{amine} \]

At pH > 9 the m-NO₂ is reduced via four-electronic process to the corresponding hydroxylamine:

\[ \text{m-NO}_2 \rightarrow \text{hydroxylamine} \]

The p-NO₂ derivative (Ie, Fig. 2) showed similar behaviour except at pH > 9 where the wave height associated with the nitro group reduction still corresponded to 6-electronic process. This is well known behaviour accompanying the polarographic reduction of the aromatic nitro group in the p-position where usually a quinoid form is involved in the electroc process which can be schemed as follows:

\[ \text{p-NO}_2 \rightarrow \text{quinoid} \]
Spectrophotometric $pK_a$:

Spectrophotometric runs of $5 \times 10^{-5}$M, 40% alcoholic Britton Robinson buffers at roughly increasing 0.5 pH unit for the parent compound ($I_a$) as a representative example for (this series) are illustrated in Fig. 3. The spectra are characterized by an absorption band at $\lambda_{274}$nm and an isobestic point at 300 nm. These points cover all the pH range indicating the presence of an equilibrium between the acid form and its conjugate base as the only equilibrium existing in such solutions. The
Fig. 2: Schematic representation of the polarograms of 5 x 10^{-3} M 2-N-(p-N0-phenyl) acetoacetyl-L4-2-indandione (I) in 40% V/V ethanol - Britton - Robinson buffers.
Fig 3: (a) Electronic absorption spectra of 5 \times 10^{-5}M (I_p) in 40% V/V ethanolic Britton-Robinson buffers. (b) log \((A - A_{\text{min}})/(A_{\text{max}} - A)\) - pH plot.
pK\textsubscript{a} values, calculated from plots of pH vs. log (A - A\textsubscript{min}) / (A\textsubscript{max} - A) are compiled in Table 1.

<table>
<thead>
<tr>
<th>Compound</th>
<th>(I_a) H</th>
<th>(I_b)</th>
<th>(I_c) p-Cl</th>
<th>(I_d) m-NO\textsubscript{2}</th>
<th>(I_e) p-NO\textsubscript{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>pK\textsubscript{a}</td>
<td>10.50</td>
<td>10.80</td>
<td>10.30</td>
<td>9.60</td>
<td>9.40</td>
</tr>
</tbody>
</table>

Structure-Reactivity Relationship:

The influence of substituents of the reduction wave of the \(\text{C-N}\) group (wave A) and the acid-base equilibrium constant pK\textsubscript{a} for the series under investigation were examined. The correlation of half-wave potentials for \(I_{a-e}\) at pH 4.0, 6.0 and 8.0 with sigma constants \(\sigma\) as taken from the tabulation of Retchie and Sagar\textsuperscript{17} is shown in Fig. 4. The coordinates for the nitro derivatives were not included in the correlation at pH > 4 due to the interference of the reduction waves of the nitro group with that of the azomethine ligand; also a better correlation could be observed when using values for NH\textsubscript{2} which results from reduction of the NO\textsubscript{2} group. The data were treated statistically using the least square method according to Jaffe\textsuperscript{18}. Detailed calculations were summarized in Table 2. It is obvious that a weak correlation exists between E\textsubscript{1/2} - \(\sigma\) since the reactivity parameter \(\varphi\) oscillates between \(+0.03\) and \(+0.07\). This is to be expected since water molecule is involved in the electrochemical process (cf. introduction). For wave (B) the correlation showed complete independency of E\textsubscript{1/2} on \(\sigma\) values. This confirms the electroreduction scheme previously suggested for these compounds\textsuperscript{8} since the substituents is separated in the aniline portion and thus has absolutely no effect.

On the other hand the correlation of pK\textsubscript{a} - \(\sigma\) sets (\(\sigma\), \(\sigma^0\), \(\sigma^+\)) shown in Fig. 5 reflects a quite fair correlation which is also in accordance with expectation, i.e. p-CH\textsubscript{3}(I\textsubscript{b}) exhibits the higher pK\textsubscript{a} whereas the p-NO\textsubscript{2} (I\textsubscript{c}) exhibits the lower one. It is obvious from Table 3 that the values of \(\varphi\) are positive, signifying that the substrate with an electron withdrawing substituents facilitates the ionization process, hence lower pK\textsubscript{a} values compared to the standard substrate. From the other hand, electron donating substituents increases the negative cloud at the ionization center leading to higher pK\textsubscript{a} values than that of the parent compound.
Fig. 4: Dependence of $E_{1/2}$ on $\sigma$ constants at pH 4.6 and 8.
Fig. 5: Dependence of the dissociation constant $pK_a$ on $\sigma$ constants.
Table 2

Values of reaction constant \( q \) from \( E_{1/2} \) vs. \( \sigma \) plots for compounds \( I_{n-e} \) at different pH’s (wave A).

<table>
<thead>
<tr>
<th>pH</th>
<th>( +q )</th>
<th>( r^a )</th>
<th>( \pm ) s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>0.03</td>
<td>0.892</td>
<td>0.002</td>
</tr>
<tr>
<td>6.0</td>
<td>0.07</td>
<td>0.901</td>
<td>0.002</td>
</tr>
<tr>
<td>8.0</td>
<td>0.06</td>
<td>0.852</td>
<td>0.005</td>
</tr>
</tbody>
</table>

\( a \) Correlation coefficient

\( b \) Standard deviation

Table 3

Values of reaction constant \( q \) from plots of \( pK_a \) vs. \( \sigma \) sets.

<table>
<thead>
<tr>
<th>( \sigma )</th>
<th>( +q )</th>
<th>( r^a )</th>
<th>( \pm ) s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma_0 )</td>
<td>+ 1.4</td>
<td>0.997</td>
<td>0.007</td>
</tr>
<tr>
<td>( \sigma^+ )</td>
<td>+ 1.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References


