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by

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Communications de la Faculté des Sciences de l'Université d'Ankara

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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 σ sets showed a weak dependence while pK_a-σ 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 spectometric 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 $>C=N$- linkage according to:
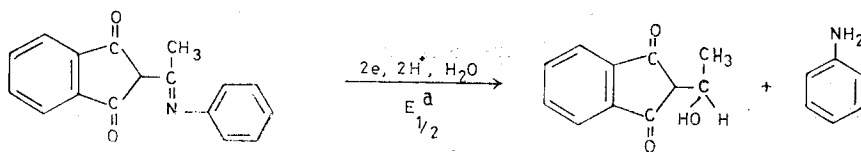

Wave A

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

Wave B
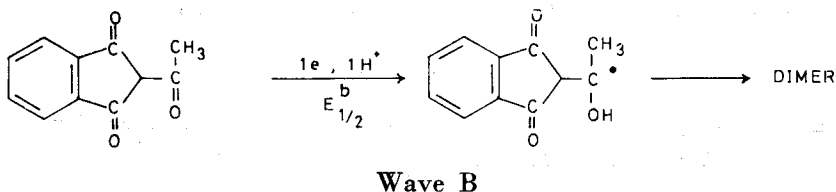
In continuation to this direction we report here the effect of electron-withdrawing groups (p-Cl, m-NO_2, p-NO_2) and electron-donating group (p-CH_3) on the polarographic reduction waves (A) and (B) and the degree of ionization of H in position 2 of 2-[N-(phenyl) acetomidoyl]-1,3-indandione:
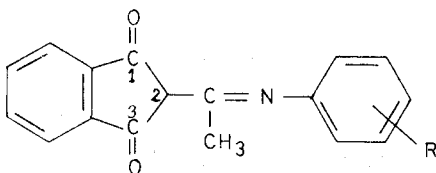
I_a	I_b	I_c	I_d	I_e

R =   H CH_3-p   Cl-p NO_2-m NO_2-p

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 σ sets.

Experimental

Organic Syntheses:

Compounds I_{a-e} were prepared following procedures previously reported by Amer et al.[9] 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_2O 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 $\pm$ 2°C. The
half-wave potentials were measured graphically and expressed versus
the saturated calomel electrode (SCE) with an accuracy $\pm$ 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 x 10^{-5} M in 20 ml of 40 % (V /V) ethanolic buffer.
Controlled Potential Electrolysis:

Mercury pool electrolysis was carrried 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 flack 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 transis
torized potentiostat at -1.0 V vs. SCE (i.e. on the limiting current pla-
teau of wave A). The progress of the electrolysis was followed by recor-
ding 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[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 5×10^{-5}M I_{a-e}, 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_a was then calculated using the equation[13].

$$pH = pK_a + \log (A - A_{min.}) / (A_{max.} - A)$$

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

Results And Discussion

Polarographic Reduction:

The polarographic behaviour of the p-CH$_3$ and p-Cl substituents (compounds I_b & I_c) were found identical with that reported for the parent compound I_a[8]. On the other hand the polarograms obtained with the m-NO$_2$(I_d) and p-NO$_2$ (I_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 $> C=N-$ linkage. Thus at pH < 4 the nitro group of the m-NO$_2$ 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 $> C=N-$ 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 $> C = N-$
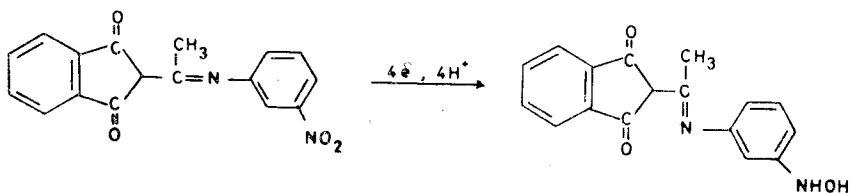
Fig 1: Schematic representation of the polarograms of 5×10^{-5}M 2- N-(m-NO$_2$-phenyl) aceto-midoyl -1,3-indandione (I$_d$) in 40 % V/V ethanolic Britton-Robinson buffers.
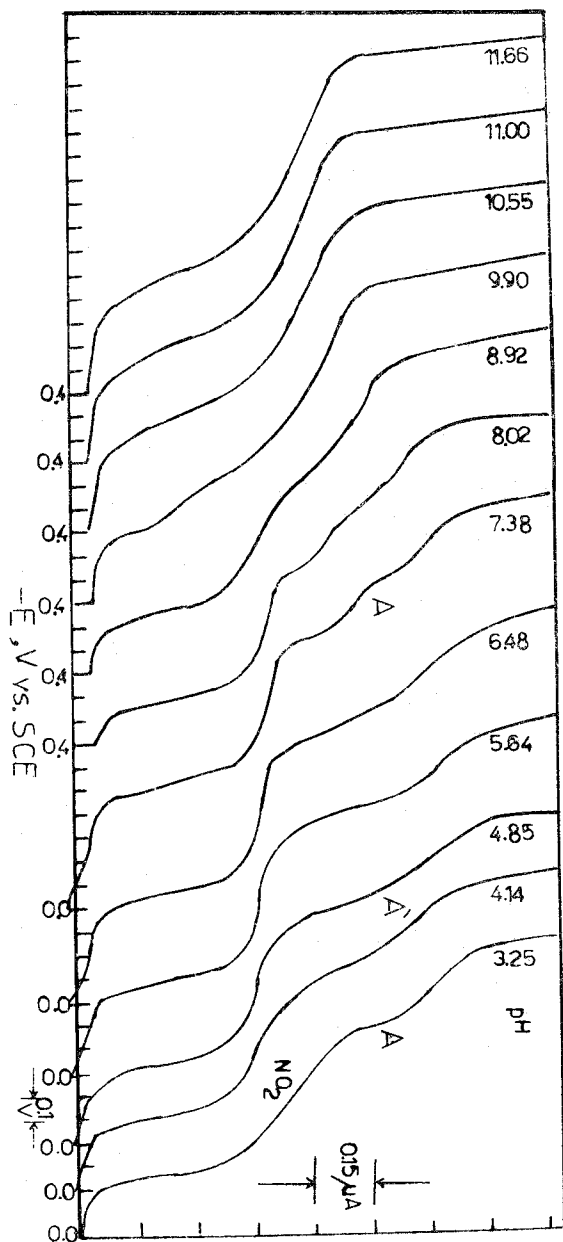
group) decreases in height with pH increase[8] and the more positive wave to reduction of the NO_2group. At pH $>$ 9 the reduction waves of the nitro decreases in height to a four electronic process and remains constant up to the highest pH. In acidic, neutral and fairly alkaline media (pH $<$ 9) the m-NO_2group reduces to the recpective amine along six electronic process as follows:
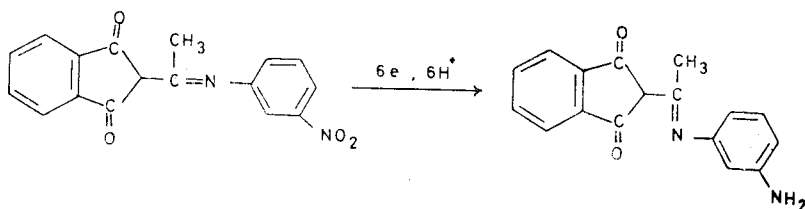
At pH $>$ 9 the m-$NO_2$is reduced via four-electronic process to the corresponding hydroxylamine:

The p-NO_2derivative (I_e, 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 quininoid[14,15,16] form is involved in the electrodic process which can be schemed as follows:
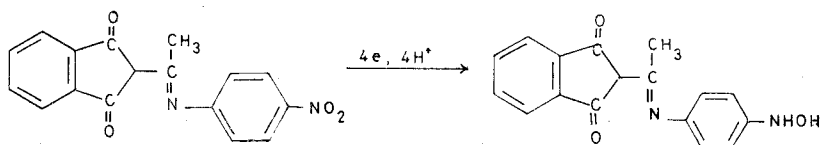
Spectrophotometric pK_a:

Spectrophotometric runs of 5 x 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 λ_{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
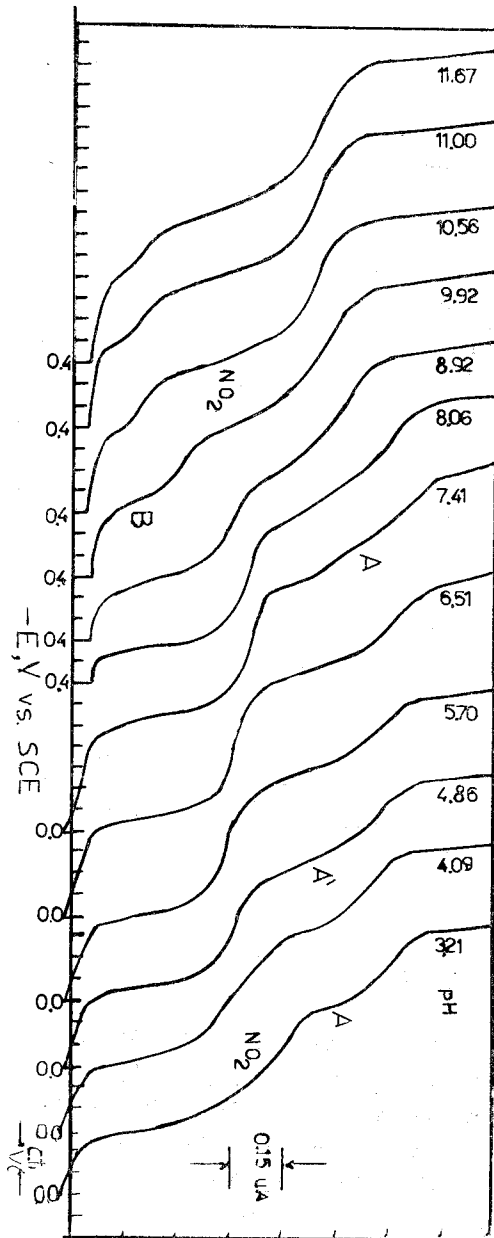
Fig 2: Schelatic representation of the polarograms of 5 x 10⁻⁵M 2- N-(p-NO₂-phenyl) aceto-midoyl 1,3-indandione (I$_e$) in 40 % V/V ethanolic Britton - Robinson buffers.
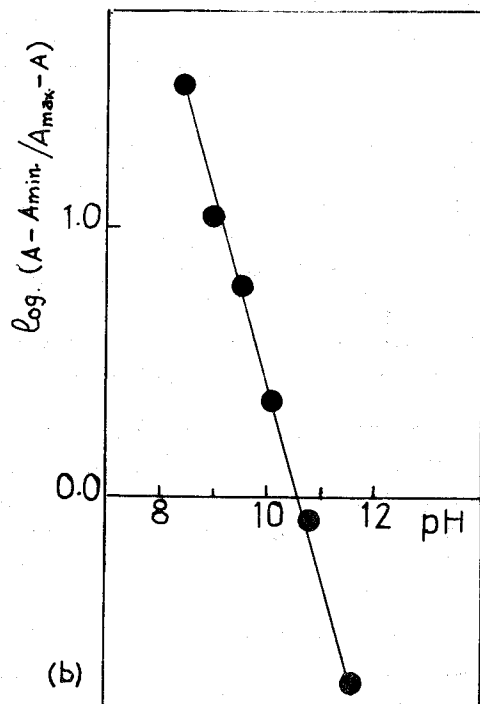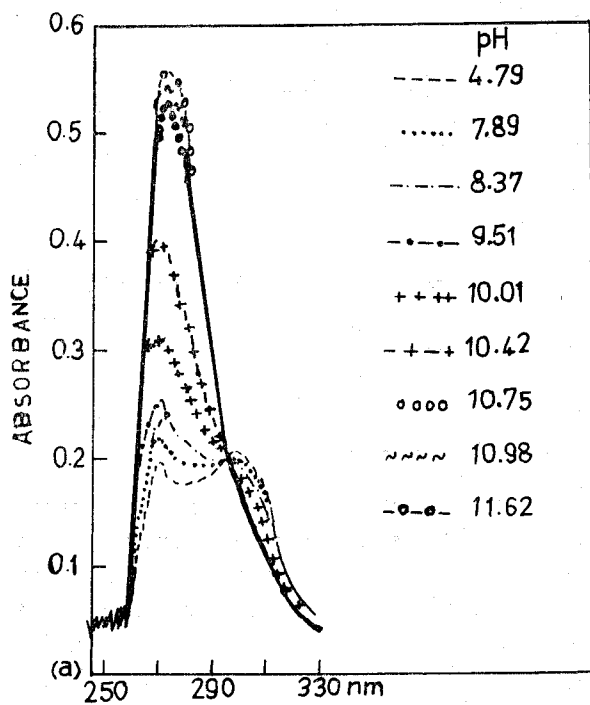
Fig 3: (a) Electronic absorption spectra of 5×10^{-5}M (I_a) in 40 % V/V ethanolic Britton-Ronin-son buffers. (b) log (A - A_{min}) (A_{max}- A) - pH plot.

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pK$_a$ values, calculated from plots of pH vs. log $(A - A_{min})$ / $(A_{max} - A)$ are compiled in table 1.

Table 1

Spectrophotometric pK$_a$ for compounds I$_a\beta_e$.

Compound	I$_a$, H	I$_b$,	I$_c$, p-Cl	I$_d$, m-NO$_2$	I$_e$, p-NO$_2$
pK$_a$	10.50	10.80	10.30	9.60	9.40

Structure-Reactivity Relationship:

The influence of substituents of the reduction wave of the $>$C$=$N-group (wave A) and the acid-base equilibrium constant pK$_a$ for the series under investigation were examined. The correlation of half-wave potentials for I$_{a-c}$ at pH 4.0, 6.0 and 8.0 with sigma constants σ as taken from the tabulation of Retchie and Sagar[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 lingake; also a better correlation could be observed when using values for NH$_2$ which results from reduction of the NO$_2$ group. The data were treated statistically using the least square method according to Jaffe[18]. Detailed calculations were summarized in Table 2. It is obvious that a weak correlation exists between E$_{1/2}$-σ since the reactivity parameter ϱ oscillates between + 0.03 and + 0.07. This is to be expected since water molecule is involved in the electrodic process (cf. introduction). For wave (B) the correlation showed complete independency of E$_{1/2}$ on σ values. This confirms the electroreduction scheme previously suggested for these compounds[8] since the substituents is separated in the aniline portion and thus has absolutely no effect.

On the other hand the correlation of pK$_a$- σ sets (σ, σ^o, σ^+) shown in Fig. 5 reflects a quite fair correlation which is also in accordance with expectation, i.e. p-CH$_3$(I$_b$) exhibits the higher pK$_a$ whereas the p-NO$_2$ (I$_c$) exhibits the lower one. It is obvious from Table 3 that the values of ϱ are positive, signifying that the substrate with an electron withdrawing substituents facilitates the ionization process, hence lower pK$_a$ 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$_a$ values than that of the parent compound.
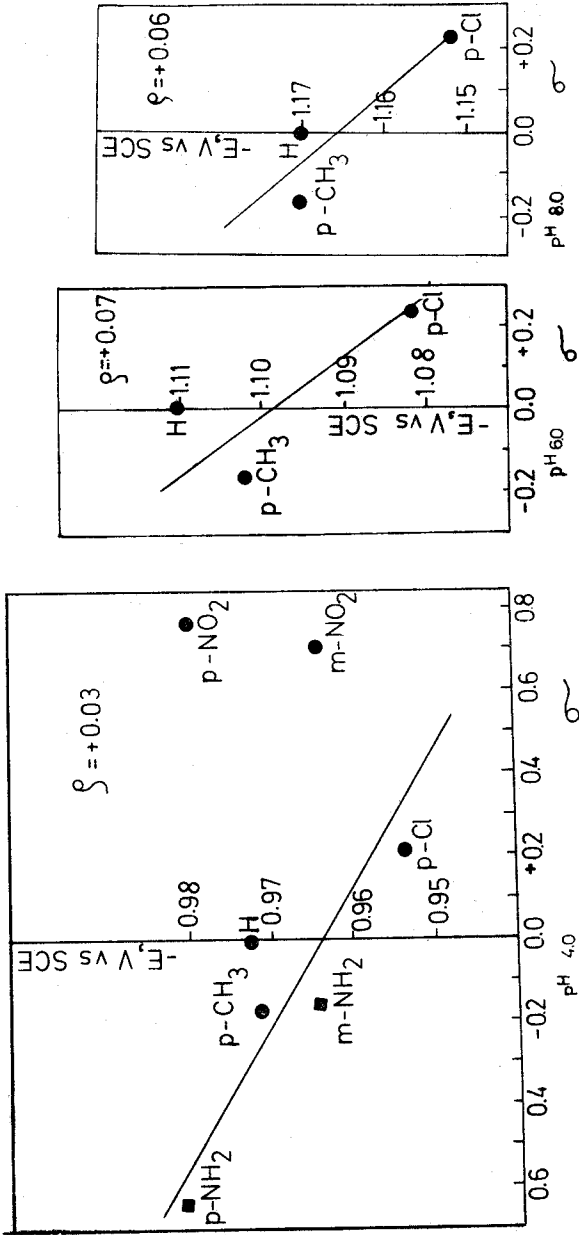
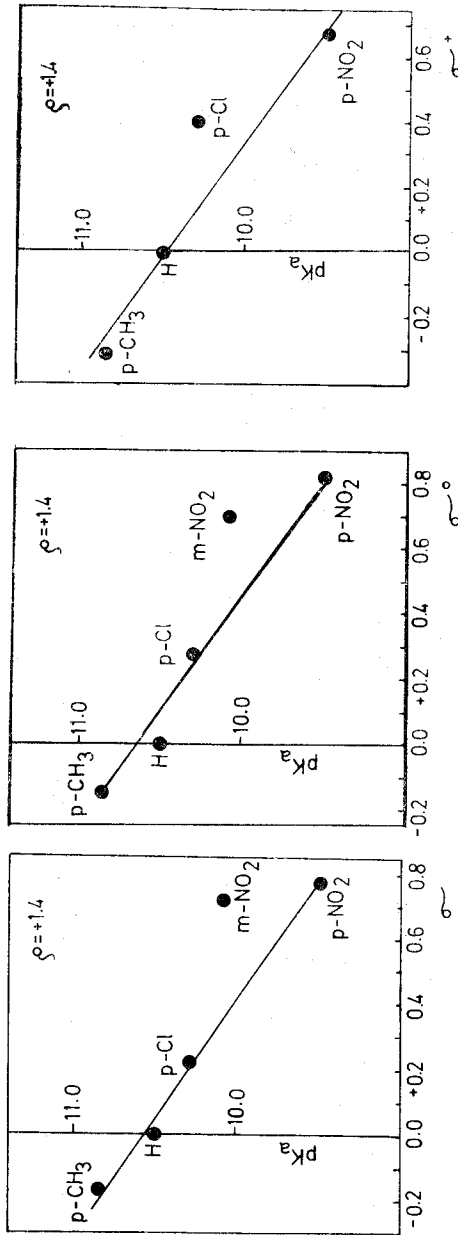Fig 4: Dependence of $E_{1/2}$ on σ constants at pH 4,6 and 8.

Fig 5: Dependence of the dissociation constant pK_a on σ constants.

Table 2

Values of reaction constant ϱ from $E_{1/2}$ - σ plots for compounds I_{a-e} at different pH's (wave A).

pH	+ ϱ	r^a	± s.d.
4.0	0.03	0.892	0.002
6.0	0.07	0.901	0.002
8.0	0.06	0.852	0.005

a) Correlation coefficient   b) Standard deviation

Table 3

Values of reaction constant ϱ from plots of pK_a- σ sets.

+ ϱ			r^a	± s.d.[b]
σ	σo	σ^+		
+ 1.4	+ 1.4	+ 1.4	0.997	0.007

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