

## ON PHTHALIDES AND INDANDIONES. XLVIII.\*

A STUDY OF THE POLAROGRAPHIC REDUCTION  
AND OF THE TRANSMISSION OF ELECTRONIC EFFECTS  
IN SUBSTITUTED 3-ARYLMETHYLENEPHTHALIDESA. BEŇO<sup>a</sup>, P. HRNČIAR<sup>b</sup> and M. LÁCOVÁ<sup>b</sup><sup>a</sup> Department of Analytical Chemistry and<sup>b</sup> Department of Organic Chemistry, Komenský University, Bratislava

Dedicated to Professor S. Stankoviánsky on the occasion of his 65th birthday.

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The polarographic reduction of substituted 3-arylmethylenephthalides *I*, 3-aryloxymethylenephthalides *II* and 3-arylthiomethylenephthalides *III* was studied in Britton-Weldorf buffers. It was found that at pH 5–9 in all the systems studied the methylenic C=C bond is reduced. At pH > 10 hydrolytic cleavage of the lactone ring of the phthalides takes place, giving rise to corresponding 2-phenylacetylbenzoic acids. In all the series the values of  $E_{1/2}$  can be well correlated with  $\sigma$  substituent constants. The coefficients of the transmission of substituent effects through oxygen and sulphur atoms, calculated from the obtained reaction constants, are confronted with literature data.

Polarographic reduction of phthalide and especially of its derivatives has been the subject of several works<sup>1–4</sup>. It was found that the half-wave potentials of these compounds in the medium of tetraalkylammonium salts are highly negative (c.  $-2$  V), and in aqueous-ethanolic buffers they do not give cathodic waves. Sugawara and Sugahara<sup>5</sup> have prepared 3-phenylmethylenephthalide, the electroreduction of which yielded the product with the reduced C=C bond.

In the present work we have studied polarographic reduction of series of substituted 3-phenylmethylenephthalides *I*, 3-phenoxy methylenephthalides *II* and 3-phenylthiomethylenephthalides *III* in methanolic Britton-Weldorf buffers. In connection with our previous studies devoted to the examination of transmission of electronic effects of substituents in series *I–III* by infrared spectroscopy in the region of C=O stretching vibrations<sup>6,7</sup> and by PMR spectroscopy<sup>8</sup>, we have also been interested in the effects of substituents on the values of  $E_{1/2}$  as well as in the transmission of these effects through oxygen and sulphur atoms of the studied systems.

## EXPERIMENTAL

*Instruments.* Polarographic curves were recorded with Model OH-202 polarograph (Radelkis, Budapest) equipped with a modified Kalousek vessel with separated standard calomel electrode (s.c.e.). At working height of the mercury reservoir (69 cm) the capillary had flow rate 2.15 mg s<sup>-1</sup>

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and the time of drops 2.8 s in 0.1M-KCl at 0.0 V. The pH values of the buffers and polarographed solutions were measured with pH-meter, Model PHM-26 (Radiometer, Copenhagen) equipped with G 200B glass electrode and the standard calomel electrode of type K 401. The half-wave potentials of studied derivatives,  $E_{1/2}$ , were measured by three-electrode system with respect to nonpolarized s.c.e. with the use of QTK-compensator (Metra, Blansko), the precision being  $\pm 2$  mV. Parameters of the linear correlations were calculated on a Gier digital computer from statistic relations<sup>9</sup>.

**Chemicals.** All the phthalides *I*–*III* were prepared according to the literature<sup>10–13</sup>. Their purity was checked by melting point determination, which was carried out prior to use, after recrystallizing the substances from appropriate solvents. The other chemicals were of analytical purity (Lachema, Brno).

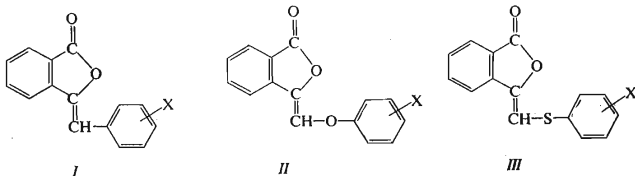
**Procedure.** The measurements were made with  $5 \cdot 10^{-4}$  M methanolic solutions of the phthalides. After mixing the solutions with Britton–Weldorf buffers<sup>14</sup> ( $\text{KH}_2\text{PO}_4$ –NaOH) of pH 5–12 the concentration of depolarizator in polarographed solutions in the medium of 40% methanol was  $1 \cdot 10^{-4}$  M. The dissolved oxygen was removed by blowing through the nitrogen purified by alkaline solution of pyrogallol for the period of 5 min at the 50 mm  $\text{H}_2\text{O}$  overpressure. All the measurements were carried out at 20°C.

## RESULTS AND DISCUSSION

From the study of the character of limit currents it followed that they are controlled by diffusion, since they were linearly dependent on the square root of the Hg-reservoir height and on depolarizator concentration. The temperature coefficient did not exceed 1.8% per 1°C.

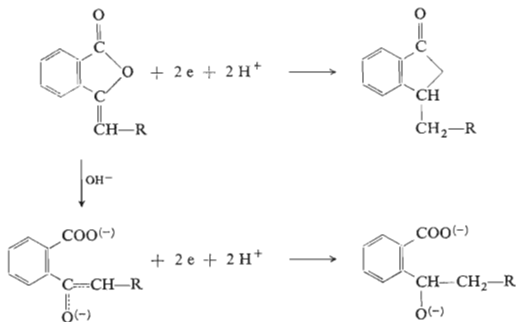
Polarographic characteristics for series *I*–*III* measured at pH 8.7 are presented in Table I. The  $E_{1/2}$  values for the studied derivatives do not change with increasing pH and are dependent only on substituents on the phenyl group.

The course of polarographic reduction of 3-phenylmethylenephthalide derivatives *I* is analogous to that of the parent compound. In an acidic medium with pH < 5 no polarographic wave is formed. The reduction at pH > 5 manifests itself by one cathodic wave which does not change its form up to pH ~ 9. Around this value limit currents of the wave begin to decrease and a new wave at more negative  $E_{1/2}$  is being formed. The first wave disappears at pH ~ 10 and the new wave is approximately of the same height. Phthalides *II* and *III* resemble in their behaviour phthalides *I* up to pH ~ 10. At pH > 10 the new wave is formed at a more negative  $E_{1/2}$  but the first wave does not disappear at a higher pH, only its limit currents decrease to the



half value. The character of both waves does not change even at  $\text{pH} \sim 13$ . At this  $\text{pH}$  the waves are equal in height and their sum equals to the height of the original wave formed at  $\text{pH} < 10$ . This fact indicates that in the case of both waves in the series *I* and the first wave in series *II* and *III* ( $\text{pH} < 10$ ) the equal number of electrons is exchanged during the electroreduction. Phthalides *III* are reduced at  $E_{1/2}$  by 20 to 40 mV more positive and phthalides *II* at  $E_{1/2}$  by 80–120 mV more negative than are derivatives *I*. The fact that the reduction proceeds most easily with derivatives *III* can be explained by enhanced polarization of the  $\text{C}=\text{C}$  bond caused by the sulphur atom. This finding agrees well with the results obtained with other systems containing similar arrangement of bridge atoms<sup>15</sup>.

On the basis of the results of the study of phthalides *I–III* and similar substances<sup>16</sup> as well as of the model compounds, 2-phenyl-1,3-indandione and 2-phenylacetylbenzoic acid, we can conclude that the wave formed at  $\text{pH} 5\text{--}9$  in the electroreduction of all the derivatives studied corresponds to two-electron reduction of the  $\text{C}=\text{C}$  bond. The wave at more negative potentials ( $\text{pH} > 10$ ) is characteristic of two-electron reduction of the anion of substituted 2-phenylacetylbenzoic acids, which are formed by hydrolytic cleavage of the lactone ring of the corresponding 3-arylmethylenephthalides<sup>17</sup>. These reduction processes can be depicted as follows:



where  $\text{R} = \text{C}_6\text{H}_4\text{X}$ ,  $\text{OC}_6\text{H}_4\text{X}$  and  $\text{SC}_6\text{H}_4\text{X}$ .

In the electroreduction of the derivatives of series *II* and *III* it can be assumed that both electrode processes proceed simultaneously, since the lactone ring-opening of these substances is not quantitative. This is evidenced by the fact that even in strong alkaline medium these derivatives give two polarographic waves. The derivatives of 2-phenyl-1,3-indandione, formed from 3-phenylmethylenephthalides in the medium of alcoholates, which could be alternative reaction products, are reduced, however, at more positive half-wave potentials (approximately by 100 mV).

TABLE I  
Polarographic Characteristic of Series of Phthalide Derivatives I—III (pH 8·7) and  $\sigma$  Substituent Constants

No	X	$-E_{1/2}$ , V	$i_d/c$	$n \cdot \alpha$ (ref. 22)	$\sigma$
Series I					
1	4-NH <sub>2</sub>	1·572	4·3	1·14	-0·66
2	4-OCH <sub>3</sub>	1·537	3·8	1·25	-0·27
3	4-CH <sub>3</sub>	1·515	4·3	1·21	-0·17
4	3-CH <sub>3</sub>	1·508	4·2	1·08	-0·07
5	4-NHCOCH <sub>3</sub>	1·502	4·2	0·88	-0·01
6	H	1·495	3·7	1·11	0·00
7	4-F	1·483	4·4	1·04	0·06
8	3-OCH <sub>3</sub>	1·472	3·8	1·26	0·12
9	4-Cl	1·458	3·7	1·08	0·23
10	4-Br	1·462	1·8	1·33	0·23
11	3-F	1·444	4·5	1·00	0·34
12	3-I	1·448	4·5	0·96	0·35
Series II					
13	4-NH <sub>2</sub>	1·648	6·9	1·10	-0·66
14	3,4-(CH <sub>3</sub> ) <sub>2</sub>	1·624	2·8	1·08	-0·24
15	4-CH <sub>3</sub>	1·611	3·2	1·18	-0·17
16	3-CH <sub>3</sub>	1·615	4·9	1·04	-0·07
17	3-C <sub>2</sub> H <sub>5</sub>	1·610	5·7	1·08	-0·07
18	H	1·601	7·2	0·98	0·00
19	4-F	1·602	5·9	1·04	0·06
20	3-CH <sub>3</sub> , 4-Cl	1·587	2·2	1·08	0·16
21	4-Cl	1·590	2·4	1·24	0·23
22	3-F	1·582	6·7	0·98	0·34
23	3-Cl	1·580	2·3	1·20	0·37
Series III					
24	4-NH <sub>2</sub>	1·498	2·3	0·90	-0·66
25	4-OH	1·472	3·4	1·24	-0·36
26	4-NHOH	1·482	1·7	1·12	-0·34
27	4-CH <sub>3</sub>	1·469	3·3	1·22	-0·17
28	4-NHCOCH <sub>3</sub>	1·465	3·4	0·92	-0·01
29	H	1·461	3·7	1·00	0·00
30	4-Cl	1·443	1·8	0·96	0·23
31	4-Br	1·444	1·9	0·84	0·23
32	4-I	1·438	2·3	0·74	0·27
33	3-Cl	1·432	1·9	0·92	0·37

In all the series studied the values of  $E_{1/2}$  can be correlated with  $\sigma$  taken from<sup>18</sup>. The results are summarized in Table II and graphically represented in Fig. 1. The magnitude of the reaction constant  $\rho$  for the reduction of the series I ( $\rho_I = 0.132$ ) indicates that these compounds are most sensitive toward substituent effects. The values of  $\rho$  for the other series are substantially smaller ( $\rho_{II} = 0.068$  and  $\rho_{III} = 0.061$ ). On the basis of the obtained results it can be concluded that the insertion of oxygen or sulphur between the C=C bond and the substituted phenyl in 3-arylmethylene-phthalides brings about a decrease in the transmission of substituent effects on the reaction center. In comparison with the series I the oxygen and the sulphur atom of phthalides II and III acts as a partial isolator of electronic effects transmission. The corresponding transmission coefficients  $\pi'$ , for oxygen and sulphur, obtained

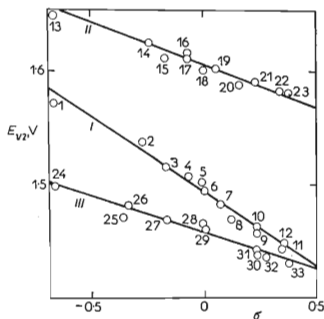


FIG. 1

The Plot of  $E_{1/2}$  vs  $\sigma$  for Series of Phthalides I—III (pH 8.7)

The numbering of experimental points is identical with that used in Table I.

TABLE II

Statistic Parameters of Linear Dependence of  $E_{1/2}$  on  $\sigma$  for Methylene-phthalides I—III

Symbols:  $n$  the number of the derivatives used in correlation,  $\rho$  the slope of the dependence,  $E_{1/2}^0$  the calculated value for unsubstituted derivative,  $r$  the correlation coefficient,  $s$  the standard deviation.

Parameter	Series		
	I	II	III
$n$	12	11	10
$\rho$	$0.132 \pm 0.006$	$0.068 \pm 0.004$	$0.061 \pm 0.004$
$E_{1/2}^0$	-1.493	-1.604	-1.458
$r$	0.991	0.984	0.981
$s$	0.006	0.004	0.004

TABLE III  
Polarographic Characteristic of 3-Arylmethylenephthalides *I* (pH 12.2)

No	X	$-E_{1/2}, V$	$i_d/c$	$n \cdot \alpha$
1	4-NH <sub>2</sub>	1.630	4.3	1.04
2	4-OCH <sub>3</sub>	1.615	4.9	0.94
3	4-CH <sub>3</sub>	1.611	7.8	0.91
4	3-CH <sub>3</sub>	1.608	5.2	0.82
5	4-NHCOCH <sub>3</sub>	1.592	5.6	0.89
6	H	1.595	4.4	0.96
7	4-F	1.598	5.2	0.84
8	3-OCH <sub>3</sub>	1.592	5.2	0.80
9	4-Cl	1.583	6.2	0.84
10	4-Br	1.586	3.2	0.83
11	3-F	1.572	7.6	0.85
12	3-I	1.580	7.8	0.85

from the ratios of the reaction constants  $q_{II}/q_I$  and  $q_{III}/q_I$ , equal to 0.52 and 0.42, respectively. On taking into account statistic data on the slopes for series *II* and *III*, the coefficients indicate that here substituent effects are somewhat better transmitted through oxygen than through sulphur. This can be demonstrated by the coefficient  $\eta = q_{III}/q_{II}$  which equals to 0.89, in accordance with the value obtained from spectral data<sup>7</sup> (0.86). The results of polarographic measurements agree well also with the results of the studies<sup>6,7</sup> in which the transmission of substituent effects in the above compounds was followed by infrared spectroscopy. Again, the authors found that the effects are better transmitted through oxygen than through sulphur.

Different results have however been obtained in a study of the <sup>1</sup>H-NMR spectra of the series *I* and *III*. Unexpectedly, the  $\rho$  constant of the dependence of methine proton chemical shifts  $\tau$  on  $\sigma$  was greater for the series *III* than for the series *I*. This fact was attributed to the direct interaction of methine hydrogen with bridge sulphur atom.

In strongly alkaline medium (pH  $\sim$  12) substituent effects were followed only in the series *I*, the derivatives of which give in this medium only one wave, corresponding to the reduction of the anions of substituted 2-phenylacetylbenzoic acids. By putting the experimental and calculated values given in Table III to the relations<sup>19</sup>  $\Delta E_{1/2} = \rho\sigma$  and  $\Delta E_{1/2} = E_{1/2}^{\text{substd.}} - E_{1/2}^H$  we have obtained the following parameters:

$$E_{1/2}^{\text{substd.}} = -1.597 + (0.056 \pm 0.005)\sigma; \quad r = 0.967, \quad s = 0.004,$$

where  $r$  and  $s$  is the correlation coefficient and the standard deviation, respectively.

The magnitude of the  $\rho$  constant indicates a decreased conjugation in substituted 2-phenylacetylbenzoic acids, relative to 3-phenylmethylenephthalides.

The discussed results are in harmony with studies<sup>20,21</sup> of substituent effects in 2-aryl-1,3-indandiones. These compounds are reduced in strongly alkaline medium (pH  $\sim 12$ ) in the form of enolate-anions, the constants  $\rho$  and  $\rho^0$  being +0.05 and 0.04, respectively. It can be assumed that the effects of substituents in 2-phenylacetylbenzoic acids, formed by hydrolytic cleavage of 3-phenylmethylenephthalides, are at pH  $\sim 12$  comparable with those in the enolate-anions of 2-aryl-1,3-indandiones. It seems further probable that the electroreduction of both systems in strongly alkaline medium proceeds by similar mechanism. This assumption is supported by the structure of the part of the molecule which undergoes reduction.

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